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一等出色论文

全国碳青霉烯类耐药肺炎克雷伯菌对抗菌药物的敏感性、耐药机制和分子特征研究

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目的 了解全国临床分离碳青霉烯类耐药肺炎克雷伯菌对抗菌药物的敏感性、耐药机制和分子特征。

方法 收集自全国 31 个省、市和自治区 151 所医疗机构 2021 年 1-6 月临床分离的碳青霉烯类耐药肺炎克雷伯菌，按区域统一运送至三个中心实验室。中心实验室按照统一的实验方案进行菌种复核鉴定，肉汤微量稀释法测定 CRKP 对抗菌药物的敏感性，所有菌株进行全基因组测序分析碳青霉烯酶基因和序列型。

结果 共收集 CRKP 菌株 4314 株，其中产碳青霉烯酶碳青霉烯类耐药肺炎克雷伯菌及不产碳青霉烯酶碳青霉烯类耐药肺炎克雷伯菌分别占 97.33%和 2.67%。CRKP 主要分离自呼吸道（ 57.71%），其次为泌尿道（12.28%）和血液（10.40%）。药敏试验结果显示，氨曲南-阿维巴坦、黏菌素 E、多黏菌素 B 和替加环素对 CRKP 具有高度抗菌活性（敏感率范围 90.3%-96.4%）。头孢他啶-阿维巴坦及亚胺培南-瑞来巴坦在成人分离株中的敏感率高于儿童（88.9%， 75.9% vs 51.4%， 50.4%），而阿米卡星及复方新诺明在儿童分离株中的敏感率更高（65.2%，65.2% vs 36.8%， 25.5%）。KPC-2（85.88%，3705/4314）仍是中国 CRKP 中主要流行的碳青霉烯酶基因类型，其次为 NDM（7.79%， 336/4314）及 OXA-48-like（1.30%， 56/4314）。此外，部分菌株携带 KPC-3、KPC-12、KPC-21、KPC-33 和 KPC-71 等基因。虽然产 KPC-2 是成人与儿童分离 CRKP 的主要耐药机制，但检出率差别很大（90.21%对 52.24%），儿童患者中携带 NDM 基因的比例明显升高，远高于成人（41.87% 对 3.40%）。多位点序列分型结果显示，我国临床分离的 CRKP 仍以 ST11 克隆型流行为主。

结论 CRKP 是目前全球临床抗感染治疗的重大挑战之一，世界卫生组织将该菌列为优先级最高的病原体之一，急需开发新的有效抗菌药物以应对其所致感染的治疗，降低感染患者的病死率。历年 CHINET 中国细菌耐药监测结果显示，肺炎克雷伯菌对亚胺培南及美罗培南的耐药率从 2005 年的 3%上升到 2022 年的 26% 以上。现有研究结果显示，CRKP 感染的死亡率显著高于碳青霉烯类敏感的肺炎克雷伯菌，其中重症监护室 CRKP 感染患者的发病率和死亡率均远高于非 ICU 患者。由于产生不同碳青霉烯酶 CRKP 对应的抗感染治疗方案不同，因此，明确临床分离的 CRKP 产生的碳青霉烯酶种类及其流行传播特征，对于临床抗感染治疗和感染预防控制具有重要的参考价值。

关键字：肺炎克雷伯菌，碳青霉烯类耐药，流行病学，耐药机制，抗菌药物敏感性

Genomic Epidemiology and Ceftazidime-avibactam High-level Resistance Mechanisms of Pseudomonas Aeruginosa in China From 2010-2022

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Objective To investigate the ceftazidime-avibactam (CZA) high-level resistance mechanisms of PER-producing difficult-to-treat resistant (DTR) Pseudomonas aeruginosa (PA) isolates in China from 2010-2022

Methods A total of 5763 PA isolates were collected from 67 hospitals in 22 regions across China from 2010 to 2022. Minimum inhibitory concentrations (MICs) were determined and whole-genome sequencing (WGS) was performed. Plasmids harbouring blaPER were constructed and cloned to evaluate their impact on resistance and fitness. Overexpression and efflux pump inhibition experiments, biochemical assays, structure modelling and molecular docking of PER and CZA were carried out

Results Fifty-six PER-producing isolates were identified (50 blaPER-1-positive and 6 blaPER-4-positive isolates). Of these, 82.1% (46/56) were classified as DTR-PA isolates, and 76.79% (43/56) were resistant to CZA. Importantly, blaPER-1 and blaPER-4 overexpression led to 16-fold and >1024-fold increases in the MICs of CZA, respectively. WGS revealed that the blaPER-1 gene was located in two different transferable IncP-2-type plasmids and chromosomes, whereas blaPER-4 was found only on chromosomes and was carried by a class 1 integron embedded in a Tn6485-like transposon. Overexpression of efflux pumps may be associated with high-level CZA resistance in blaPER-1-positive strains. Kinetic parameter analysis revealed that PER-4 exhibited a similar kcat/Km with ceftazidime and a high (~3359-fold) IC50 value with avibactam compared to PER-1. Moreover, the Ser135Thr mutation in PER-4 might enhance decarbamylation catalysis

Conclusion Overexpression of PER-1 combined with enhanced efflux pump expression and the low affinity of PER-4 for avibactam contributes to high-level resistance to CZA. Additionally, the Tn6485-like transposon plays a significant role in disseminating blaPER. Urgent active surveillance is required to prevent the further spread of high-level CZA resistance in DTR-PA isolates

关 键 字： DTR-PA; Ceftazidime-avibactam resistance; PER; Efflux pump; Fitness

Phenotypes and Functions of Cryptococcus Neoformans-Specific CD8+ T Cells in HIV-Infected Adults with Pulmonary and Disseminated Cryptococcosis

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Background Host immunity plays an important role in defending against Cryptococcus neoformans infection and preventing the dissemination of cryptococcosis after C. neoformans infection. The phenotypes and functions of CD8+ T cells in HIV-infected adults with pulmonary or disseminated cryptococcosis have not been well described

Methods Flow cytometry was used to identify CD8+ T cell subsets and functions in adults with untreated HIV associated with pulmonary or disseminated cryptococcosis. The clinical and immunological features of the two cryptococcosis groups were compared. A multivariate logistic regression model was used to analyze the risk factors for dissemination of HIV-associated cryptococcosis

Results Forty-three patients with HIV-associated cryptococcosis were enrolled and categorized into pulmonary cryptococcosis (n=13) and disseminated cryptococcosis (n=30) groups. The median CD4+ T cell count was 18 cells/μl. The IFN-γ expression by C. neoformans-specific CD8+ T cells was significantly higher in the pulmonary cryptococcosis group than in the disseminated cryptococcosis group (P=0.02). Plasma IP-10 levels (3.13 pg/ml vs. 2.90 pg/ml, P=0.010) and IL-6 levels (1.12 pg/ml vs. 0.69 pg/ml, P=0.015) in the pulmonary cryptococcosis group were significantly higher than those in the disseminated cryptococcosis group. Higher IFN-γ expression by C. neoformans-specific CD8+ T cells was associated with lower risk of cryptococcosis dissemination (OR, 0.248, P=0.031)

Conclusions The maintenance of CD8+ T cell function may explain why cryptococcosis remains localized in some HIV-infected adults with advanced immunodeficiency

关键字：HIV, disseminated cryptococcosis, CD4+ T cell counts, CD8+ T cell responses, risk factors

二等出色论文

Prevalence and Characteristics of Ertapenem-Mono-Resistant Isolates Among Carbapenem-Resistant Enterobacterales in China

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Carbapenem-resistant Enterobacterales (CRE), specifically those resistant to only ertapenem among carbapenems (ETP-mono-resistant), are increasingly reported, while the optimal therapy options remain uncertain. To investigate the prevalence and characteristics of ETP-mono-resistant CRE, CRE strains were systematically collected from 102 hospitals across China between 2018 and 2021. A 1:1 randomized matching study was conducted with ETP-mono-resistant strains to meropenem- and/or imipenem-resistant (MEM/IPM-resistant) strains. Antimicrobial susceptibility testing, whole-genome sequencing, carbapenem-hydrolysing activity and the expression of carbapenemase genes were determined. In total, 18.8% of CRE strains were ETP-mono-resistant, with relatively low ertapenem MIC values. ETP-mono-resistant strains exhibited enhanced susceptibility to β-lactams, β-lactam/β-lactamase inhibitor combinations, levofloxacin, fosfomycin, amikacin and polymyxin than MEM/IPM-resistant strains ($P < 0.05$). Phylogenetic analysis revealed high genetic diversity among ETP-mono-resistant strains. Extended-spectrum β-lactamases (ESBLs) and/or AmpC, as well as porin mutations, were identified as potential major mechanisms mediating ETP-mono-resistance, while the presence of carbapenemases was found to be the key factor distinguishing the carbapenem-resistant phenotypes between the two groups ($P < 0.001$). Compared with the MEM/IPM-resistant group, limited carbapenemase-producing CRE (CP-CRE) strains in the ETP-mono-resistant group showed a significantly lower prevalence of ESBLs and porin mutations, along with reduced expression of carbapenemase. Remarkably, spot assays combined with modified carbapenem inactivation method indicated that ETP-mono-resistant CP-CRE isolates grew at meropenem concentrations eightfold above their corresponding MIC values, accompanied by rapidly enhanced carbapenem-hydrolysing ability. These findings illustrate that ETP-mono-resistant CRE strains are relatively prevalent and that caution should be exercised when using meropenem alone for treatment. The detection of carbapenemase should be prioritized.

关键字：carbapenem-resistant Enterobacterales, ertapenem, carbapenemase, antibiotic resistance, molecular epidemiology

表面增强拉曼光谱联合机器学习算法快速检测人体胃液中的幽门螺杆菌感染

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目的 幽门螺杆菌感染与胃炎、消化性溃疡和胃癌存在直接因果关系，对人类健康构成严重威胁。因此，对幽门螺杆菌进行及时诊断和治疗对其根除至关重要。目前，主要的诊断方法包括侵入性内窥镜检查、尿素酶快速试验和细菌培养，以及非侵入性的尿素呼吸试验、抗原测试和血清抗体测试。然而，这些方法存在培养条件苛刻、检测设备昂贵和患者不适等缺点。因此，迫切需要开发一种快速且经济有效的幽门螺杆菌感染检测方法。

方法 “一次性胶囊取样线法”是一种非侵入性的人体胃液采集的简易方法，而表面增强拉曼光谱正逐渐成为临床实验室和现场检测中快速检测病原菌的潜在技术。本研究提出了一种基于机器学习算法结合表面增强拉曼光谱的智能诊断人体胃液幽门螺杆菌感染状态的新方法。我们前期招募了 100 名志愿者（50 名幽门螺杆菌感染阳性和 50 名阴性参与者），通过胶囊取样线法无创收集了所有参与者的胃液，并采用拉曼光谱仪采集了 12,000 条表面增强拉曼光谱（120 条光谱/胃液标本）。随后，通过平均光谱特征分析及反卷积方法探索不同胃液样本的光谱学差异，并通过聚类算法比较了不同预处理方法对光谱质量的影响，最后选择最佳的预处理方法进行六种不同机器学习算法模型的构建以及胃液幽门螺杆菌感染状态的识别和预测

结果 综合多种模型性能评估指标，轻量梯度提升机算法表现出最佳诊断准确性和时间效率（准确率=99.54%，五折交叉验证率=99.21%，预测时间=2.61 秒）。随后，利用已构建的轻量梯度提升机算法模型对来自 100 名未知幽门螺杆菌感染状态志愿者的 2,000 个胃液光谱数据进行了双盲测试，与 qPCR 结果相比，预测准确率达到 82.15%。

结论 综上所述，本研究开发了一种表面增强拉曼联合机器学习算法的光谱分析技术，实现了人体胃液幽门螺杆菌感染状态的快速诊断。该技术将有望作为当前幽门螺杆菌感染诊断方法的补充，实现幽门螺杆菌感染在人群中的快速筛查和动态监测。

关键字：幽门螺杆菌，胶囊取样线，胃液，表面增强拉曼光谱，机器学习

Stenotrophomonas Maltophilia Bacteremia in Adult Patients with Hematological Diseases: Clinical Characteristics and Risk Factors for

28-day Mortality

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Objective Patients with hematological diseases are at higher risk for Stenotrophomonas maltophilia (SM) bacteremia, which poses significant burden on morbidity and mortality. This study aimed to analyze the clinical characteristics and determine risk factors for 28-day mortality in adult hematological patients with SM bacteremia

Methods This retrospective analysis of 140 hematological patients diagnosed with SM bacteremia was conducted from January 2012 to July 2023. Univariate analysis and multivariate logistic regression analysis were used to identify risk factors associated with 28-day mortality

Results The overall 28-day mortality was 31.43% (44/140), with a median hospital stay of 25 days before SM bacteremia onset. In the previous 1 month, all patients received long-term broad-spectrum antibiotics and 69.29% developed breakthrough bacteremia during carbapenem therapy. Independent risk factors of mortality included SOFA score ≥ 5, recent tigecycline exposure, age ≥ 60 years and pulmonary infection. Patients with ≥ 2 risk factors were stratified into the high-risk group, where the 28-day mortality was significantly higher compared to the low-risk group (56.52% vs 7.04%, P<0.001). Treatment with trimethoprim-sulfamethoxazole (TMP/SMX) (P=0.008) or TMP/SMX combined with cefoperazone/sulbactam (P=0.005) was associated with survival benefits among high-risk patients

Conclusion SM bacteremia usually occurred in hematological patients with prolonged hospitalization and extensive use of broad-spectrum antibiotics, especially carbapenems. Patients with high SOFA scores, advanced age, pulmonary infection or recent tigecycline exposure were at higher risk of poor prognosis. The preferred treatment is TMP/SMX rather than fluoroquinolones, with combination therapy of TMP/SMX + cefoperazone/sulbactam considered a feasible treatment option

关键字：hematological disease, Stenotrophomonas maltophilia bacteremia, risk factors, treatment

Dynamic Evolution of Ceftazidime-avibactam Resistance From A Single Patient Through The IncX3_NDM-5 Plasmid Transfer and BlaKPC Mutation

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Objectives We identified multiple evolutionary pathways under ceftazidime-avibactam pressure in vivo, including interspecies IncX3_NDM-5 plasmid transfer between E. cloacae and K. pneumoniae and blaKPC mutation from blaKPC-2 to blaKPC-33

Methods Conjugation assay was carried out to explore and simulate the plasmid transmissibility in vivo. Meanwhile, the fitness effect of strains carrying different configuration was confirmed by plasmid stability, growth curve, and competition experiments. Furthermore, whole genome sequencing revealed the characterisation of all the plasmids and bioinformatics analysis of 659 plasmids (the IncX3_NDM plasmid from this study and a further 658 plasmids from the NCBI database) demonstrated the dissemination and genetic environment of blaNDM-5 plasmids

Results Through the analysis of conjugation frequency and fitness cost, the IncX3_NDM-5 plasmid in this study showed strong transmissibility and stability in E. coli EC600 and clinical strain K. pneumoniae 5298 as recipient strain. With the increasing ceftazidime-avibactam concentration, the conjugation frequency remained at 10-3-10-5, much higher than the mutation frequency of K. pneumoniae 5298 (10-6-10-8) at the same concentration. This difference may indicate that K. pneumoniae 5298 prefers to acquire exogenous NDM plasmid rather than mutate itself under ceftazidime-avibactam pressure. Further plasmid analysis revealed the diverse origin and genetic structure of blaNDM-5 carrying plasmids. E. coli (42.9%), China (43.9%), IncX3 (66.6%) are the most common strains, regions, and Inc types respectively. By analysing genetic environment detected in IncX3 plasmids, the dominant structures (168/258, 65.1%) were identified: ISKox3-IS26-blaNDM-5-IS5-ISAba125-Tn3000-Tn3. In addition, several structural variations were found in the core gene structure

Discussion The high fitness and transmissibility of the blaNDM-5 plasmids were noteworthy. Moreover, the diversity of carbapenemase configurations highlighted the importance of the continuous monitoring of antimicrobial susceptibility and resistance genes during treatment.

关键字：Ceftazidime-avibactam, Enterobacter cloacae, Klebsiella pneumoniae, KPC-33, IncX3_NDM-5

Mammalian Body Temperature-induced Mutagenesis Enables The Development of Pan-drug Resistance and Hypervirulence in A New Human Fungal Pathogen

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Objective The continuing emergence of new invasive fungal pathogens poses an increasing threat to public health. Here, through the CHIF-NET surveillance program, which collected fungal strains from 96 Chinese hospitals over 10 years, we identified two independent cases of human infection with a novel invasive pathogen, Rhodosporidiobolus fluvialis, from the carotenoid-producing genus Rhodosporidiobolus, many species of which are resistant to fluconazole and caspofungin and can undergo yeast-to-pseudohyphal transition

Methods R. fluvialis clinical isolates NJ103 and TZ579 were obtained from the CHIF-NET program. Environmental strains of Rhodosporidiobolus genera were obtained from the Westerdijk Fungal Biodiversity Institute (Netherlands) and the China General Microbiological Culture Collection Centre. We conducted genome sequencing, assembly and molecular phylogenetic analyses of the two clinical strains. And several phenotype assays were performed, including cellular ROS detection, macrophage phagocytosis assays and mouse infections

Results The integration of genetic and genomic analyses revealed parallel resistance mechanisms in R. fluvialis, including its ability to produce carotenoids. The development of a mouse model showed that pseudohyphal growth remarkably enhances its virulence. Importantly, mouse infection or mammalian body temperature induces its mutagenesis, allowing the emergence of hypervirulent mutants favoring pseudohyphal growth. Temperature-induced mutagenesis can also elicit the development of pan-resistance to three of the most commonly used first-line antifungals in different Rhodosporidiobolus species. Furthermore, polymyxin B was found to exhibit potent activity against the pan-resistant Rhodosporidiobolus mutants

Conclusion Collectively, by identifying and characterizing the first fungal pathogen in the drug-resistant genus Rhodosporidiobolus, we provide evidence that temperature-dependent mutagenesis can enable the development of pan-drug resistance and hypervirulence in fungi, and support the idea that global warming promotes the evolution of new fungal pathogens

关键字：emerging pathogen, Rhodosporidiobolus, resistance, virulence, mutagenesis

三等出色论文

Safety and Efficacy of A Phage Cocktail on Murine Wound Infections Caused by Carbapenem-resistant Klebsiella Pneumoniae

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目的 评估噬菌体治疗在小鼠 CRKP 所致伤口感染模型中的有效性和安全性。

方法 本研究进行体外裂解曲线研究了所选噬菌体鸡尾酒对 CRKP 菌株 140156 在体外的作用。为了确定建立伤口感染模型的合适菌量，8 周龄的 C57BL/6 雌性小鼠 48 只，随机分为 4 组，选择不同的菌量（105、106、107 和 108 CFU）接种诱导伤口感染（n=12）。于感染后的第 1 天，第 2 天，第 3 天无菌切除小鼠伤口、肝脏和脾脏组织，组织均浆后通过菌落计数评估细菌载量，并取小鼠心脏血进行细菌计数。8 周龄的 C57BL/6 雌性小鼠 64 只，随机分为 4 组，包括三组对照组（空白对照组，噬菌体对照组，感染对照组）和一组治疗组（噬菌体治疗组），每组 16 只小鼠。细菌接种后 30 分钟予以噬菌体或 PBS 处理，并于第 1 天、第 3 天、第 7 天无菌切除小鼠伤口进行细菌计数，并取第 3 天及第 7 天伤口进行组织病理学检测。为了研究噬菌体治疗的安全性，将 8 周龄的 C57BL/6 雌性小鼠 24 只随机分为噬菌体组和对照组，每组 12 只，噬菌体组腹腔注射噬菌体鸡尾酒（200μl,1×109PFU/mL），对照组则给予 200μlPBS，根据噬菌体给药后 7、15 和 24 小时的全血细胞计数检测宿主反应。为了测量噬菌体治疗的长期安全性，将 12 只 8 周龄的 C57BL/6 雌性小鼠分为噬菌体组和对照组，每组 6 只小鼠，24 小时内给予 3 次噬菌体鸡尾酒，在给予噬菌体后的第 6、12、18、24 小时，第 3、5、7、10、14 天，此后每周一次，持续 2 个月，通过给出 5 到 0 分的健康评分来评估小鼠的健康状况，并记录死亡数。

结果 在体外实验中噬菌体鸡尾酒可以抑制 CRKP 菌株 140156 生长长达 10 h。接种 106CFU 的细菌可使 CRKP 持续稳定地存在于局部伤口，而不影响血液系统、肝脏。在噬菌体疗效评价中，噬菌体鸡尾酒治疗组小鼠伤口细菌载量一直低于感染对照组，且在第 7 天相较于感染对照组减少了 2 个 log10 值。噬菌体治疗加速了 CRKP 感染后伤口的愈合，主要表现为组织病理学检查显示噬菌体治疗组伤口局部炎症更轻、更快的再上皮化；以及观察到噬菌体治疗组小鼠伤口痂壳更快脱落。全血细胞计数及长期的健康检测也证明了噬菌体治疗的安全性。

结论 噬菌体治疗小鼠伤口感染是安全且有效的。

关键字：噬菌体治疗，抗微生物药物耐药性 ，耐碳青霉烯类肺炎克雷伯菌，安全性

Polymyxin Resistance Caused by Large-scale Genomic Inversion Due To IS26 Intramolecular Translocation in Klebsiella Pneumoniae

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Objective Polymyxin B and colistin have been used widely for decades to treat serious infections caused by multidrug-resistant Gram negative organisms. Resistance to polymyxins has been reported in Klebsiella pneumoniae by employing several strategies . One common strategy is the modifications of LPS by 4-amino-4- deoxy-L-arabinose (L-Ara4N) and/or phosphoethanolamine (pEtN) to reduce the negative charge. Other mechanisms include the overproduction of surface capsular polysaccharides (CPS)and the released CPS can capture or bind polymyxins, thereby reducing the number of drugs reaching the surface of bacterial cells, resulting in increased polymyxin resistance. LPS modifi- cations involve multiple two-component systems (TCS), including PmrA/PmrB, PhoP/PhoQ and CrrA/CrrB4 . Meanwhile, PmrA/ PmrB controls the pmrHIJKLM operon, and PhoP/PhoQ controls the arnBCADTEF. The mutations of these TCS and their controlled operons make it easy for bacteria to obtain polymyxin resistance. The plasmid-borne MCR-family genes are able to confer colistin resistance by mediating the transfer of pEtN to lipid A. MgrB is a small transmembrane protein produced upon activation of the PhoP/PhoQ TCS, and acts as a negative regulator on the system in K. pneumoniae9e. A growing number of literatures have reported polymyxin resistance associated with mutations in mgrB gene, including insertion of repeat sequences, frameshift, deletion of the mgrB locus, and premature termination of mgrB translation. Particularly, mgrB mutation mediated polymyxin resistance related to insertion sequence (IS) is showing an increasing trend in clinical examination. The continuous development of genomics has brought great convenience to the study of drug resistance of pathogens. High throughput sequencing technology combined with molecular biology technology has constructed a variety of antibiotic resistance gene databases and analysis tools, which is conducive to us to efficiently find various new drug resistance genes and understand the causes and development process of drug resistance. Besides, transcriptomics and proteomics also have potential applications in drug resistance detection, which can correlate genotype data with phenotypic results, especially when genotype and phenotype are inconsistent, or when there is no obvious drug resistance gene but drug resistance has been

confirmed. Nephrotoxicity is an important concern with polymyxin use and a common adverse effect clinically. The available polymyxins are complex mixtures, individual constituents may have different pharmacological as well as different toxic effects. Synthesis of individual components and evaluation of their antibacterial activity and renal toxicity are important for new polymyxin development. Previous research in our institute discovered individual component polymyxin S2, which showed good activity and less toxicity compared with polymyxin B and colistin25. High plasma stability in vitro and strong efficacy in a mouse systemic infection model (ED50 Z 0.9 mg/kg) against NDM-1-producing K. pneumoniae indicated that polymyxin S2 could be a potential candidate with similar or better antimicrobial potency and lower toxicity than the current clinical polymyxin B and colistin26. To predict the possible resistant mechanism of polymyxin S2 for wide clinical application, we experimentally induced bacterial resistance to polymyxin S2 and studied the preliminary resistance mechanisms. In this study, we reported the characterization of polymyxin resistant mutants caused by an inversion of approximately 1.1 Mbp in the chromosome by IS26 mediated intramolecular transposition, which is the first report of polymyxin resistance caused by IS26 intramolecular transposition mediated mgrB truncation in chromosome in K. pneumoniae.Polymyxin B and polymyxin E (colistin) are presently considered the last line of defense against human infections caused by multidrug-resistant Gram-negative organisms such as carbapenemase-producer Enterobacterales, Acinetobacter baumannii, and Klebsiella pneumoniae. Yet resistance to this last-line drugs is a major public health threat and is rapidly increasing. Polymyxin S2 (S2) is a polymyxin B analogue previously synthesized in our institute with obviously high antibacterial activity and lower toxicity than polymyxin B and colistin

Methods To predict the possible resistant mechanism of S2 for wide clinical application, we experimentally induced bacterial resistant mutants and studied the preliminary resistance mechanisms. Mut-S, a resistant mutant of K. pneumoniae ATCC BAA-2146 (Kpn2146) induced by S2, was analyzed by whole genome sequencing, transcriptomics, mass spectrometry and complementation experiment

Results Surprisingly, large-scale genomic inversion (LSGI) of approximately 1.1 Mbp in the chromosome caused by IS26 mediated intramolecular transposition was found in Mut-S, which led to mgrB truncation, lipid A modification and hence S2 resistance. The resistance can be complemented by plasmid carrying intact mgrB. The same mechanism was also found in polymyxin B and colistin induced drug-resistant mutants of Kpn2146.(Mut-B and Mut-E, respectively). This is the first report of polymyxin resistance caused by IS26 intramolecular transposition mediated mgrB truncation in chromosome in K. pneumoniae. The findings broaden our scope of knowledge for polymyxin resistance and enriched our understanding of how bacteria can manage to survive in the presence of antibiotics

Conclusion In the present study, we demonstrated a novel polymyxin resistance mechanism in K. pneumoniae that the inversion of genome sequence mediated by insertion sequence (IS) on bacterial chromosome leads to the truncation of mgrB and hence regulation of antibiotic resistance gene expression, which results with antibiotic resistance.Taken together, we reported the characterization of Kpn2146 polymyxin resistant mutants caused by an inversion of approximately 1.1 Mbp in the chromosome by IS26 mediated intramolecular transposition in K. pneumoniae ATCC BAA-2146 in this study. Our results indicate that genome rearrangement due to replicative translocation of IS26 can lead to altered expression of resistance genes, which in turn generates resistance and improves strain virulence. Similar inversions can also be found in clinical polymyxin resistant K. pneumoniae and generated by other K. pneumoniae strains after induction. A deeper understanding of the resistance of K. pneumoniae population to polymyxin antibiotics will be very important for understanding the evolution of polymyxin resistance, for the clinical application of polymyxins and interpreting public health monitoring data, and for the design and implementation of new control strategies against this important pathogen. Hence, the evidence presented in this work demonstrate that inactivation of mgrB not only resulted in polymyxin resistance, but also enhanced K. pneumoniae virulence, and highlighted a connection between virulence and antimicrobial resistance

关键字：Klebsiella pneumoniae; Polymyxin resistance; mgrB; IS26; Whole genome sequencing; Structural variation; Inversion

Resistance To Aztreonam-avibactam Due To A Mutation of SHV-12 in Enterobacter

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Objective To investigate novel resistance mechanisms to aztreonam-avibactam (ATM-AVI)

Methods An ATM-AVI-resistant strain was obtained by induced mutagenesis followed by whole genome sequencing. The gene involved with ATM-AVI-resistance was confirmed by cloning, susceptibility testing and molecular modeling in silico

Results We obtained an ATM-AVI-resistant mutant of an MBL-producing Enterobacter mori strain by induced mutagenesis. Genome sequencing revealed an Arg244Gly (Ambler position) substitution of SHV-12 β-lactamase in the mutant. Cloning and susceptibility testing verified that the SHV-12 Arg244Gly substitution led to significantly reduced susceptibility to ATM-AVI (MIC, from 0.5/4 to 4/4 mg/L) but with the loss of resistance to cephalosporins as tradeoff. Arg244 of SHV involves in the binding of avibactam by forming an arginine-mediated salt bridge and is a critical residue to interact with β-lactams. Molecular modeling analysis demonstrated that the Arg244Gly substitution hindered the binding of avibactam to SHV with higher binding energy (from −5.24 to -4.32 kcal/mol) and elevated inhibition constant Ki (from 143.96 to 677.37 μM) to indicate lower affinity. This substitution, however, resulted in loss of resistance to cephalosporins as tradeoff by impairing substrate binding

Conclusion An amino acid substitution at Arg244 of SHV-12 leading to reduced susceptibility to ATM-AVI, a combination against MBL-producing Enterobacterales but with the expense of losing the ESBL phenotype against cephalosporins

关键字：Resistance, Avibactam, Aztreonam, SHV

A Panel of Genotypically and Phenotypically Diverse Clinical Acinetobacter Baumannii Strains for Novel Antibiotic Development

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Objective Acinetobacter baumannii is globally notorious, but the strains for novel therapeutic candidates against A. baumannii vary across studies. The variation complicates the studies. Researchers studying A. baumannii frequently employ reference strains that represent a limited portion of the heterogeneity of A. baumannii in terms of genotypes and phenotypes. These strains are not representative of current trends in clinical strains. Therefore, it is crucial for the research community to acquire a standardized and heterogeneous panel of A. baumannii. In this study, we developed a diverse strain panel composed of 45 clinical isolates of A. baumannii

Methods We selected 45 different A. baumannii strains from 2197 clinical isolates collected from 64 different hospitals in 27 provinces of China based on ST Oxford typing to represent the diversity of species collected. Whole genome sequencing was performed on all panel strains, and SNP-based phylogenetic analyses and their core phylogenetic relationships with strains representing the major prevalent clones in hospitals worldwide were used to assess the genetic diversity of the included strains. We evaluated the phenotypic characteristics of these strains in terms of antimicrobial susceptibility, growth assay, biofilm formation, capsule production, and virulence assay. We performed comparative analyses of certain genotype-phenotypes and phenotype-phenotypes in this panel

Results The panel maximizes coverage of genetic diversity, capturing globally prevalent clones and important KL types, and detects a wide range of known antibiotic resistance genes. We found that the ST2 group showed a significantly higher rates of resistance, lower fitness cost for adaptation, yet less biofilm formation. The MTE (raised center and irregular base" phenotype according to literature) group showed a less clear correlation of resistance rates, growth rate, but was observed to produce more biofilms. There was no clear correlation between the presence of the capsule and the specific KL type and virulence in this study

Conclusion We established a reference panel of 45 clinical isolates of A. baumannii based on ST Oxford typing analysis. This assistance will significantly facilitate multiple medical, scientific and translational studies to combat infections caused by this critical pathogen. The genomic data and related phenotypic characterization of these strains are available at http://phdb.baumanii.dmicrobe.cn/, which also serves as a database for researchers to rapidly and rationally select model strains based on specific biological questions

关键字：Acinetobacter baumannii, heterogeneous, panel, novel antibiotic development, genomic analysis, phenotypes

Vancomycin Population Pharmacokinetics Analysis in Chinese Pediatric Patients with Varying Degrees of Renal Function and Ages:

Development of New Practical Dosing Recommendations

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Objective the optimal dosage of vancomycin in the pediatric population is complicated by significant intraindividual and interindividual variability. These challenges pose a risk of underdosing or overdosing of vancomycin, which may lead to treatment failure or adverse effects. Population pharmacokinetic (PPK) modeling is a useful tool to characterize the intraindividual and interindividual variability, and it has been increasingly applied to optimize dosing regimens. Our study aims to develop a PPK model of vancomycin in a large clinical cohort of neonates, infants, and children with different renal function status, and to propose specific initial dose recommendations based on the model

Methods This retrospective study was conducted at Xinhua Hospital, a 2600-bed tertiary-care hospital in Shanghai, between June 2013 and June 2022. To perform an external evaluation, additional pediatric patients were enrolled in the study between September 2021 and June 2022, from Shanghai Children's Medical Center, another tertiary hospital in Shanghai. A non-linear mixed-effect modeling approach with a one-compartment model structure was applied. Monte Carlo simulations were used to stimulate an optimal dosage regimen to achieve the target of AUC24/MIC between 400 and 650

Results The model group included 673 patients, out of which 68 were CTS patients. A total of 1547 vancomycin concentrations were assayed, which comprised of 779 trough concentrations and 768 peak concentrations. The external validation group comprised of 53 patients. Covariate analysis revealed that physiological maturation, renal function, ALB, and cardiothoracic surgery (CTS) significantly affected vancomycin pharmacokinetics. The typical clearance and volume of distribution, standardized to 70 kg, were 7.75 L/h (2.3% RSE) and 36.2 L (1.7% RSE), respectively. The parameter estimates were within the bootstrap 95% CI. The goodness-of-fit and validity of the model were confirmed by GOF plots, and NPDE. The pvcVPC plots indicated a good predictive performance with a good agreement between simulated and observed data across all subgroups. As part of the external evaluation, the pvcVPC plots for the validation group similarly demonstrated good predictive performance. The prediction errors were small in both the model and validation groups. Simulations were conducted to determine the optimal dosing regimen for pediatric patients with varying ages and eGFRs, aiming to achieve a target AUC24/MIC between 400 and 650 for both non-CTS and CTS patients. The findings of these simulations show that the optimal dosage varies depending on patient's age and eGFR. Notably, the dose required for CTS patients is considerably lower than that for non-CTS patients. Most pediatric patients with an eGFR > 60 mL/min/1.73m2 could achieve the target AUC24/MIC on the first day of treatment without the need for a loading dose when given with the optimal dosing regimen (Figure 4). Nevertheless, for children with an eGFR < 60 mL/min/1.73m2, AUC values were notably lower on the first day if a loading dose was not administered. Our simulations showed that a loading dose of 20 mg/kg achieves desirable results

Conclusion We established vancomycin pharmacokinetic parameters in Chinese pediatric patients and proposed a dosing guideline integrating eGFR, age, and CTS status, potentially improving clinical outcomes and reducing nephrotoxicity risk

关键字：Vancomycin, population pharmacokinetics, pediatric

利奈唑胺在医院获得性肺炎合并肾功能不全患者中的群体药代动力学/药效学研究

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目的 在肾功能不全患者中，治疗耐药革兰氏阳性菌导致的医院获得性肺炎(hospital-acquired pneumonia, HAP)的最佳策略仍然具有挑战性。本研究的目的是比较在 HAP 合并肾功能不全患者中接受利奈唑胺与替考拉宁治疗的结局指标是否具有差异性，并探讨利奈唑胺的最佳给药策略。

方法 研究 1 比较了替考拉宁与利奈唑胺治疗 HAP 合并肾功能不全患者的有效性、安全性及谷浓度(trough concentration, Cmin)达标情况。在研究 2 中，使用从肾功能不全患者中收集的利奈唑胺浓度进行群体药代动力学(population pharmacokinetics, PPK)分析，并通过蒙特卡罗模拟确认最佳给药策略。

结果 与替考拉宁组相比，利奈唑胺组的细菌清除率更高(87.9% vs. 63.4%，P<0.001)，出现至少一次不良反应的比例更高 (50.6% vs.31.6%，P=0.015)。利奈唑胺组 Cmin 超标、未达标比例显著高于替考拉宁组(经校正 P<0.05)。来自肾功能不全患者的 231 个利奈唑胺浓度用于 PPK 分析，年龄和肌酐清除率(creatinine clearance, CrCL)被确定为影响清除率的重要协变量。模拟结果表明，对于 CrCL 为 60 或 45 mL/min 的患者，300mg q12h 是最佳给药方案，对于 CrCL 为 30 或 15 mL/min 的患者，推荐 200mg q12h 的给药方案。

结论 医院获得性肺炎合并肾功能不全患者接受利奈唑胺治疗比接受替考拉宁治疗具有更高的细菌清除率、谷浓度超标率和不良反应率。肾功能不全患者减少利奈唑胺剂量可提高达到最佳暴露的可能性。

关键字：利奈唑胺，群体药代动力学，药效学，肾功能不全，医院获得性肺炎

基于物联网技术的远程持续体温监测系统在发热患者体温测量中的信效度检验

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目的 检测基于物联网技术的远程持续体温监测系统在成年发热患者体温测量中的信效度。

方法 采用连续抽样法，选取 2023 年 3 月-8 月上海某三甲医院感染病科收治的发热患者为研究对象。患者住院期间，使用水银体温计按护理常规和治疗需求测量患者口温，使用体温监测系统连续测量患者腋温，并对比两者测温结果。

结果 共纳入 111 例病人，共计 2824 个体温测量点。体温监测系统测量的腋温比水银体温计测量的口温低（0.372±0.525）℃，Bland-Altman 图显示，95%LoA 上限为 1.400℃，下限为-0.656，表明在平均温度范围内具有±1.028℃一致性。体温监测系统测温的灵敏度为 75.1%，特异度为 91.1%，ROC 曲线下面积为 0.894，95%Cl（0.879~0.908），Kappa 值为 0.672。111 例患者平均使用体温监测系统监测体温 8.350±4.729 天，非必要监测中断发生率为 0.850%。体温监测系统测温准确性与 BMI 和测温传感器腋下粘贴部位有关。

结论 基于物联网技术的远程持续体温监测系统可以用于成年发热患者体温测量，具有较好的测温准确性和可靠性，但对于 BMI 高的患者存在遗漏发热的可能。

关键字：物联网；体温；体温监测系统；持续测温；移动医疗

Emergence and Clonal Expansion of Aeromonas Hydrophila ST1172 That Simultaneously Produces MOX-13 and OXA-724

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Objective Aeromonas hydrophila infections can cause gastrointestinal symptoms such as diarrhea; however, deep infections are rarely reported. Outbreaks of A. hydrophila are reported more frequently in fish, poultry, and snakes than in humans. This study aimed to track clonal relatedness of deep infections caused by A. hydrophila using whole genome sequencing (WGS)

Methods We collected three isolates of A. hydrophila in July 19 to August 29, 2019, from patients that underwent spine surgery. Accurate species identification was performed using whole-genome average nucleotide identity (ANI). Antimicrobial susceptibility testing was performed using a VITEK 2 automated AST-N334 Gram-negative susceptibility card system. Antimicrobial resistance and virulence genes were identified using the Comprehensive Antibiotic Resistance Database and Virulence Factor Database VFanalyzer

Results All three isolates were identified as A. hydrophila based on ANI and multilocus sequence typing analysis revealed that A. hydrophila belonged to a novel sequence type (ST1172). All three isolates were susceptible to amikacin and levofloxacin; however, they were resistant to piperacillin/tazobactam, ceftriaxone, cefuroxime, cefoxitin, and imipenem. Isolate 19W05620 (patient 3) showed increased ceftazidime resistance (minimum inhibitory concentration ≥ 64 μg/mL). All three isolates possessed the same chromosomally encoded β-lactamases, including blaOXA-724(β-lactamase), imiH (metallo-β-lactamase), and blaMOX-13(AmpC) in plasmids

Conclusions Our study validated the transmission of a novel carbapenem-resistant A. hydrophila sequence type (ST1172) in patients that underwent spine surgery. Control measures should be developed to prevent dissemination of A. hydrophila in the hospital setting

关键字：Aeromonas hydrophila; Carbapenem resistance; ST1172

Pharmacist-Driven Dosing Service and Pharmaceutical Care Increases Probability of Teicoplanin Target Concentration Attainment To Improve Clinical and Economic Outcomes in Non-Critically Ill Patients

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Objective Pharmacist-driven (PD) dosing and monitoring services have been shown to improve the clinical and economic outcomes in patients treated with

different antibiotics other than teicoplanin. This study validates the effect of a PD dosing and pharmaceutical care on clinical and economic outcomes of non-critically ill patients treated by teicoplanin

Methods A single-center retrospective study was designed. The patients were assigned to the PD group and the non-PD (NPD) group. The primary outcomes were defined as attainment of target concentration and a composite endpoint of all-cause mortality, admission to the intensive care unit (ICU) and the development of sepsis or septic shock during the hospital stay or within 30 days after hospital admission. Cost of teicoplanin, drug cost and total cost during hospital stay was also compared

Results A total of 163 patients from January to December 2019 were enrolled and evaluated. Seventy patients were assigned to the PD group and ninety-three were in the NPD group. More patients attained the target trough concentration in the PD group (54% vs. 16%, $p < 0.001$). Approximately 26% of the patients in the PD group and 50% of the patients in the NPD group reached the composite endpoint during hospital stay ($p = 0.002$). The PD group had significantly lower rate of sepsis or septic shock, shorter length of hospital stay and lower drug cost and total cost

Conclusion Our study demonstrates that pharmacist-driven teicoplanin therapy can improve the clinical and economic outcomes of non-critically ill patients

关键字：teicoplanin, clinical pharmacist, pharmaceutical care, therapeutic drug monitoring, MRSA, non-critically ill patients

Clinical Features and Risk Factors for Pyogenic Liver Abscess Caused by Multidrug-resistant Organisms: A Retrospective Study

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Objective The incidence rate of pyogenic liver abscess caused by multidrug-resistant bacteria has increased in recent years. This study aimed to identify the clinical characteristics and risk factors for pyogenic liver abscess caused by multidrug-resistant bacteria

Methods We conducted a retrospective analysis of the clinical features, laboratory test results, and cause of pyogenic liver abscesses in 239 patients admitted to a tertiary hospital. Multivariable logistic regression was used to identify risk factors for multidrug resistance

Results Among 239 patients with pyogenic liver abscesses, 55 cases (23.0%) were caused by multidrug-resistant organisms, and 71 cases (29.7%) were associated with biliary tract disease. Patients with pyogenic liver abscesses caused by multidrug-resistant organisms had a significantly higher likelihood of polymicrobial infection and increased mortality (7/44 [15.9%] vs. 3/131 [2.3%]; P =.003). The Charlson Comorbidity Index (adjusted odds ratio [aOR]: 1.32, 95% confidence interval [CI]: 1.06–1.68), hospitalization (aOR: 10.34, 95% CI: 1.86–60.3) or an invasive procedure (aOR: 9.62; 95% CI: 1.66–71.7) within the past 6 months, and gas in the liver on imaging (aOR: 26.0; 95% CI: 3.29–261.3) were independent risk factors for pyogenic liver abscess caused by multidrug-resistant bacteria. A nomogram was constructed based on the risk factors identified. The nomogram showed high diagnostic accuracy (specificity, 0.878; sensitivity 0.940)

Conclusion Multidrug-resistant organisms causing pyogenic liver abscesses have specific characteristics. Early identification of patients at high risk of infection with multidrug-resistant organisms could help improve their management and enable personalized treatment

关键字：Pyogenic liver abscess, multidrug resistant organisms, Klebsiella pneumoniae, Escherichia coli; risk factors, gas in liver

Adherence and Central Line-associated Bloodstream Infections (CLABSIs) Occurrence During Insertion and Maintenance of Intravascular Catheters (IVC): Evidence From 20 Tertiary Hospitals

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Objective To investigate the adherence to intravascular catheters (IVC) insertion and maintenance in Chinese tertiary-level A hospitals, and to provide a basis for the further development of various aspects such as a clinically realistic verification form

Methods A cross-sectional survey was conducted from July to September 2022 in 20 tertiary hospitals in China using a questionnaire survey of adult inpatients with IVC, each of whom had at least one vascular catheter. One clinical staff member from each department in each hospital was assigned to participate in completing the questionnaire. The questionnaires were uniformly collected and reviewed after 3 months.A total of 2993 questionnaires were distributed, and 2993 questionnaires were recovered, with a recovery rate of 100%. . After analysis, the research team retained the questionnaires with a response rate of ≥80%, and finally determined that 2894 questionnaires were valid, with an

effective recovery rate of 96.69%

Results A total of 2894 patients were included in this study, and each patient had at least one vascular catheter. The study included 1815 cases (62.69%) of CVC, 471 cases (16.27%) of PICC, 461 cases (15.92%) of PORT, and 147 cases (5.08%) of HC. Over 90% of IVC operators have undergone CLABSIs training and are familiar with the CLABSIs quality control indicators that were introduced in China in 2021.In addition to 93.63% of PICC insertion being nurses, the remaining IVC insertion operators consist of doctors.Statistically significant differences were observed in the adherence of various types of IVC during insertion, specifically in relation to the insertion checklist, the insertion standard operating procedure, and the insertion environment($P<0.05$).There was no statistically significant difference in compliance between different types of IVC insertion during placement in terms of hand hygiene and skin disinfection prior to placement($P>0.05$).More than 99% of patients with IVC placement had standard operating procedures for catheter care and quality standards for catheter care during maintenance($P>0.05$). Practice adherence during IVC maintenance was not all the same among the four types of IVC insertion patients in other aspects such as availability of IVC maintenance verification forms, daily scrubbing of the catheterized patients, and catheter connection methods, and the differences were statistically significant ($P<0.05$).After IVC insertion, a total of 386(14.88%) patients developed fever, 1086(41.87%) patients were treated with therapeutic antibiotics, 16(0.62%) patients developed CLABSIs, 2(0.07%) patients developed local skin infection, and 6(0.21%) patients developed deep vein thrombosis.There were significant differences in the incidence of CLABSIs among the four types of IVC

Conclusion The adherence to the four types of IVC insertion and maintenance is not the same, there is a certain gap between the recommended measures and the actual operation of the guideline. So it is necessary to further enhance training and develop checklists to prevent central line-associated bloodstream infections (CLABSIs).We propose the following recommendations: 1) the use of pre-filled catheter flushing solution for flushing and sealing; 2) the study of the effect of chlorhexidine rubbing; 3) the study of the replacement time of infusion connectors; 4) the study of the effectiveness of antimicrobial IVCs in reducing the incidence of CLABSIs

关键字：Central Line-associated Bloodstream Infections; Intravascular Catheters; Adherence

Identification and Risk Assessment of Distinct Prognostic Subtypes in Sepsis Patients Requiring Invasive Mechanical Ventilation Using Machine Learning and Deep Learning Models

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Objective Sepsis is a global health threat, and invasive mechanical ventilation (MV) is crucial but may lead to complications. We hypothesized that ML and DL models could identify prognostic subtypes in sepsis patients requiring invasive MV

Method A retrospective cohort study included sepsis patients from MIMIC-IV, using various ML and DL models (e.g., RF, XGBoost, CNN, etc.), with eICU data for external validation. AUCs and SHAP values assessed model performance and feature importance

Result 12,929 MIMIC-IV and 1,437 eICU patients were analyzed. RF, Adaboost, Catboost, LGBM, ANN, and CNN exhibited robust discriminatory power in MIMIC-IV (AUCs: 0.82-0.84). RF excelled across both databases (sensitivity: 0.825, specificity: 0.863, AUC: 0.844), with critical predictors of clinical death identified through SHAP values. A risk calculator for clinical death risk in sepsis patients was developed based on the RF model

Conclusion The RF model assists in assessing in-hospital mortality risk in sepsis patients undergoing invasive MV, offering valuable insights for clinical decisions

关键字：infection,sepsis, ventilation, machine learning, deep learning

壁报交流

细菌真菌感染的流行病学

Strong Homology between Colonizing and Bloodstream Carbapenem-resistant Acinetobacter Spp.: Implications for Empiric Antibiotic Therapy in Hematological Patients

Jia Li Sizhou Feng*

Strong homology between colonizing and bloodstream carbapenem-resistant Acinetobacter spp.: implications for empiric antibiotic therapy in hematological patients

Objective This study aimed to assess the impact of colonization status on the outcomes of Acinetobacter spp. bloodstream infection (BSI) and investigate the homology and within-host evolution between colonizing and bloodstream carbapenem-resistant Acinetobacter spp. (CRA) to inform antibiotic therapeutic decisions

Methods We analyzed clinical outcomes of 46 hematological patients with Acinetobacter spp. BSI and performed whole-genome sequencing on the remaining CRA isolates

Results Among the patients, 39.1% (n=18) had prior Acinetobacter spp. colonization. Colonized patients had higher rates of polymicrobial BSI (50.0% vs. 21.4%, P=0.044) and CRA BSI (72.2% vs. 17.9%, P<0.001), resulting in elevated inflammatory markers and increased 30-day mortality. Each of the eight pairs of the remaining respiratory colonizing and bloodstream CRA strains belonged to the same genomospecies. Each pair exhibited definitive agreement in at least 21 of the 22 most representative antibiotic susceptibility tests. The minimum spanning tree based on multilocus sequence typing (MLST) and phylogenetic trees based on MLST and single nucleotide polymorphism (SNP) all indicated that each pair shared the same minimum branch. Very few non-synonymous SNPs in genic regions were identified during the transition from respiratory colonization to bloodstream infection, with minimal changes in virulence genes. Homology analysis suggested that CRA BSI originated from colonizing isolates in the respiratory tract

Conclusion Strict infection control measures are needed to manage Acinetobacter spp. colonisation in hematological patients. Appropriate empirical therapy can be administered for suspected CRA BSI based on the antimicrobial minimum inhibitory concentration of CRA colonising the respiratory tract

关键字：Acinetobacter, colonization, bloodstream infections, homology, therapy, carbapenem-resistant

Prevalence and Clonal Diversity of Carbapenem-resistant Klebsiella Pneumoniae Causing Neonatal Infections: A Systematic Review of 128 Articles Across 30 Countries

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Background Klebsiella pneumoniae is the most common pathogen causing neonatal infections, leading to high mortality worldwide. Along with increasing antimicrobial use in neonates, carbapenem-resistant K. pneumoniae (CRKP) has emerged as a severe challenge for infection control and treatment. However, no comprehensive systematic review is available to describe the global epidemiology of neonatal CRKP infections. We therefore performed a systematic review of available data worldwide and combined a genome-based analysis to address the prevalence, clonal diversity, and carbapenem resistance genes of CRKP causing neonatal infections

Methods We performed a systematic review of studies reporting population-based neonatal infections caused by CRKP in combination with a genome-based analysis of all publicly available CRKP genomes with neonatal origins. We searched multiple databases (PubMed, Web of Science, Embase, Ovid MEDLINE, Cochrane, bioRxiv, and medRxiv) to identify studies that have reported data of neonatal CRKP infections up to June 30, 2022. We included studies addressing the prevalence of CRKP infections and colonization in neonates but excluded studies lacking the numbers of neonates, the geographical location, or independent data on Klebsiella or CRKP isolates. We used narrative synthesis for pooling data with JMP statistical software. We identified 8,558 articles and excluding those that did not meet inclusion criteria. We included 128 studies, none of which were pre-prints, comprising 127,583 neonates in 30 countries including 21 low- and middle-income countries (LMICs) for analysis. We found that bloodstream infection is the most common infection type in reported data. We estimated that the pooled global prevalence of CRKP infections in hospitalized neonates was 0.3% (95% confidence interval [CI], 0.2%-0.3%). Based on 21 studies reporting patient outcomes, we found that the pooled mortality of neonatal CRKP infections was 22.9% (95% CI, 13.0%-32.9%). 535 neonatal CRKP genomes were identified from GenBank including Sequence Read Archive, of which 204 were not linked to any publications. We incorporated the 204 genomes with a literature review for understanding the species distribution, clonal diversity and carbapenemase types. We identified 146 sequence types (ST) for neonatal CRKP strains and found that ST17, ST11, and ST15 were the three most common lineages. In particular, ST17 CRKP has been seen in neonates in eight countries

across four continents. The vast majority (75.3%) of the 1,592 neonatal CRKP strains available for analyzing carbapenemase have genes encoding metallo-β-lactamases and NDM (New Delhi metallo-β-lactamase) appeared to be the most common carbapenemase (64.3%). The main limitation of this study is the absence or scarcity of data from North America, South America, and Oceania

Conclusions CRKP contributes to a considerable number of neonatal infections and leads to significant neonatal mortality. Neonatal CRKP strains are highly diverse, while ST17 is globally prevalent and merits early detection for treatment and prevention. The dominance of blaNDM carbapenemase genes imposes challenges on therapeutic options in neonates and supports the continued inhibitor-related drug discovery

[Author summary]

Why was this study done?

l Klebsiella pneumoniae is a leading cause of neonatal infections with high mortality, representing a severe global problem.

l Carbapenem-resistant K. pneumoniae (CRKP) has emerged as a particularly severe challenge for infection control and treatment.

l Understanding the global burden of neonatal infections caused by CRKP and their clonal background could provide critical insights for guiding countermeasures, but no systematic review has been accomplished to address this gap.

What did the researchers do and find?

l We systematically reviewed all published articles addressing CRKP in neonates and included a total of 128 studies comprising 127,583 neonates in 30 countries and 2,057 neonatal CRKP isolates.

l We estimated a 0.3% pooled prevalence of CRKP infections in hospitalized neonates with a 22.9% pooled mortality. We found that neonatal CRKP strains were diverse in clonal background and most lineages did not exhibit inter-country dissemination.

l We utilized publicly available CRKP genomes with neonatal origins in GenBank to complement the literature for data about species, strain types and carbapenemase types.

l However, we observed inter-continental distribution of ST17, representing a particular widespread CRKP lineage associated with neonates, and most neonatal CRKP strains encode a metallo-β-lactamase, particularly NDM (New Delhi metallo-β-lactamase).

What do these findings mean?

l CRKP is a severe threat to this vulnerable population worldwide, in particular for those in LMICs.

l Most CRKP lineages in neonates appeared to emerge locally.

l Individualized approaches that are informed by local data may be needed for designing countermeasures.

l The dominance of carbapenemase genes impose challenges to effective treatment of neonatal infection. Our findings support the need for on-going research into effective therapeutics.

关键字：neonate, newborn, Klebsiella pneumoniae, CRKP, ST17, NDM

Molecular Epidemiological Investigation of Multi-drug Resistant Pathogenic Fungus Candida Pelliculosa in Chinese Hospitals

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Objective Fungal infection is still an important issue of global public health concern, although Candida albicans is the organism most often associated with serious fungal infections, rare yeast infections are also on the rise due to an increase in people with immunodeficiency or severe medical conditions in recent years. Candida pelliculosa can cause bloodstream infections with a mortality rate of 16.7%-41.2%. It is a serious threat to newborns and immunocompromised patients. China Hospital Invasive Fungal Surveillance Net (CHIF-NET) has monitored that the clinical isolation rate and drug resistance rate of Candida pelliculosa have increased significantly from 2009 to 2021, which poses severe challenges to clinical treatment and infection control

Methods In our research, isolates were identified as C. pelliculosa by a previously-established algorithm incorporating matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) using the Vitek MS system (software version V2.0, bioMérieux). MIC of 309 C. pelliculosa isolates from 42 hospitals in China were evaluated in vitro using in-house prepared 96-well plates following CLSI broth microdilution methods. Susceptibility to ten antifungal agents, including five azoles (fluconazole, voriconazole, itraconazole, isavuconazole and posaconazole), three echinocandins (caspofungin, micafungin, and anidulafungin), 5-flucytosine, and amphotericin B were determined. Then we explored drug-resistant related mutation sites and drug resistance expansion regularity of Candida pelliculosa in China, based on populational genomics

Results More than one-third of the 309 strains of C. pelliculosa were obtained from the Northeast region in China, and individuals aged 46-65 years and newborns emerged as the primary sources of infection. The predominance of C. pelliculosa isolates in blood samples highlights the significance of bloodstream infections caused by this organism

Through drug sensitivity analyses conducted in

vitro, we discerned that C. pelliculosa exhibits notable resistance, particularly evident with three drugs—5-fluorocytosine, voriconazole, and fluconazole—with non-wild type ratios reaching 43.3%, 48.5%, and 34.3%, respectively. The issue of co-resistance between 5-fluorocytosine and fluconazole is particularly concerning. Conversely, the fungus demonstrated sensitivity to echinocandins and amphotericin B (MIC50/90, ≤0.25 mg/L).

Noteworthy genetic markers associated with drug resistance, including ERG11, MRR1, TAC1, CDR1, and CDR2, were identified in azole-resistant isolates. An analysis of the FST index of genomic differentiation in C. pelliculosa across China unveiled an expansion spanning multiple geographic regions.

Further examination through SNP evolutionary tree analysis disclosed that clusters of multiple drug-resistant strains were predominantly isolated from the same hospital. This implies a pressing concern of intra-hospital outbreaks and the potential transmission of drug-resistant isolates from patient to patient.

Conclusion In conclusion, our study offers crucial and updated insights at the national level in China regarding the antifungal susceptibility of C. pelliculosa, the emergence of azole drug resistance poses a significant threat to C. pelliculosa, underscoring the ongoing need for surveillance.Out findings will provide new targets for the specific diagnosis of drug resistance, and provide theoretical guidance for the monitoring of drug resistance epidemic and the formulation of infection control strategies for C. pelliculosa

关键字：Candida pelliculosa, antifungal susceptibility,epidemiology

广州地区 ICU 念珠菌血流感染患者临床特征及预后影响因素分析

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目的 探讨广州地区重症监护室（Intensive Care Unit，ICU）念珠菌血流感染患者的临床特点及预后相关影响因素，为其诊治及预后改善提供理论依据。

方法 回顾性分析 2018 年 1 月-2023 年 3 月广东省人民医院 ICU 念珠菌血流感染患者的临床资料及预后情况，并对生存和死亡患者间的相关危险因素进行比较分析。

结果 134 例 ICU 念珠菌血流感染患者中，白念珠菌检出率最高（49 株，36.6%），其次为近平滑念珠菌（28 株，20.9%）、光滑念珠菌（23 株，17.2%）和热带念珠菌（20 株，14.9%）等，药敏结果显示光滑念珠菌和热带念珠菌对唑类抗真菌药物的耐药率较高。134 例患者中死亡 42 例，死亡率为 31.3%，且死亡组平均年龄高于生存组（t=-2.255，P=0.026）。单因素分析显示：患者伴有恶性肿瘤、＞3 种基础疾病、使用糖皮质激素和碳青霉烯类药物以及＞3 种抗菌药物联用与预后相关，Logistic 回归分析显示：＞3 种基础疾病和使用糖皮质激素可能是影响患者预后的重要危险因素。

结论 ICU 念珠菌血流感染患者死亡率高，同时临床需尽早完善患者血培养送检，并加强药物管理及临床护理工作，以降低念珠菌血流感染风险，改善患者预后。

关键字：念珠菌血流感染；重症监护室；临床特征；预后

Clinical Characteristics and Prognosis of Patients with Cryptococcus Neoformans Bloodstream Infection

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Objective To investigate the clinical characteristics and prognosis of Cryptococcus neoformans bloodstream infection, providing a foundation for clinical diagnosis and treatment to enhance patient outcomes

Methods The data of 11 patients diagnosed with Cryptococcus neoformans bloodstream infection in Guangdong Provincial People's Hospital from January 2018 to December 2022 were collected. Subsequently, conducting a comprehensive analysis of their clinical characteristics, laboratory detection indicators, diagnosis, treatment, and prognosis

Results There were 7 males and 4 females among the 11 patients with Cryptococcus neoformans bloodstream infection, with a median age of 49 years and a median length of hospital stay of 27 days. Ten patients had underlying diseases, including a history of steroid/immunosuppressive drug treatment in 7 cases, diabetes and kidney disease in 4 cases each, and autoimmune disease and cardiovascular disease in 3 cases

each. Clinical manifestations included fever in 9 cases, cough in 5, headache in 4, rash in 2, and abdominal pain in 2. Some cases presented with concurrent infections at other sites, comprising 3 cases of cryptococcal meningitis, 1 case of pulmonary cryptococcosis, and 1 case of both concurrent cryptococcal meningitis and pulmonary cryptococcosis. Additionally, 7 cases exhibited an increase in leukocyte count and C-reactive protein, 8 cases had an elevated neutrophil ratio, 10 cases showed increased procalcitonin levels, and albumin levels decreased in all cases. The antimicrobial susceptibility testing indicated that one strain of Cryptococcus neoformans had acquired resistance to fluconazole, while the others had not. Out of the 11 patients, 9 showed improvement, while 2 did not well recover

Conclusion Cryptococcus neoformans bloodstream infection is prevalent in immunodeficient or immunosuppressed populations, typically manifesting clinically with fever. Therefore, emphasizing the management of susceptible populations and the monitoring of strain resistance can positively impact infection control and contribute to improved prognosis

Cryptococcus neoformans is a widely distributed opportunistic pathogenic fungus, primarily originating from the environment. It can be isolated from various sources, including bird droppings, soil, fruits, plant materials, decaying wood, and even wooden products[1]. According to the Fungal Priority Pathogens List (FPPL) released by the World Health Organization in 2022, Cryptococcus neoformans holds the top position[2]. Capable of causing life-threatening cryptococcosis, its high mortality is primarily attributed to delayed diagnosis and treatment. It most commonly invades the lungs and central nervous system[3], while bloodstream infections are relatively rare. By collecting data on patients admitted to Guangdong Provincial People's Hospital diagnosed with Cryptococcus neoformans bloodstream infections, this study will analyze their clinical characteristics, treatment, and prognosis, aiming to provide valuable insights for the prevention and treatment of cryptococcosis and the enhancement of patient outcomes.

1 Materials and Methods

1.1 Study Subjects

Clinical records of 11 patients with Cryptococcus neoformans bloodstream infections at Guangdong Provincial People's Hospital from January 2018 to December 2022 were systematically collected through the medical record system. In adherence to the diagnostic criteria for bloodstream infections[4], patients with positive blood cultures identified as Cryptococcus neoformans infections were diagnosed and included, whereas those with concurrent infections involving other pathogens and incomplete clinical data were excluded.

1.2 Instruments and Reagents

Blood cultures were conducted using the French bioMérieux Virtuo BacT/ALERT system, along with its corresponding blood culture bottles. Strain identification and antimicrobial susceptibility testing were performed using the French bioMérieux VITEK MS mass spectrometry system and fungal susceptibility test kits. Cryptococcus neoformans was cultured through blood agar and Potato Dextrose Agar (PDA) culture media. Adhering to the standards outlined in the Clinical and Laboratory Standards Institute (CLSI) Fungal Susceptibility Test M59[5], the epidemiological cutoff values (ECV) for Cryptococcus neoformans antifungal drugs were as follows: Amphotericin B (AmB): 0.5 μg/mL, 5-Fluorocytosine (5-FC): 8 μg/mL, Fluconazole (FLU): 8 μg/mL, Voriconazole (VORI): 0.25 μg/mL, Itraconazole (ITRA): 0.25 μg/mL.

1.3 Research Methods

Utilizing the electronic medical record system to gather essential information on patients, including their basic details, underlying conditions, clinical manifestations, diagnostic and therapeutic processes, as well as outcome data. Subsequently, retrieving pertinent data from the laboratory information system, organizing and comprehensively analyzing patients' microbiological culture, identification, susceptibility testing results, and relevant laboratory test indicators.

关键字：Cryptococcus neoformans; Bloodstream infection; Clinical characteristics; Clinical prognosis; Antifungal drug

Antimicrobial Resistance Changes of Multidrug-resistant Organisms Among Critically Ill Patients before and after The COVID-19 Outbreak: An Interrupted Time Series Analysis in A Teaching Hospital in Guangzhou, China

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Objective The emergence of infections caused by multidrug-resistant organisms (MDROs) has emerged as a paramount concern in the realm of global public health and hospital infection control endeavors. According to the World Health Organization (WHO), the ongoing COVID-19 pandemic has precipitated an upsurge in antibiotic utilization, thereby heightening the perils associated with antimicrobial resistance, which is significantly contributing to augmented disease burdens and mortalities

Previous studies have revealed that between 3-12% of hospitalized patients in developed countries will develop nosocomial infections, with over 20% of these infections being acquired in the ICU. Despite ICUs accounting for less than 10% of hospital beds, the risk of

MDRO infections is high due to high rates of antimicrobial resistance and mortality. Patients in the ICU have a higher risk of MDRO infection due to their complex health conditions, decreased organ function, and weakened immune systems. A case of multi-center validation study showed that MDRO causes a higher mortality rate (37.6%, n = 53) in the ICU than non-MDRO patients (26.2%, n = 37). In addition, the inappropriate use of antibiotics can exacerbate the problem of resistance among pathogens. To avoid the potential of increased mortality due to delayed antibiotic treatment, broad-spectrum antibiotics are commonly used for critically ill patients in the ICU. However, prolonged exposure to antibiotics will raise the risk of MDRO infections.

Additionally, during the pandemic, the global health management system has faced significant strain, resulting in numerous adjustments to clinical practice that could potentially influence AMR. The COVID-19 pandemic highlighted the challenge that an emerging pathogen provides in adapting prevention measures of MDROs regarding the change of characteristics of resistance. The Carbapenem-Resistant Acinetobacter baumannii (CRAB) outbreak at an acute care hospital in the United States during COVID-19 was particularly severe among ICU patients, largely due to breaches in infection control and persistent environmental pollution. A study in Iran showed that in ICU up to 68.7% of the drug-resistant strains in patients with COVID-19 were multi-drug-resistant strains. The study in mainland China reported K. pneumoniae and CRKP infections in ICU elderly infected patients had decreased during the COVID-19 pandemic which deserved great attention. Therefore, it is imperative to gather comprehensive data on the prevalence of AMR infections before and after the pandemic to asses effectively the global AMR threat at both local and global levels.

It is challenging to assess the impact of the outbreak on MDROs in many regions due to disruptions in routine drug resistance surveillance and reporting, missing baseline data, and other factors. Urgent action is needed to conduct a long-term monitoring study that captures the changes in antimicrobial resistance during the COVID-19 pandemic, especially in ICUs where medical resources are strained and resistance is a serious problem.

Methods This retrospective interrupted time series analysis was performed at a tertiary teaching hospital in Guangdong Province, China. The hospital has a capacity of 7,400 beds across 4 wards and sees an average of 18,000 outpatient visits per day. The teaching hospital is well-known for its strong medical and technical expertise and is considered a leading institution in the country. Notably, the hospital's clinical laboratory has successfully established an extensive database encompassing nosocomial infection pathologies and drug resistance, ensuring utmost data integrity and accuracy. The intensive care units included the surgical Intensive Care Unit (SICU), medical intensive Care Unit (MICU), pediatric intensive care unit (PICU), emergency intensive care unit (EICU), and cardiac intensive care Unit (CCU), which had 1464, 1222, 37439 and 254 patient admissions, respectively, during the study period. As a tertiary referral hospital, the general hospital has a full range of departments and receives referrals from both regional and remote areas of the country frequently. As a result, the collected microbial data covers diverse patient and specimen types and is quite representative

The data was collected from April 2018 to September 2021, encompassing the period before and after the COVID-19 outbreak. The collected data included information on nosocomial infections and drug susceptibility. Patient information comprised patient ID, sex, age, ward type, department, source of the specimen, species of the infectious pathogen from the nosocomial infection surveillance system, and susceptibility to major antibiotics from the drug resistance surveillance network. For each surveillance period, only one result was reported for each patient per surveyed specimen type and surveyed pathogen. For comparative purposes, We also obtained national data on the distribution of pathogens and drug resistance from the China Antimicrobial Resistance Surveillance System (CARSS) from 2018 to 2021, which was used to compare with the drug resistance data of the hospital and provide a national data reference for the changes of bacterial drug resistance during COVID-19 in Guangdong Province.

We used Quasi-Poisson regression to fit the interrupted time-series-model. January 2020 was selected as the time break point for the impact of COVID-19 in Guangzhou. The main basis is that on January 23, 2020, Guangdong Province launched a top level response to a major public health event. The Durbin Watson (DW) method was used to detect the presence of first-order autocorrelation in the time series, with DW values ranging from 0 to 4 and values close to 2 indicating no autocorrelation. The model diagnosis was based on the Akaike information criterion (AIC)values.

The dependent variable (Y) for the study was the monthly isolated strains of drug-resistant bacteria in the ICU of a tertiary teaching hospital from April 2018 to September 2021. ln (Count) is used to incorporate the total count of the detected bacteria strains as an offset. The breakpoint for the analysis was the outbreak of COVID-19 in January 2020. The time variable (count variable) was represented by values of 1, 2, ..., for each month from 2018 to 2021. The value of the COVID-19t variable was 0 before the outbreak and 1 after the outbreak (starting from January 2020). The time after the outbreak was represented by the (TIME following the COVID-19)t variable, with values of 0 before January 2020 (including January 2020) before the breakpoint and values of 1,2,3... after the breakpoint. Month, Age, Gender, Ward, and Specimen were the controllable variables. An interrupted time series Poisson regression

model was fitted:

Y ~ Poisson (μ)

ln (μt) = ln(count) + β0 + β1*timet + β2*COVID-19t + β3*(TIME following the COVID-19)t + δ*Moutht + γ*age + η*Gender + ρ*Ward + σ*Specimen

Where β0 represented the baseline level in January 2020, β1 represented the monthly change in the number of drug-resistant strains of pathogens before the outbreak of COVID-19. β2 and β3 represented the level and trend of drug-resistant strains (relative to β0 and β1) since the outbreak, respectively. A t-test or z-test was performed to verify the statistical significance of the difference between the changes in level and slope.

Results In this study, the period analyzed was from April 13, 2018, to September 30, 2021. The proportion of Acinetobacter baumannii remained the highest during this time frame. The proportion of Acinetobacter baumannii and Pseudomonas aeruginosa declined over the study period, whereas the proportion of Stenotrophomonas maltophilia showed a significant increase in 2020

There was a decrease in the detection proportion of Acinetobacter baumannii by 12.59% from January to February 2020, with the lowest point observed in December 2020 (3.92%). There was a decrease of 9.79% in the proportion of Escherichia coli and a decrease of 2.79% in the proportion of Klebsiella pneumoniae. On the other hand, the proportion of Stenotrophomonas maltophilia and Pseudomonas aeruginosa increased by 8.39% and 9.56%, respectively. In the period between December 2020 and January 2021, there was a decrease of 35.54% in the proportion of Pseudomonas aeruginosa detected.

Taking January 2020 as the cut-off point, the number of drug-resistant bacteria detected in the ICU from April 2018 to September 2021 was applied to analyze using the Segmented quasi-Poisson Regression model. Carbapenem-resistant Acinetobacter baumannii (RR=1.031, 95%CI: 1.016~1.046), third- or fourth-generation cephalosporin-resistant Acinetobacter baumannii (RR=1.033, 95%CI: 1.017~1.048), carbapenem-resistant Klebsiella pneumoniae (RR=1.141, 95%CI: 1.079~1.206), third- or fourth- generation cephalosporin-resistant Klebsiella pneumoniae (RR=1.053, 95%CI: 1.015~1.093), meticillin-resistant Klebsiella pneumoniae (RR=1.094, 95%CI: 1.041~1.150), third- or fourth- generation of cephalosporin-resistant Pseudomonas aeruginosa (RR=1.060, 95%CI: 1.011~1.110) and Methicillin-resistant Staphylococcus aureus (RR=1.685, 95%CI: 1.189~2.388) showed an increasing trend before the COVID-19 pandemic, while carbapenem-resistant Escherichia coli (RR=0.689, 95%CI: 0.526~0.904) showed an decreased trend before the COVID-19 pandemic.

At the outset of the COVID-19 outbreak in January 2020, there was a significant decrease in carbapenem-resistant Klebsiella pneumoniae (RR=0.240, 95%CI: 0.081-0.711) and Methicillin-resistant Staphylococcus aureus (RR=0.001, 95%CI: 0~0.108). However, there was a significant increase in the detection of carbapenem-resistant Pseudomonas aeruginosa (RR=1.750, 95%CI: 1.341~2.282) and Methicillin-resistant Escherichia coli (RR=9.622, 95%CI: 1.254~73.819).

After the outbreak of COVID-19, a long-term decreasing trend was observed in carbapenem-resistant Klebsiella pneumoniae (RR=0.890, 95%CI: 0.818~0.969), methicillin-resistant Klebsiella pneumoniae (RR=0.915, 95%CI: 0.845~0.990), carbapenem-resistant Pseudomonas aeruginosa (RR=0.927, 95%CI: 0.907~0.947) and third- or fourth- generation of cephalosporin-resistant Pseudomonas aeruginosa (RR=0.888, 95%CI: 0.819~0.962) in the ICU. However, a long-term increasing trend was shown in the carbapenem-resistant Escherichia coli (RR=2.267, 95%CI: 1.166~4.409).

Conclusion This study collected dynamic monitoring data of nosocomial infection and used an interrupted time series model to explore the impact of COVID-19 on MDROs in the ICU, which provided evidence for ICU antimicrobial stewardship and infection control during the pandemic. The interrupted time series model has a wider time frame compared with similar studies, controlled for the effect of time, and attempted to fit different types of distribution models, which can provide a reference for subsequent studies. After the outbreak of COVID-19, the risk of multi-drug resistance in Klebsiella pneumoniae and Pseudomonas aeruginosa decreased significantly, while the resistance to the carbapenems in Escherichia coli showed an upward trend, suggesting that during the COVID-19 pandemic, continuous control and surveillance of hospital infections caused by MDROs deserved great concern, especially Escherichia coli and the rational use of carbapenems

关键字：multidrug-resistant organisms, intensive care unit; nosocomial infection, COVID-19, interrupted time series

Epidemiological Characteristics and Impact on Patient Outcomes of Bacterial and Fungal Infections in Severe Pneumonia From 2004 To 2023

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Objective Severe pneumonia presents a significant public health challenge globally, not only causing high mortality rates but also prevalently affecting patients with compromised immune systems. Over the past two decades (2004-2023), the treatment and management of severe pneumonia have become increasingly complex due to the rise in bacterial and fungal resistance, along with the emergence of new pathogens. This study aims to comprehensively analyze the epidemiological characteristics of bacterial and fungal infections in severe pneumonia during this period, and their impact on patient outcomes

Methods This research conducted a retrospective analysis of clinical data from 18,935 severe pneumonia patients collected by the National Respiratory Medicine Center in the southern region from 2004 to 2023. It detailed the types, incidence rates, resistance patterns, and treatment outcomes of bacterial and fungal infections. Furthermore, multivariable regression analysis was used to evaluate the impact of different pathogen characteristics on patient outcomes (including hospital stay duration, treatment costs, and mortality rates)

Results Among the 18,935 patients, bacterial infections predominated (65%), followed by fungal infections (25%) and mixed infections (10%). Streptococcus pneumoniae, Staphylococcus aureus, and Klebsiella pneumoniae were the most common bacterial pathogens; Aspergillus and Candida were the most common fungal pathogens. Significant increases in resistance to various commonly used antibiotics and antifungal drugs were observed, especially the resistance rate of Klebsiella pneumoniae to carbapenems, which surged from 20% in 2004 to 60% in 2023. The analysis indicated that the mortality rate of patients with fungal infections (35%) was significantly higher than that of patients with bacterial infections (20%) and those without infections (10%). Multivariable regression analysis suggested that the type of pathogen, resistance, and patients' baseline health conditions were significant factors affecting outcomes

Conclusion This study reveals the complex epidemiological characteristics of bacterial and fungal infections in severe pneumonia from 2004 to 2023 and their significant impact on patient outcomes. Fungal infections, in particular, are associated with poorer treatment outcomes, indicating the need for early identification and intervention in high-risk patients in clinical settings. Additionally, the escalating issue of bacterial and fungal resistance urgently demands the development of new antibiotics and antifungal medications, as well as the reinforcement of rational drug use management. Continuous monitoring and research are essential to adapt to potential epidemiological changes in the future, ensuring that patients with severe pneumonia can receive effective prevention, diagnosis, and treatment services

关键字：severe pneumonia, bacteria, fungi, infections, epidemiology

Clonal Aggregation of Fluconazole Resistant Candida Tropicalis in Clinical Sterile Body Fluid Specimens From Patients in Hefei，China

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Background C. tropicalis, a human conditionally pathogenic yeast, is distributed globally, especially in Asia-Pacific. The increasing morbidity and azole-resistance of C. tropicalis have made clinical treatment difficult. There is a correlation between clonality and antifungal susceptibility of clinical C. tropicalis isolates

Objectives To study the putative correlation between fluconazole non-susceptible (FNS) of C. tropicalis isolated from multicentric clinical sterile body fluid specimens and distinct clonal complex (CC) formation, and to explore epidemic C. tropicalis CCs in Hefei

Methods 256 clinical C. tropicalis isolates were collected, 30 of which were FNS. Genetic profiles of 63 isolates (30 FNS and 33 fluconazole-susceptible (FS)) were characterized using multilocus sequence typing (MLST). Phylogenetic analysis of the datas in this study and the MLST database were conducted. MLST clonal clusters were analysed using the BioNumerics 8.1

Results MLST identified six gene fragments, among which ICL1, SAPT2, and ZWF1α presented the highest typing efficiency. Among 35 differentiated diploid sequence types (DSTs), 16 DSTs and 1 genotype were identified as novel. 35 DSTs were assigned to five major CCs. The predominant FNS CC1 (containing DST 376, 505, 507, 1221, 1222, 1223,1226, and 1229) accounted for 86.7% of the FNS isolates. However, the genetic relationships among the FS isolates were relatively decentralised.The local FNS CC1 belongs to a large FNS CC8 in global isolates, of which the putative founder genotype was DST225. Unique FNS CCs have also been found in Singapore (CC6) and India (CC11and CC48)

Conclusions The putative correlation between MLST types and fluconazole susceptibility of clinical C. tropicalis isolates in Hefei showed that DSTs are closely related to FNS clones

关键字：Candida tropicalis, fluconazole resistance, genetic diversity, multilocus sequence typing (MLST).

Epidemiological Characteristics of 7 Respiratory Pathogens in 14549 Patients During The COVID-19 Pandemic in Guangzhou, China

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Objective To analyze the epidemiological characteristics of 7 respiratory pathogens in 14549 patients during the COVID-19 pandemic in Guangzhou, China and to explore the causes

Methods Respiratory pathogens, namely influenza A virus (FluA), influenza B virus (FluB), respiratory syncytial virus (RSV), human parainfluenza virus (PIV), adenovirus (AdV), Mycoplasma pneumoniae (MP) and Chlamydia pneumoniae (Cpn), were selected from a total of 14549 patients from December 1, 2019 to November 30, 2022. The differences in the positive constituent ratios and detection rates of each pathogen were analyzed and compared among different years, ages, genders, and seasons

Results The detection rate of RSV (1.03%) was higher than that of FluA (0.42%), PIV (0.41%), MP (0.23%), AdV (0.10%), FluB (0.06%) and Cpn (0.01%), and the difference was statistically significant. There was a statistically significant difference between two comparisons of the detection rates of FluA in different years, with the lowest in 2021 (0%) and the highest in 2022 (1.32%). The detection rate of RSV in 2021 (0.80%) showed a decreasing trend compared to 2020 (1.43%). FluA replaced RSV in 2020 and 2021 as the dominant strain in 2022. The detection rates of RSV (5.21%), PIV (1.88%) and AdV (0.47%) in children were higher than those of 0.97%, 0.44% and 0.09% in young and middle-aged adults, respectively. They were also higher than 0.20%, 0.10% and 0.03% in the elderly, respectively, with statistically significant differences. The detection rate of FluA in children (0.89%) was higher than that in the elderly (0.36%), with a statistically significant difference. There was a statistically significant difference in the detection rates of RSV and PIV between young and middle-aged adults and the elderly. RSV was the predominant strain in both children and young and middle-aged adults, but it was replaced by FluA in the elderly. The detection rates of RSV (1.31%) and PIV (0.58%) were higher in female than in male (0.88% and 0.32%, respectively), and the differences were statistically significant. The predominant strain in both male and female was RSV. There were seasonal differences in the detection rates of FluA, RSV and PIV. The detection rate of FluA was highest in summer (1.34%), followed by winter (0.47%), spring and autumn were lowest, both were 0%. The detection rate of RSV was highest in autumn (2.19%), followed by summer (1.32%), spring and winter were lower (0.32% and 0.45%, respectively). The detection rate of PIV was highest in winter (1.01%), and 0.16%, 0.23%, and 0.21% in spring, summer, and autumn, respectively. The dominant strain was RSV in spring, summer and autumn, which was replaced by PIV in winter. Among the 13,270 patients who were screened for all seven of these pathogens simultaneously, the top four pathogen-positive composition ratios were RSV (41.54%), FluA (21.15%), PIV (18.46%) and MP (10.38%). Single pathogen infection was dominated by RSV infection, accounting for 0.81%, and two pathogen infections were dominated by FluA+PIV and RSV+ MP infection, with one case each

Conclusions RSV was more prevalent and Cpn was less common among respiratory pathogens infections in Guangzhou under non-pharmacological intervention during the New Coronavirus-19 pandemic. Annual differences existed in the detection rates of FluA and RSV. The detection rates of RSV and PIV were highest in children, followed by young and middle-aged adults, and the elderly. The detection rates of RSV and PIV were higher in females than in males. There were seasonal differences in the detection rates of FluA, RSV and PIV, with the highest detection rates of FluA in summer, RSV in autumn and PIV in winter. Infection patterns were more common with single pathogens. The predominant strain was mostly RSV, except in 2022 and in the elderly was replaced by FluA, and was replaced by PIV in winter

关键字：COVID-19, respiratory pathogens, Guangzhou, season

Etiology, Microbiological Isolates, and Antibiotic Susceptibilities in Inpatients with Refractory Auricular Perichondritis: A 10-Year Retrospective Study

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Objective This study aimed to elucidate the etiologies, microbiological profiles, antibiotic susceptibilities of bacteria and outcomes of patients with auricular perichondritis

Methods This was a single-center retrospective study. Inpatients diagnosed with auricular perichondritis at a university teaching hospital in eastern China between January 2013 and December 2022 were included in this study

Results A total of 127 patients were enrolled, with an average age of 50.6 ± 16.9 years. In addition to cases in which the etiology remained undetermined in 37% of the patients, postoperative infection emerged as the predominant cause (37.8%), followed by trauma (18.1%). Among the 61 cultured isolates, 21.3% were

gram-positive bacteria, 55.7% were gram-negative bacteria, and 23.0% were fungal isolates. The most frequent isolate was Pseudomonas aeruginosa (30/61, 49.2%). Notably, the incidence of fungal infections was markedly higher among postoperative patients than among post-traumatic patients (41.7% vs 7.1%, p = 0.03). The proportions of gram-negative bacteria (60.0% vs 50.0%) and fungal isolates (28.6% vs 15.4%) exhibited an increasing trend during the period of 2018–2022, as compared to the previous period of 2013–2017. The bacterial isolates exhibited high susceptibility to vancomycin (100%), amikacin (100%), cefepime (94.6%), and ceftazidime (90.9%). In contrast, overall susceptibility to fluoroquinolones was relatively low (65.2–67.4%), demonstrating a declining trend in the susceptibility of Pseudomonas aeruginosa. Notably, 78.7% of the patients received an initial treatment regimen covering Pseudomonas aeruginosa. Within 30 days of discharge, 8.5% (6/71) experienced an infection recurrence

Conclusion Auricular perichondritis predominantly originates from iatrogenic (postoperative) infections. Antibiotic therapy covering Pseudomonas aeruginosa is a sensible and appropriate empirical treatment in the majority of patients with auricular perichondritis. However, increased resistance to fluoroquinolones has become a notable concern, suggesting the need to seek new, more aggressive strategies

关键字：auricular perichondritis, antibiotic sensitivity, Pseudomonas aeruginosa, fluoroquinolones

Genetic Characteristics and Potential Pathogenic Agents in Campylobacter Upsaliensis Based on Genomic Analysis

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Campylobacter upsaliensis is the most common Campylobacter species in pets' gastrointestinal tracts and has been isolated from patients with bacteremia, hemolytic-uremic syndrome, spontaneous abortion, and Guillain-Barré syndrome. However, the genetic characteristics and the full extent of its significance as a human pathogen remain to be fully understood. This study involved an investigation for genomic analysis of 154 strains from different sources and additional drug resistance profiles of 26 strains for this species. The genomes contained 1,558 – 1,971 CDS and the genome sizes were estimated to vary from 1.53 Mb to 1.86 Mb, with an average GC content of 34.71%. The entire analyzed genomes could be divided into three clades (A, B, and C) based on ANI and phylogenomic analysis. Significantly, nearly all strains in Clade B were isolated from human diseases, and the virulence associated FlgD, GmhA, and CdtC may serve as determining factors for the classification of Clade B. Half of the tested isolates had MIC values over 64 μg ml-1 for nalidixic acid, gentamicin, and streptomycin. Isolates from pets in China carried more resistant elements on the genomes. This study both provided a comprehensive profile of C. upsaliensis for its genomic features and also put forward some pathogenic agents for human infection of this species.

关键字：Campylobacter upsaliensis; pathogenic agent; comparative genomics; virulence factor; antimicrobial resistance

Screening for Clostridioides Difficile Mixed Infection Is Necessary in Patients with Ulcerative Colitis

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Objective Clostridioides difficile (C. difficile) is the leading cause of antibiotic-associated diarrhea enteritis. The risk of C. difficile infection(CDI) is greatly increased in patients with ulcerative colitis(UC). Moreover, the severity and duration of disease are greatly increased in patients with clinical UC combined with a CDI. C. difficile mixed infections are concurrent infections in the same host with different genotype strain types,which may have potential effects on the disease process and host immunity

Given that clinical screening for C. difficile mixed infections is rarely performed and that many cases of C. difficile mixed infections may be missed. The prevalence of mixed C. difficile infections in UC patients and whether mixed infections result in increased disease severity, prolonged treatment cycles, and subsequent CDI recurrence is unknown. Therefore, the objectives of the current study were as follows: determine the incidence of C. difficile mixed infections during a clinical CDI by culture identification of multiple isolates from the same specimen; compare the susceptibility factors and disease severity of mixed infections with single infections by retrospectively investigating the underlying clinical UC and other diseases; and investigate the potential relationship between mixed infections and disease recurrence based on in vitro experiments with mixed infection strains.

Methods 1. Collection of clinical CDI cases: patients with clinical symptoms of diarrhea along with Gene Xpert (+) or glutamate dehydrogenase antigen/toxin (+) in several hospitals in Hebei from August 2022 to September 2023 were enrolled according to the

diagnostic criteria for CDI defined according to the national guidelines of the Infectious Diseases Society of America (IDSA), and their fecal specimens used for the diagnosis of the disease were collected

2. Detection of C. difficile mixed infection: patients with clinical CDI were tested for C. difficile mixed infection by PCR-ribotyping and multilocus sequence typing (MLST).

3. Detection of antibiotic resistance of mixed infection strains: Minimum inhibitory concentration (MIC) of mixed infection strains to different antibiotics was determined by agar dilution method.

4. Biofilm formation ability of mixed infection strains: Different genotypes of C. difficile were cultured separately or mixed 1:1 for 120h in BHISG, and the biofilm formation ability of the strains cultured separately and mixed was quantified by crystal violet staining.

Results A total of 31 (11.3%) mixed infections were detected by PCR-ribotyping and MLST in 274 cases of CDI, of which 30 were double-strain infections and 1 was triple-strain infection. The main types of mixed infections were ST54, ST3, ST42. Statistical analysis showed that patients with chronic recurrent ulcerative colitis had a substantially increased risk of mixed infection with C. difficile (OR=3.843, 95%CI 1.779-8.301, P=0.001). The heterogeneous resistance rate among strains of mixed infections was 83.9%, with levofloxacin, rifaximin, chloramphenicol and tetracycline being more likely to show heterogeneous resistance. The results of the in vitro experiments showed that the level of biofilm formation in mixed cultures was more in favor of the strains with a high biofilm-forming capacity in mono-culture

Conclusion Our study showed that a percentage of C. difficile mixed infections occur during clinical CDIs, and that UC, especially chronic recurrent UC, may increase the risk of C. difficile mixed infections. In addition, the emergence of multidrug-resistant strains of C. difficile and recurrent CDIs after discontinuation of medication may also be associated with mixed infections. Therefore, patients with UC should be screened for C. difficile mixed infections and individualized medications should be administered to reduce recurrence and the development of multidrug-resistant strains

关键字：Clostridioides difficile , mixed infection, ulcerative colitis, MLST, PCR-Ribotyping

中国多中心侵袭性感染季也蒙念珠菌复合体流行病学分析

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目的 季也蒙念珠菌是侵袭性念珠菌感染中重要的致病病原体，分离率位列非白念珠菌的第四位，近年来呈现增长趋势。本研究旨在分析中国多中心侵袭性感染季也蒙念珠菌复合体的流行病学现状。

方法 本研究共纳入中国医院侵袭性真菌病监测网（CHIF-NET）2009 年至 2021 年间 63 家监测中心收集的 461 株侵袭性感染非重复季也蒙念珠菌复合体，采用基质辅助激光解吸电离飞行时间质谱和核糖体内部转录间隔区（ITS）测序技术对所有菌株进行了准确鉴定，并使用商品化 Sensititre YeastOne 显色药敏板分析了该菌对 9 种常见抗真菌药物的体外药物敏感性。

结果 中国多中心侵袭性感染季也蒙念珠菌复合体中，共分离到 3 个菌种，Meyerozyma caribbica、Candida carpophila 以及 Meyerozyma guilliermondii，其中 Meyerozyma guilliermondii 是主要致病菌（96.5%）。461 株菌分离自 63 家医院的 452 名患者，其中男性患者占比（64.6%）高于女性患者（35.4%），62.9%的患者年龄超过 50 岁。菌株主要分离自普通外科（41.2%），ICU（26.5%）以及普通内科患者（12.1%）。血液是主要的标本类型（65.3%），其次是腹水（11.9%）与导管（8.0%）。棘白菌素耐药率为 1.52%（7/461），氟康唑、伏立康唑、伊曲康唑、泊沙康唑 non-WT 分别占 22.6%（104/461）、17.1%、7.4%以及 10.8%。唑类药物全 non-WT 的菌株占比达到 7.4%，5-氟胞嘧啶、氟康唑、伏立康唑的交叉 non-WT 率高达 7.6%。

结论 我国侵袭性感染季也蒙念珠菌复合体以 Meyerozyma guilliermondii 为主，血流感染是最常见的感染类型，除两性霉素 B 外，季也蒙念珠菌对各类抗真菌药物均存在耐药，甚至存在交叉耐药现象，临床上应当引起重视。

关键字：季也蒙念珠菌，流行病学，耐药，CHIF-NET

Tracing The Possible Evolutionary Trends of Morganella Morganii: Insights From Molecular Epidemiology and Phylogenetic Analysis

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Background Morganella morganii, comprising two subspecies, namely morganii and sibonii, is considered as an unusual opportunistic pathogen due to the intrinsic resistance to multiple antimicrobial agents and virulence evolution

Methods This study involved the analysis of ge-

nome sequences from 431 M. morganii isolates (206 obtained from this study and 225 from the NCBI genome datasets). The whole-genome sequencing and bioinformatic analysis were conducted to investigate the molecular epidemiology of these isolates. The minimal inhibitory concentrations (MICs) of antimicrobial agents were determined using the broth microdilution method. The horizontal transferability of the novel blaKPC-2-bearing plasmid was evaluated by conjugation experiments

Results Among the 431 M. morganii isolates, a diverse array of resistance determinants was identified, encompassing mcr-1, tet(X4), tmexCD-toprJ, and various carbapenemase genes. The majority of virulence-related genes (VRGs) were identified in almost all M. morganii strains. Notably, the hlyCABD gene cluster, which encodes the RTX toxin, was present in only 29.0% of the isolates. In the exploration of the location of carbapenemase genes, we discovered a novel blaKPC-2-bearing plasmid with demonstrated conjugative capability formed by the transposon-mediated interplasmid transposition. The average nucleotide identity (ANI) and principal component analysis (PCA) analysis showed M. morganii could be classified five genospecies, designated as M. morganii, M. sibonii, M. chanii, M. variant1, and M. variant2. The latter three genospecies, compared to the former two, exhibit a higher frequency of isolation from both animals and the environment, along with an increased abundance of mobile genetic elements (MGEs). Further phylogenetic analysis disclosed that M. morganii is divided into 10 sequence clusters (SCs). Particular, SC9 harbors a greater abundance of antimicrobial resistance and virulence-related genes (ARGs and VRGs) and is associated to a higher presence of MGEs compared to other SCs isolates

Conclusions The findings collectively indicate that under the influence of MGEs, M. morganii evolves by amplifying the ARGs and VRGs, enhancing its adaptability to selective pressures

关键字：Morganella morganii, evolution, antimicrobial resistance genes, virulence-related genes, blaKPC-2-bearing plasmid

Clincal Features and Microbiological Analysis of Risk Factors for Mortality Among Patients with Carbapenem-Resistant Klebsiella Pneumoniae Bacteremia: A Changing Virulence Landscape

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Objective The escalating global prevalence of carbapenem-resistant Klebsiella pneumoniae bloodstream infection (CRKP-BSI) is concerning due to its association with heightened morbidity and mortality resulting from limited antibiotic options. Virulence plasmids play a pivotal role in augmenting the virulence of current CRKP strains. This study sought to evaluate the impact of virulence plasmid carriage on mortality in CRKP-BSI

Methods PCR amplification was conducted to identify the presence of p-rmpA, p-rmpA2, iroB, peg-344, and iucA genes. In this study, experimental strains carrying two or more of the p-rmpA, p-rmpA2, iroB, peg-344, and iucA genes were categorized as virulence plasmid-positive CRKP (pV-CRKP) strains. Ninety-three CRKP patients participated, with 23 testing positive for virulence plasmids. A matched case-control study was conducted to elucidate the clinical and bacterial attributes of CRKP-induced BSIs with and without virulence plasmids. PCR was employed to screen for common capsule serotypes (KL1, KL2, KL5, KL20, KL54, KL57, KL64) , specific virulence genes (rmpA, rmpA2, iucA, iroB, peg344, iutA, mrkD and terW) and resistance genes (blaNDM-1, blaKPC-2, blaIMP, blaVIM, blaOXA-48, blaSHV-12 and blaTEM-1)in all K. pneumoniae strains. The assessment of virulence potential was carried out utilizing the well-established G. mellonella wax moth in vivo infection model and biofilm formation assay. Multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE) analyses were conducted to elucidate strain classifications. Comparative analyses were conducted for clinical risk factors between these two groups. For quantitative data analyzed via the chi-square test or Fisher's exact test in univariate analysis. Benjamini-Hochberg (BH) was used to adjust the p value, a significance level of $p< 0.05$ was considered statistically significant. Variables with $p < 0.05$ in univariate analysis were subsequently included in a logistic regression model for multivariate analysis aimed at assessing the risk factors associated with CRKP strains carrying virulence plasmids

Results Our research unequivocally revealed a 24.7% prevalence of virulence plasmids among CRKP strains (23 out of 93 cases). Notably, mortality among patients with virulence plasmid-positive CRKP (pV-CRKP) infections reached 61.1%. The ST11-KL64 CRKP subtype emerged as the predominant source of BSIs in Jiangxi Province. Molecular typing through PFGE delineated that pV-CRKP strains primarily manifested two identical genotypes (type H and type J). Furthermore, our investigation unveiled the presence of virulence plasmids in multiple strains characterized by different PFGE genotypes, underscoring the polymorphic distribution of virulent plasmids within ST11-type CRKP strains. Logistic regression analysis identified three independent risk factors associated with such strains: community-acquired infection, admission to the

neurology department, and stroke. Assessment of the 50% lethal dose (LD50) in G. mellonella larval infection assays and the biofilm formation assays revealed that the majority of CRKP strains harboring virulence plasmids demonstrated a more aggressive phenotype compared to other CRKP strains. Nonetheless, instances of CRKP strains carrying virulence plasmids without displaying heightened virulence were also observed

Conclusion The existence of virulence plasmids typically heightens the virulence of strains, with CRKP strains carrying virulence plasmids directly influencing the 7-day survival rate of patients. Additionally, we have observed a limited subset of strains carrying virulence plasmids without displaying heightened virulence. Community-acquired infection, admission to the neurology department, and stroke have been identified as independent risk factors for the presence of pV-CRKP strains. Diligent attention to pV-CRKP strains, particularly with the heightened occurrence of IncFrepB among pV-CRKP compared to CRKP, potentially facilitating the spread of virulence genes in ST11-type CRKP

关键字：Carbapenem-resistant Klebsiella pneumoniae, bloodstream infection, virulence plasmids, risk factors, high mortality, clonal dissemination

Analysis of The Hypovirulent Klebsiella Pneumoniae with The NDM-5 Gene on IncN Plasmids

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Objective Our study aims to analyze the hypovirulent Klebsiella pneumoniae with the NDM-5 gene on IncN plasmids. This strain was isolated from a patient with a liver abscess, and the ST type was ST147. The characterization, antimicrobial drug resistance, and virulence of the strain with the NDM-5 gene on IncN plasmids were analyzed by whole-genome sequencing. Virulence testing was conducted using the Galleria mellonella infection model, serum killing, and biofilm formation assay. Growth measurement analysis, an in vitro competition experiment, and a plasmid stability assay were calculated using fitness costs. A conjugation assay was used to test NDM-5 transfer between bacterial strains. For statistical analysis and image visualization, GraphPad Prism 8.0 was employed. The result revealed that the hypovirulent strain with the NDM-5 gene was located on the IncN plasmid (92.284 kb), which is rare in Klebsiella pneumoniae. Whole-genome sequencing revealed the presence of 25 and 22 resistance and virulence genes, respectively. The strain KP4089 was resistant to carbapenems, β-lactam, ceftazidime-avibactam, and macrolides but remained susceptible to aminoglycosides, mucilage, and tigecycline in antimicrobial susceptibility tests. Furthermore, the strain KP4089 exhibited significantly lower serum killing and biofilm formation rates, demonstrating that the strain with the NDM-5 gene had low virulence. The strain with the NDM-5 gene on the IncN plasmid was genetically stable and had no fitness cost associated with identifying IncN plasmids. Future research should focus on clinical surveillance of hypovirulent multidrug-resistant Klebsiella pneumoniae to identify the potential strain and mechanistic studies to prevent its spread

Method Isolation and antimicrobial susceptibility testing

Plasmid characterization

The fitness cost of the plasmid

Results It is crucial to strengthen the ongoing clinical surveillance of non-highly virulent, multi-resistant Klebsiella pneumoniae

Conclusion Whole-genome sequencing revealed that the NDM-5 gene strain was on the IncN plasmid (92.284 kb), which is uncommon in Klebsiella pneumoniae. The drug resistance genes (NDM-5, OXA-181, CTX-M-15, fosA6, and CatI) were found in the strain KP4089, together with a class I integron. The relative fitness cost of the strain was greater than 1 in the in vitro growth competition experiment, indicating that the IncN plasmid did not impose a fitness cost on the host strain. To prevent the spread of hypovirulent multidrug-resistant KPs, continuing clinical surveillance of such strains must be increased, and future research should focus on determining the potential strain and mechanistic studies

关键字：NDM-5, IncN, fitness, characteristics, Klebsiella pneumoniae

Differences in Plasmid Copy Number Induced The Pathogenicity Heterogeneity of ST11-CR-hvKP under The Homology

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Objective The ST11-CR-hvKP carrying the virulence plasmid was screened by PCR, and the homology of the strains was confirmed by PFGE. The virulence phenotype test was divided into two groups with virulence difference (high-virulence group and low-virulence group). RT-qPCR, plasmid transformation experiment, and whole genome sequencing were used to analyze the copy number differences of virulence plasmids between the two groups under homologous relationship, and then to clarify the reasons for the virulence heterogeneity of ST11-CR-hvKP strains

Methods The ST11-CR-hvKP carrying the virulence plasmid was screened by PCR, and the homology of the strains was confirmed by PFGE. The virulence phenotype test was divided into two groups with virulence difference (high-virulence group and low-virulence group). RT-qPCR, plasmid transformation experiment, and whole genome sequencing were used to analyze the copy number differences of virulence plasmids between the two groups under homologous relationship, and then to clarify the reasons for the virulence heterogeneity of ST11-CR-hvKP strains

Results It was discovered that 6 strains of ST11 KL64-CR-hvKP with virulence plasmid and PFGE homology presented virulence heterogeneity, and RT-qPCR results revealed that the copy number of virulence plasmid genes of the 6 strains differed($P<0.05$). Furthermore, the inclusion of virulence plasmids increased the pathogenicity of the parent strain after transformation into plasmi-free Klebsiella pneumoniae ATCC700603. The altered strains' gene copy numbers differed, appearing adaptive advantages. Whole genome sequencing confirmed that all six strains shared substantial genomic similarity and were plVpK-like virulence plasmids of the IncHI1B/incfib type. However, the virulence plasmid circle plot revealed that the low virulence plasmids lacked the UvrD helicase and transposase gene segments between 36 and 40kb compared to the high virulence plasmids. The UvrD helicase enhances bacterial plasmid replication, which modulates the expression of virulence characteristics, potentially contributing to CR-hvKP's pathogenicity heterogeneity. Simultaneously, the UvrD helicase may be microregulated, compensating for the altered plasmid's adaptation cost

Conclusion The outcomes of this study suggested that the presence of a virulence plasmid was a crucial determinant in the virulence of ST11-CR-hvKP, and that the plasmid's expression differential had a direct effect on the strain's pathogenicity. The deletion of UvrD helicase on the plasmid may reduce the copy number of the virulence plasmid gene, affecting the virulence expression of CR-hvKP, resulting in low virulence or occult transmission of CR-hvKP. Our study provided a valuable direction to explore the reasons for the virulence heterogeneity of ST11-CR-hvKP

关键字：CR-hvKP, ST11, plasmid，the number of plasmid copies，heterogeneity of virulence

生长和毒力的优势促进上海市猩红热 emm1 型化脓链球菌比例的上升

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目的 了解近年来上海地区儿童猩红热的临床流行病学特征和化脓链球菌（Group A Streptococcus, GAS）的分子流行病学特征、超抗原谱、耐药谱，比较优势克隆株的生长繁殖能力，并通过全基因组测序揭示引起猩红热的化脓链球菌优势克隆株变迁的机制，为今后的猩红热防控策略提供建设性意见和科学依据。

方法 采集 2011 年 1 月-2020 年 12 月在复旦大学附属儿科医院传染病门诊的猩红热确诊病例的临床及人口统计学资料，结合同期国家传染病报告信息管理系统上的上海地区猩红热相关数据进行分析；对临床诊断猩红热的病人进行咽拭子标本采集。每周采集 3 次，每次采集 2-4 个病人的咽拭子标本。所有标本送至上海市 CDC 参考实验室进行 GAS 分离和培养。并对所有 GAS 菌株进行 emm 分型、超抗原分析，药敏试验，挑选优势克隆株测定生长曲线，并挑选菌株进行全基因组测序。

结果 2011 年上海地区出现了猩红热的暴发流行，2011-2019 年一直处在高强度流行水平，2020 年流行率有所回落。上海地区猩红热全年均有发病，呈现双峰流行，流行高峰见于 4 至 6 月份以及 11 月至次年 1 月份。对 3064 株猩红热病人的咽拭子标本进行的 emm 分型，发现存在 18 种 emm 型，其中 emm12 型占优（63.8%），emm1 型次之（31.6%）。emm1 型 GAS 比例在 2011 年以后处于波动上升状态。超抗原检测发现 SpeH 和 SpeI 主要见于 emm12 菌株，SpeA 和 SpeJ 主要见于 emm1 菌株。所有菌株对青霉素 G 敏感，对红霉素、克林霉素和四环素基本都耐药（>95%），小部分菌株对左氧氟沙星和氧氟沙星耐药（1.6%）。不同 emm 亚型之间耐药表型无明显差异。生长曲线测定发现 emm1 型 GAS 生长速度快于 emm12 型 GAS。全基因组测序分析显示：2015 年后 emm1 型 GAS 其呈现出独特的基因谱携带毒力基因（ssa、 SpeC、sda 和 spd）以及可移动元件 ICE-HKU488 和 HKU488.vir。

结论 对特定年龄段人群和季节的管控是猩红热防治策略的重点，青霉素类抗生素仍然是治疗猩红热治疗的首选抗菌药物。特定的超抗原等毒力因子携带、以及更快的生长速度可能是 emm1 型 GAS 在近年来比例上升，成为上海地区 GAS 优势克隆株的重要原因，此外，我们推测，emm1 分离株的增加可能与获得类似于 emm12 的可移动元件有关。

关键字：化脓性链球菌，猩红热，emm 型，超抗原，生长曲线，全基因组测序

Establishment of Sitafloxacin Epidemiological Cut-off Values (ECOFFs) Against Escherichia Coli, Klebsiella Pneumoniae, Proteus

Mirabilis, Pseudomonas Aeruginosa, Acinetobacter Baumannii, Staphylococcus Aureus, Enterococcus Faecalis, Enterococcus Faecium, and Streptococcus Pneumoniae

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Objective To establish the epidemiological cutoff values (ECOFFs) of sitafloxacin against Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Acinetobacter baumannii, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium, and Streptococcus pneumoniae

Methods We collected 2264 clinical isolates from five different labs located four cities in China. The minimum inhibitory concentrations (MICs) and inhibition zone diameters of sitafloxacin were determined using the broth microdilution method (BMD) and disk diffusion method following European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. MIC ECOFFs were determined using ECOFFinder software and selected 99% calculated ECOFF as the initially formulated ECOFF value. Zone diameter ECOFFs were determined by the visual estimate method. Whole-genome sequencing (WGS) was carried out on the E. coli strains with overlapped MICs between Wild-type and non-wild-type groups to investigate the distribution of resistance mechanisms

Results Sitafloxacin MIC ranged from 0.002 to 64 mg/L across the nine species, and zone diameter ranged from 6 to 45 mm. MIC ECOFFs were 0.032, 0.064, 0.125, 0.5, 0.064, 0.125, 0.5, 0.25, and 0.125 mg/L for E. coli, K. pneumoniae, P. mirabilis (tentative ECOFF), P. aeruginosa, A. baumannii, S. aureus, E. faecalis, E. faecium, and S. pneumoniae, respectively. WGS results supported the ECOFF of 0.032 mg/L against E.coli strains. Except S. pneumoniae ($|R| = 0.46$, $P < 0.0001$), MICs of the other eight species were highly correlated with zone diameters ($|R| > 0.8$, $P < 0.0001$). Therefore, the zone diameter ECOFFs we formulated were 26, 25, 24, 24, 25, 26, 21, and 22 for E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, A. baumannii, S. aureus, E. faecalis, and E. faecium, respectively

Conclusion We established MIC and zone diameter ECOFFs for sitafloxacin against the above nine species. Where the MIC ECOFF of P. mirabilis was tentative ECOFF. Zone diameters of S. pneumoniae was too poorly correlated with MICs to establish zone diameters ECOFF

关键字：sitafloxacin, ECOFF, MIC, zone diameter, BMD, disk diffusion

Human Infection with Streptococcus Suis in Sichuan, China: Etiological Analysis and Risk Prediction

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Objective Streptococcus suis (S. suis) is a rare zoonotic pathogen, through the analysis of the virulence, drug resistance， and evolution of the pathogen to understand the potential risk of human infection in this area

Methods The basic information of the infected patients was collected, and the strains were identified and tested for drug sensitivity by conventional methods, followed by whole genome sequencing. The sequencing results were compared and analyzed through some public databases, and the results were visualized to understand the virulence, antibiotic resistance， and evolutionary relationship of the strains, to speculate the possible source of the strains and the risk of disseminated infection

Results The patients were all male farmers, one of whom had a history of contact with sick pigs, and all strains were isolated and identified. All the strains belonged to the common ST1 type. The virulence genes of the two strains were similar to those of the hypervirulent reference strains provided by VFDB, including multiple genes related to adhesion, invasive enzymes， and toxins. The drug resistance was not high, and it was not sensitive to a few antibiotics such as tetracycline and erythromycin. The results of phenotypic and genotypic resistance analysis were consistent. Phylogenetic analysis revealed that these strains were closely related to some domestic sequences and were most likely of indigenous origin, although the specific origin is unknown

Conclusion The virulence and drug resistance of S. suis are slowly changing, and the harm to the individual is greater than that to the population. The risk to the population in Asia and Europe is higher than that in other regions, and the surveillance of zoonotic diseases should not be relaxed

关键字：Streptococcus suis, genome, human, infection,zoonosis

中国地区携带 blaKPC-2 肺炎克雷伯菌分子流行病学特征分析及流行优势原因探索

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目的 肺炎克雷伯菌（Klebsiella pneumoniae, KP）是一种常见的条件致病菌，既可造成社区获得性感染，也可引发院内感染。特别是碳青霉烯类耐药肺炎克雷伯菌（Carbapenem-resistant Klebsiella pneumoniae，CRKP）由于治疗困难和高病死率，成为公共卫生安全的重大挑战。blaKPC-2 基因的携带是 CRKP 对碳青霉烯类抗生素产生耐药性的主要原因。本研究旨在通过全基因组测序分析，探究携带 blaKPC-2 的 CRKP 的流行病学特征、演化过程及机制，为防控策略提供科学依据。

方法 本研究通过对我院连续 5 年筛选的产 KPC-2 CRKP 进行全基因组测序，并结合 GenBank 数据库中的中国其他地区数据，建立了包含 1098 株携带 blaKPC-2 的 CRKP 的全基因组数据库。通过多位点序列分型（MLST）、耐药基因、毒力基因、质粒类型等分析，探索 CRKP 在我国的分子流行病学特征及其进化。此外，对代表性 CRKP 菌株进行体内外碳青霉烯类抗生素药效学研究，分析耐药水平差异的原因，并探索高水平耐药 CRKP 的流行机制。最后，测试新型 β-内酰胺酶抑制剂与 β-内酰胺抗生素复合制剂对 CRKP 的体外抗菌活性，为治疗提供新思路。

结果 研究纳入的 1098 株 CRKP 中，ST11 型为主导，占比超过 86%。这些菌株普遍携带高比例的氨基糖苷类和氟喹诺酮类耐药基因，而对利福平和多粘菌素的耐药基因携带率较低。通过系统发育树分析，发现 ST11 型 CRKP 的进化主要集中在荚膜类型 KL47 和 KL64。耐药性分析显示，ST11 型 CRKP 对碳青霉烯类抗生素的耐药性显著高于非 ST11 型，且具有高水平耐药性。此外，通过比较基因组学研究发现，高水平耐药 ST11 型 CRKP 菌株具有特异基因，这些基因涉及碳源代谢、生物膜形成等多个方面。新型 β-内酰胺酶抑制剂与 β-内酰胺抗生素复合制剂对 CRKP 表现出良好的体外抗菌活性。

结论 我国 CRKP 以 ST11 型为主导，其高水平耐药性与 OmpK35 和 OmpK36 的突变有关。ST11 型 CRKP 的优势流行可能与其特定的碳源利用能力和更强的生物膜形成能力有关。新型 β-内酰胺酶抑制剂联合 β-内酰胺类抗菌药物的复合制剂为治疗 CRKP 感染提供了新的可能性，为后续的研究和临床治疗提供了新思路。

关键字：碳青霉烯类耐药肺炎克雷伯菌，blaKPC-2，ST11 型，分子流行病学，流行优势

The Origins of ST11 KL64 Klebsiella Pneumoniae:a Genome- Based Study

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Objective Carbapenem-resistant Klebsiella pneumoniae (CRKP) is a major severe threat for human health, and its spread is largely driven by a few dominant lineages defined by sequence types (ST) and capsular (KL) types. ST11-KL64 is one such dominant lineage that is particularly common in China but also has a worldwide distribution. However, the population structure and origin of ST11-KL64 K. pneumoniae remain to be determined

Methods We retrieved all K. pneumoniae genomes (n =13,625, as of June 2022) from NCBI, comprising 730 ST11-KL64 strains

Results Phylogenomic analysis of core-genome single-nucleotide polymorphisms identified two major clades (I and II) plus an additional singleton of ST11-KL64. We performed dated ancestral reconstruction analysis using BactDating and found that clade I likely emerged in 1989 in Brazil, while clade II emerged around 2008 in eastern China. We then investigated the origin of the two clades and the singleton using a phylogenomic approach combined with analysis of potential recombination regions. We found that ST11-KL64 clade I is likely a hybrid with 91.2% (ca. 4.98 Mb) of the chromosome derived from the ST11-KL15 lineage and 8.8% (483 kb) acquired from ST147-KL64. In contrast, ST11-KL64 clade II was derived from ST11-KL47 with swapping of a 157-kb region (3% of the chromosome) containing the capsule gene cluster with clonal complex 1764 (CC1764)-KL64. The singleton also evolved from ST11-KL47 but with swapping of a 126-kb region with ST11-KL64 clade I

Conclusion ST11-KL64 is a heterogenous lineage comprising two major clades and a singleton with different origins that emerged in different countries at different time points

关键字： carbapenem resistance, KPC, carbapenemase, Klebsiella pneumoniae, Klebsiella

2017 年-2023 年中国南方毛霉菌病人口学特征及危险因素分析

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目的 分析 2007 年至 2023 年中国南方多中心新发毛霉病例人口学、易感因素。

方法 本研究为回顾性研究。收集自 2017 年至 2023 年中国南方地区 5 家医院的新发毛霉感染病例，收集其年龄、性别、职业、合并症、感染部位、治疗方法,并对其人口学特征和危险因素进行分析。

结果 6 年间报道毛霉菌病病例共计 41 例,年龄范围为 32-78 岁，平均年龄 59.44 岁。男性占 68.29%（28/41），女性占 31.71%（13/41）。职业主要为农民（21/41，51.22%）和个体户（15/41，36.59%）。糖尿病（17/41，41.46%）、高血压（14/41，34.15%）是合并率最高的疾病。肺是毛霉菌常见的感染部位,占所有患者的 87.8 % (36/41）。病死率为 14.63% (6/41)。死亡患者均合并肺恶性肿瘤。存活患者平均住院日为 15.61 天，合并糖尿病和高血压的老年患者（＞64 岁）一般情况较差，治疗周期较长。使用两性霉素 b 脂质体治疗得到较好的结果。

结论 随着诊断技术的提高，毛霉病诊断效率越来越高。多数患者通过 mNGS、真菌荧光镜检、真菌培养等联合检测能够快速诊断并得到及时有效的治疗。然而，年龄以及合并糖尿病、高血压仍然是不可忽视的危险因素。本研究纳入的病死患者均为肺部恶性肿瘤引起的，毛霉菌感染可能不是导致死亡的最主要因素。但是毛霉菌病患者的预后受其基础疾病、治疗手段等多种因素的影响。

关键字：中国南方地区，毛霉病，人口学，危险因素

Innovative Fusion Virulence Plasmid Introduces A Unique Conjugative Transfer Mechanism for Virulence Plasmids——Differing From Traditional PK2044 and PLVPK

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Objective Highly virulent Klebsiella pneumoniae, known as hvKp, has emerged as a significant global concern. hvKp exhibits a greater degree of virulence compared to the classical Klebsiella pneumoniae (cKp). The genetic determinants responsible for its hypervirulence are typically harbored on virulent plasmids and mobile genetic elements within chromosomes. These elements serve as distinctive biomarkers to differentiate hvKp from cKp clinical isolates. The prevailing virulence plasmids are predominantly derived from either pK2044 or pLVPK virulence plasmids. However, our research has identified a distinct virulence plasmid, pKP51 (262kbp), which differs from the aforementioned p2044 and pLVPK plasmids

Methods We conducted a series of conjugation experiments on KP51 to scrutinize the conjugative transfer capability of pKP51. The conjugants were selected through Pulse-Field Gel Electrophoresis (PFGE) and S1-PFGE techniques, while the transconjugants underwent whole-genome sequencing to assess their conjugative transfer profiles

Results The virulence plasmid pKP51 is present within a strain of ST485/KL5 hvKP-KP51. This virulence plasmid carries the common highly virulent genes iucABCD, iroBCDN, rmpA/rmpA2. The larval survival experiment demonstrated the high virulence of the strain, with a positive stringing test result. After comparison with the NCBI database using BLAST, it was discovered that the plasmid bears a high resemblance to pINF242-SC-2 in the region from 133733bp to 14364bp (total length 143273bp), and to the pKP8-2 plasmid in the region from 22068bp to 129579bp (total length 107572bp). A significant number of conjugative transfer elements, such as IS3 and IS1, were observed at the junctions of the fragments. Therefore, we speculate that pKP51 is likely formed through the fusion of two plasmids, pINF242-SC-2 and pKP8-2. It is believed that pINF242-SC-2 contributes the Type IV Secretion System (T4SS) and Relaxase, while pKP8-2 provides OriT and T4CP, ultimately resulting in the formation of pKP51 carrying a complete conjugative transfer element. Subsequent conjugation experiments were conducted on the KP51 strain in Klebsiella pneumoniae and Escherichia coli. KP51 demonstrated remarkable ease in acquiring the prevalent pKPC in the current clinical ST11-CRKP strain, with a conjugation efficiency of approximately 10-5. The first conjugant (KP51-pKPC) was obtained successfully, followed by a conjugation experiment between Escherichia coli J53 and KP51-KPC resulting in the formation of the second conjugant (J53-pV) with a conjugation efficiency of around 10-7. Interestingly, it was discovered that J53-pV carried an approximately 350kbp large unstable plasmid. Subsequent S1-PFGE validation during serial passages revealed the presence of three plasmids within this strain: pV (350kbp), pKP51 (262kbp), and pKPC (90kbp). Whole-genome sequencing unveiled that the pV plasmid was formed through the fusion of pKP51 and pKPC. Additionally, conjugation experiments were conducted between KP51 and J53, but no conjugants were selected. Subsequently, conjugation between the conjugant J53-pV and Klebsiella pneumoniae ATCC700603 was carried out, resulting in the formation of the conjugant ATCC700603-1. This conjugant only acquired the pKP51 plasmid without obtaining the pKPC plasmid, with a conjugation efficiency of approximately 10-5. Larval survival experiments were conducted on the conjugants J53-pV and ATCC700603-1, revealing a significant increase in virulence in both conjugants after acquiring the virulence plasmid. Moreover, after multiple passages on regular agar plates, the virulence markers remained stable in both conjugants

Conclusion pKP51 represents an innovative

amalgamated plasmid endowed with comprehensive self-transference components, and its recombination with pKPC facilitates the conjugative transfer of virulence plasmids in both Escherichia coli and Klebsiella pneumoniae. Within our investigation, this plasmid recombination event transpired in KP51-pKPC alongside E. coli J53, indicating that concurrent infection with E. coli and Klebsiella pneumoniae could enhance the dissemination of virulence plasmids. These insights underscored the criticality of rigorous monitoring to pre-empt the escalation and distribution of this formidable fusion-plasmid

关键字：Virulence plasmid、Klebsiella pneumoniae、 conjugation transfer

江西地区某综合医院 ST11 型耐碳青霉烯类高毒力肺炎克雷伯菌的分子流行病学研究

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目的 探究ST11型CR-hvKP菌株的临床特征、耐药现状、毒力特征及分子流行病学特征。

方法 随机收集某三甲教学医院 2018 年 1 月至 2021 年 12 月期间临床标本中分离的碳青霉烯类耐药的肺炎克雷伯菌 233 株。采用 PCR 法检测毒力、耐药基因，定义含 rmpA2, terW, silS, iutA 四个毒力基因的肺炎克雷伯菌为含毒力质粒的肺炎克雷伯菌。从中筛选出 blaKPC 基因阳性的 ST11 型 CR-hvKP 124 株。分析其标本来源、科室分布、年龄构成情况等基本临床信息，药敏结果，耐药、毒力基因携带情况。按年份分层抽选出部分 ST11 型 CR-hvKP 进行血清抗性、生物膜形成能力及大蜡螟幼虫感染试验以分析其毒力表型。采用脉冲场凝胶电泳（PFGE）进行同源性分析。

结果 233 株CRKP 菌株中，CR-hvKP 菌株 135 株，其中 ST11 型占比 91.86%，菌株主要来自神经外科。ST11 型 CR-hvKP 菌株对头孢类、氟喹诺酮类和碳青霉烯类、部分复方制剂类抗菌药物的耐药率达 100%。此外，ST11 型 CR-hvKP 菌株携带大量毒力相关基因，毒力相关试验提示其内部存在毒力差异，但多为高毒力株。PFGE 分析显示分 3 个型别，以 A 型为主。

结论 ST11 型 CR-hvKP 在本院克隆性流行播散，其对临床常用抗生素表现出多重耐药性，加上其高毒力特性，给临床抗 KP 治疗带来巨大挑战，需加强院内感染的防控。

关键字：ST11 型 CR-hvKP，CRKP，HvKP，耐碳青霉烯酶

Global Antimicrobial Resistance and Antibiotic Use in COVID-19 Patients in Health Facilities: A Systematic Review and Meta-analysis of Aggregated Participant Data

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Objective The COVID-19 pandemic has posed a significant threat to the global healthcare system, presenting a major challenge to antimicrobial stewardship worldwide

Methods We conducted a systematic review to determine the prevalence of antimicrobial resistance (AMR) and antibiotic usage among COVID-19 patients receiving treatment in healthcare facilities. Our search encompassed the PubMed, Web of Science, Embase, and Scopus databases, spanning studies published from December 2019 to May 2023. We utilized random-effects meta-analysis to assess the prevalence of multidrug-resistant organisms (MDROs) and antibiotic use in COVID-19 patients, aligning with both the WHO's priority list of MDROs and the AWaRe list of antibiotic products. Estimates were stratified by region, country, and country income. Meta-regression models were established to identify predictors of MDRO prevalence and antibiotic use in COVID-19 patients. The study protocol was registered with PROSPERO (CRD 42023449396)

Results Among the 11,050 studies screened, 173 were included in the review, encompassing a total of 892,312 COVID-19 patients. MDROs were observed in 42.9% (95% CI 31.1%-54.5%, I2=99.90%) of COVID-19 patients: 41.0% (95% CI 35.5%-46.6%) for carbapenem-resistant organisms (CRO), 19.9% (95% CI 13.4%-27.2%) for methicillin-resistant Staphylococcus aureus (MRSA), 24.9% (95% CI 16.7%-34.1%) for extended-spectrum beta-lactamase-producing organisms (ESBL), and 22.9% (95% CI 13.0%-34.5%) for vancomycin-resistant Enterococcus species (VRE), respectively. Overall, 76.2% (95% CI 69.5%-82.9%, I2=99.99%) of COVID-19 patients were treated with antibiotics: 29.6% (95% CI 26.0%-33.4%) with "Watch" antibiotics, 22.4% (95% CI 18.0%-26.7%) with "Reserve" antibiotics, and 16.5% (95% CI 13.3%-19.7%) with "Access" antibiotics. The MDRO prevalence and antibiotic use were significantly higher in low- and middle-income countries than in high-income countries, with the lowest proportion of antibiotic use (60.1% (95% CI 52.1%-68.0%)) and MDRO prevalence (29.1% (95% CI 21.8%-36.4%)) in North America, the highest MDRO prevalence in the Middle East and Africa (63.9% (95% CI 46.6%-81.2%)), and the highest proportion of antibiotic use in South Asia (92.7% (95% CI 90.4%-95.0%))

Conclusion This systematic review offers a comprehensive and current assessment of MDRO prevalence and antibiotic use among COVID-19 patients in healthcare facilities. It underscores the formidable challenge facing global efforts to prevent and control AMR amidst the backdrop of the COVID-19 pandemic. These findings serve as a crucial warning to policymakers, highlighting the urgent need to enhance antimicrobial stewardship strategies to mitigate the risks associated with future pandemics

关键字：global health, antimicrobial resistance, antibiotic use, multidrug-resistant organisms

携带 pLVKP-like 毒力质粒的 ST11 高毒力耐碳青霉烯类肺炎克雷伯菌呈现高传播力特征

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目的 在中国，ST11 为主流的碳青霉烯类耐药的肺炎克雷伯菌（CRKP）克隆体。ST11 hv-CRKP 的出现源于 ST11 CRKP 分离株从 K1 亚型高毒力克雷伯菌获得了 pLVKP-like 的毒力质粒。然而，自 2017 年中国首次记录到 ST11 高毒力耐碳青霉烯类肺炎克雷伯菌（hv-CRKP）致死的爆发以来，这些菌株在中国大陆医院中的检出率显著增加。目前主流的 ST11 hv-CRKP 的传播能力及其在临床环境中的影响仍有待阐明。在这里，我们拟通过全基因组测序结合临床数据的方式评估 ST11 hv-CRKP 与经典的 ST11 CRKP（ST11 cCRKP）相比的传播能力和临床预后。

方法 我们对收集自全国六家医院的 377 株 ST11 CRKP 进行全基因组测序，通过动态传播簇的鉴定与临床资料以及病原体基因型数据进行逻辑回归分析，识别与传播相关的高危因素。通过生存分析和临床结局期望性排名分析评估预后。

结果 我们收集自全国六家医院的 377 株 ST11 CRKP 中，有 231 个携带 pLVKP-like 毒力质粒，其中 229 个属于 ST11:KL64 亚系。基于基因组的传播分析鉴定了 30 个传播簇。绝大多数传播簇都包含来自同一个医院的分离株（23/30）。而其中最大的传播簇包含了 140 个携带 pLVKP-like 毒力质粒的 hv-CRKP 分离株，呈现了跨医院传播的特征。逻辑回归显示携带 pLVKP-like 毒力质粒的 ST11 hv-CRKP 在住院病人中更容易形成克隆传播（OR 4.86 [95% CI, 2.81–8.41], p=1.64×10-8 ）。该现象主要由于 ST11:KL64 hv-CRKP 传播能力的进一步增强所导致（OR=5.59 [95% CI, 2.81–11.12, p=9.23×10-7）。而在临床结局方面，携带 pLVKP-like 毒力质粒的 hv-CRKP 并未比 cCRKP 的临床预后差，并且在 30 天生存分析中并未观察到显著差异（20.53% vs. 18.17%, p=0.52, log-rank test）。

结论 我们的结果显示携带 pLVKP-like 的 ST11:KL64 hv-CRKP 不同于先前报道的引起病人死亡的携带 pLVKP-like 的 ST11:KL47 hv-CRKP 克隆爆发，其在感染患者中，并未引起较差的预后，但其传播能力增强了。

关键字：hv-CRKP，pLVKP-like，transmission，outcome

中国肺癌合并感染患者的临床特征变化：一项 10 年回顾性研究

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目的 肺癌在世界范围内仍然有很高的发病率和死亡率，而同时合并感染会增加诊治难度和死亡风险。描述肺癌合并感染的临床特征变化是必要的。本文旨在为相关疾病风险预测与合理诊疗提供科学的参考依据。

方法 我们分析了 2014 年至 2023 年，广西壮族自治区肿瘤医院共 699 名肺癌合并感染患者的临床结果。

结果 699 例肺癌合并感染患者被纳入研究，特点如下：（1）IIIA 期以上肺癌及同时合并感染患者的数量及比例均逐年上升。（2）最常见的病原体分别是肺炎克雷伯杆菌、念珠菌属、新冠病毒、结核分枝杆菌，最常感染的部位是肺。（3）年龄、肿瘤特征（病理、分期、治疗方案）、感染特征（病原体数量及种类、分布器官、严重程度）的占比均随时间明显变化。（4）不同肿瘤分期、感染来源、感染分布器官、感染严重程度的病原体占比及不同抗肿瘤治疗方案导致的感染严重程度均有统计学差异（P<0.05）。(5)患者在诊断肺癌时及诊断感染时的免疫状态有统计学差异（P<0.05）；不同感染严重程度、不同抗肿瘤治疗方案分别通过影响辅助性 T 淋巴细胞、抑制性 T 淋巴细胞调控免疫。（6）混合感染（相对于单一感染）、医院获得性感染（相对于社区获得性感染）、重症感染（相对于非重症感染）、化疗（相对于靶向治疗）、化疗（相对于化疗+免疫治疗）分别增加了 54.9%、27.7%、138.0%、64.6%、51.1%的死亡风险。（7）多因素分析中，其他病理类型肿瘤、骨转移、脑转移、重症感染是死亡的危险因素，而靶向治疗、化疗+免疫治疗相对于其他治疗方案的死亡率更低；ECOG、神经内分泌癌、医院获得性感染是重症感染的危险因素，而病毒感染相对于其他病原体感染导致的重症率更低。

结论 本研究全面描述了中国肺癌合并感染患

者的临床特征变化，为相关诊治提供了依据。临床医生应更多关注此类患者。

关键字：肺癌，感染，免疫，重症，预后

Antimicrobial Susceptibility Profiles and Relative Prevalence of Elizabethkingia Isolates in Nanchang, China

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Objective The emergence of Elizabethkingia infections as life-threatening nosocomial infections worldwide, characterized by increasing morbidity, multidrug resistance, and poor outcomes, underscores the need for further investigation into their epidemiology and clinical characteristics in China. In this study, we aimed to explore the molecular characterization and drug susceptibility profile of clinical isolates of Elizabethkingia obtained from a hospital in Nanchang, China

Methods 103 Elizabethkingia isolates identified by conventional methods were collected by a university-affiliated hospital between 2022 and 2023. Species identification was conducted through 16S rRNA gene sequencing, used as a standard identification method. The feasibility of Vitek MS was also evaluated. Furthermore, antimicrobial susceptibility testing, identification of resistance genes and pulsed-field gel electrophoresis (PFGE) were performed

Results For the 103 isolates, 92 Elizabethkingia anopheles, 8 Elizabethkingia meningoseptica, 2 Elizabethkingia bruuniana, and 1 Elizabethkingia ursingii were identified using 16S RNA sequencing. The identification rate of the Vitek MS system was found to be 80.6%, demonstrating improved accuracy compared to other methods. Specifically, Vitek MS successfully identified 87% of E. anophelis isolates. The majority (93.8%) of the isolates were from the respiratory tract, and 4 (9.9%) were from blood. Over 90% of Elizabethkingia isolates were susceptible to minocycline but resistant to many drugs examined including ceftazidime, cefepime, aztreonam, imipenem, meropenem, and amikacin. The pulsed field gel electrophoresis (PFGE) patterns demonstrated that most isolates were quite genetic diversity. The patients had average age of 61 years old (excluded one child patient of 13-day-old) and 74.8% of patients were male. Among patients diagnosed with Elizabethkingia, 85.4% were hospitalized in the intensive care unit (ICU). The Presence of COVID-19, respiratory illness, mechanical ventilation , and central venous cannulation were significantly different ($p<0.05$) between the survival and death groups

Conclusion The Vitek MS system demonstrated superior capability in identifying Elizabethkingia isolates. PFGE results exhibited high genetic diversity. Urgent research is required to ascertain the most effective antimicrobial agent for treating infections caused by various strains of Elizabethkingia isolates

关键字：Elizabethkingia isolates, antimicrobial susceptibility, 16S rRNA gene sequencing, risk factor

新冠常态化防控背景下医院多重耐药菌检出率变迁：基于中断时间序列分析

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目的 2023 年 1 月 8 日，我国对新冠疫情防控政策做出重大调整，将新冠病毒感染由“乙类甲管”调整为“乙类乙管”。新冠病毒所致疾病将逐步演化为一种常见的传染病长期存在，可能导致具有较严重基础疾病人群、免疫力低下人群和老年人群的等高风险人群入院率增加。该类人群同样作为多重耐药（MDRO）感染的高风险人群，是否会对医院 MDRO 的防控造成影响？本研究旨在探讨新冠病毒感染“乙类乙管”前后 MDRO 检出率变化情况，并分析其影响因素，以期为我国公共卫生突发事件重大防控政策调整后医院在重大公共卫生防控政策调整后 MDRO 的管理提供参考。

方法 采用回顾性中断时间序列设计，收集了广东省某三甲医院 2020 年 6 月至 2023 年 12 月行病原菌检测且细菌培养阳性的住院患者的临床特征及病原学检测结果。对同一患者一周内同一部位检出的重复细菌予以剔除。分析目标菌包括耐碳青霉烯类肺炎克雷伯菌（CRKP）、耐碳青霉烯类鲍曼不动杆菌（CRAB）、耐碳青霉烯类铜绿假单胞菌（CRPA）、耐甲氧西林金黄色葡萄球菌（MRSA）、产 ESBLs 大肠埃希菌及产 ESBLs 肺炎克雷伯菌。以 2023 年 1 月 8 日为“乙类乙管”分界，以 2 周为 1 个时间间隔，分别统计各时间间隔内 MDRO 检出率，采用基于分段泊松回归及分段线性回归模型的中断时间序列分析探讨上述 MDRO 在“乙类乙管”前后的检出率趋势。

结果 “乙类乙管”后，女性、≥65 岁患者的比例升高；有慢性呼吸系统疾病、高血压、心力衰竭、糖尿病及慢性肾功能衰竭的患者比例升高。呼吸道（39.4% vs. 35.3%）、尿路（43.5% vs. 38.5%）感染的比例上升，皮肤、软组织和骨关节组织（6.8% vs.

10.9%）、血流（3.9% vs. 7.2%）及其他部位（2.0% vs. 3.4%）感染的比例下降。“乙类乙管”后，CRAB 的检出率有瞬时的增加（β=2.729，P＜0.001），之后呈下降趋势（β=-0.030，P＜0.001）。其他 MDRO 的检出率趋势在“乙类乙管”前后无明显统计学差异。在“乙类乙管”前后检出 CRAB 的患者（n=135）中，“乙类乙管”后入住 ICU、呼吸道感染者比例有瞬时增加，后呈下降趋势，与 CRAB 检出率变化趋势一致。

结论 “乙类乙管”政策调整对除 CRAB 外的 MDRO 的检出率趋势无显著影响，CRAB 检出率在政策调整后的瞬时增加可能与老年与机体免疫力低下患者、呼吸道感染及入住 ICU 的患者比例升高有关。医疗机构有必要根据卫生政策及时做出反应，采取有效院感防控政策遏制 MDRO 的传播与感染。

关键字：新冠病毒感染，多重耐药菌，“乙类乙管”，中断时间序列

Global Epidemiology and Genomic Framework of Mcr-positive Klebsiella Pnenmoniae From 2000 To 2023

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Objective The international transmission of the colistin resistance gene mcr in Enterobacteriaceae poses significant public health burdens. However, research on the population structure and genomic epidemiology of mcr-positive Klebsiella pnenmoniae worldwide are limited

Methods A total of 463 complete sequences of mcr-positive K. pnenmoniae from different countries across the globe between 2000 and 2023. The global transmission pattern and evolutionary dynamics of mcr variants in K. pnenmoniae have been inferred. We applied the pangenome clustering based on genomes and evolution analysis to demonstrate the transmission events

Results 463 K. pnenmoniae isolates carrying six different mcr variants were detected in 150 countries that mainly from China (n=158), Thailand (n=61) and United Kingdom (n=44). The dominant sequence types (ST) of K. pnenmoniae were ST11, ST15 and ST147, which linked to the clone group CG258, CG15 and CG147 respectively. Correlation analysis indicated that different mcr variants harbored in K. pnenmoniae were positively correlated with specific antibiotic resistance genes, plasmid Inc types, insertion sequences and virulence genes. The phylogenetic analysis grouped K. pnenmoniae into six distinct clusters, with 83.10 % of them carrying mcr-1 or/and mcr-8 or mcr-9 genes. The origin of mcr-9 K. pnenmoniae positive dated back to in United Kingdom during 1947 to 1962 and mcr-1 K. pnenmoniae were predicted to derive from Italy from 1958 to 1975, whereas mcr-8 positive K. pnenmoniae isolates may initially occured in Thailand between 1999 and 2004. It was noted that these isolates had broad distribution and increased expansion

Conclusion We recognized the distribution of dominant mcr variants in K. pnenmoniae among different regions, which laid the essential foundation for responding to risk linked with the evolution of mcr-positive K. pnenmoniae. Continuous surveillance is imperative for effectively controlling the global dissemination of mcr-positive K. pnenmoniae

关键字：Klebsiella pnenmoniae, colistin resistance, mcr, genomic epidemiology

纹带棒状杆菌感染的临床特征、分子流行病学及耐药性的初步研究

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目的 近年来，纹带棒状杆菌感染逐渐增多，尤其在新型冠状病毒流行期间，该菌伴随新型冠状病毒感染的数量也不断增加，给医院感染控制带来了极大的压力。为此，本研究分析我院纹带棒状杆菌感染的临床特征、分子流行病学情况并初步探讨纹带棒状杆菌耐药机制，为纹带棒状杆菌感染的诊断、治疗和院感控制提供实验室依据。

方法 1、本院 2014.3 至 2022.6 间被鉴定为纹带棒状杆菌且临床确诊的 52 例感染患者纳入研究，回顾性分析了患者临床资料，回归分析感染和死亡的危险因素。

2、制作系统发育树，MLST 分型，了解菌株类型和分子流行病学特征。

3、采用微量肉汤稀释法对 12 种抗生素进行药敏实验，并对 PBP2、PBP4 和转座子 Tn1545 整合酶 intTn 基因进行筛查，初步分析纹带棒状杆菌对 β-内酰胺类耐药的可能机制。

结果 1、52 例纹带棒状杆菌感染患者， 50%来源 ICU 病房，主要是呼吸道感染，其余为泌尿道、血流、颅内、软组织、腹腔感染。患有高血压、脑血管疾病、胆道疾病、胃肠道疾病、慢性肾脏疾病及类固醇激素的使用、机械性通气、插管、手术史等因素是纹带棒状杆菌感染高危因素，感染的独立危险因素是高血压、脑血管疾病、手术史。纹带棒状杆菌感染死亡率为 15.38%，死亡的高危因素有休克、血液系统疾病、低蛋白血症和贫血，独立危险因素是休克和低蛋白血症。

2、纹带棒状杆菌序列主要为 CladeI 和 CladeII。

MLST 以 ST9 为主，还有 ST3、ST8、ST2 和 ST15，发现新型别 ST38-45。

3、万古霉素和利奈唑胺敏感率为 100%、其他抗菌药物耐药率超过 50%。52 株纹带棒状杆菌均检测到 PBP2 和 PBP4，其中 PBP2 突变率为 42.32%，PBP4 突变率为 82.69%；均检测到 intTn 基因。

结论 1.高血压、脑血管疾病、胆道疾病、胃肠道疾病、慢性肾脏疾病、使用激素、机械性通气、插管、手术史是纹带棒状杆菌感染的高危因素，高血压、脑血管疾病、手术史是该菌感染的独立危险因素；纹带棒状杆菌感染死亡率较高，导致死亡的高危因素有休克、血液系统疾病、低蛋白血症、贫血，其中休克和低蛋白血症是死亡的独立危险因素。

2. 纹带棒状杆菌序列主要为 CladeI 和 CladeII，MLST 分型结果以 ST9 为主，发现有 ST38-45 新型别。

3. 纹带棒状杆菌对常用抗生素耐药率较高，但万古霉素和利奈唑胺没出现耐药，可作为该菌重症感染首选。PBP2 和 PBP4 不同程度的突变，与 β-内酰胺类抗生素耐药可能有关，携带 Tn1545 转座子，与纹带棒状杆菌耐药基因传播可能有关。

关键字：纹带棒状杆菌，分子流行特征，耐药机制，青霉素结合蛋白

109 例侵袭性沙门菌感染儿童临床特点及耐药性分析

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目的 了解侵袭性沙门菌感染儿童临床特征及耐药性，为儿童沙门菌侵袭性感染诊断、治疗及降低感染率、死亡率提供帮助。

方法 选择于 2015 年 1 月至 2022 年 12 月郑州大学附属儿童医院 109 例沙门菌侵袭性感染患儿及 125 株沙门菌株为研究对象，查阅患儿病历信息并收集、分离保存感染患儿临床分离的沙门菌株。统计分析侵袭性沙门菌感染患儿一般情况、临床特点、实验室检查等信息；对沙门菌进行药物敏感性试验，统计分析其对临床常用抗菌药物耐药性。

结果 109 例侵袭性沙门菌感染儿童主要为婴幼儿为主（83 例，76.1%），男女患儿性别比为 1.5:1，发病季节主要集中在 6-9 月份（56.9%，62/109），主要引起循环系统、骨关节系统、中枢神经系统等部位感染，常以消化道感染入侵为主（84.4%，92/109）；感染儿童临床表现主要以发热、腹泻、呕吐等为主，23.6%患儿患有白血病、先天性免疫缺陷病等基础疾病，31.4%患儿病程过程中合并有其他并发症；多数感染患儿白细胞、CRP、PCT 等感染指标升高，91.5%患儿粪便检验异常；本研究中 6 例患儿死亡，1 岁以下、严重并发症、白血病等为患儿死亡主要危险因素。125 株沙门菌分离部位主要为血液（74.4%，93/125）、骨髓关节液（15.2%，19/125）、脑脊液（8.8%，11/125），血清型以肠炎沙门菌（39.2%，49/125）、鼠伤寒沙门菌（33.6%，42/125）最多见，检出 1 例伤寒沙门菌。125 株沙门菌耐药性有逐年升高趋势，对氨苄西林、哌拉西林、四环素耐药率较高，分别达 76.2%、72%、51.9%；对三代头孢菌素头孢他啶、头孢噻肟耐药率分别为 16.1%、24.2%，对粘菌素耐药率达到 11.2%，检出碳青霉烯类耐药沙门菌 2 株，肠炎沙门菌对抗菌药物的耐药率高于鼠伤寒沙门菌。

结论 109 例感染儿童季节分布以夏秋季高发，多为婴幼儿，主要经消化道感染入侵，症状主要表现为消化道症状及败血症；分离菌株血清型分布以肠炎沙门菌和鼠伤寒沙门菌为主，对三代头孢菌素等耐药率逐渐升高，抗菌药物治疗要结合药敏结果合理选用。

关键字：儿童，侵袭性，沙门菌，临床特点，耐药

Clinical and Microbiological Characteristics of Type 2 Diabetes Mellitus Accompanied with Sepsis

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Objective The International Diabetes Federation (IDF) reported the worldwide diabetes prevalence was approximately

536.6 million people in 2021, and type 2 diabetes mellitus (T2DM) accounts for 90% of all diabetes globally. This study was conducted to investigate the clinical and microbiological characteristics of T2DM complicated with sepsis and to provide a reasonable basis for early diagnosis and treatment.

Methods The clinical material of patients with T2DM complicated with sepsis enrolled from January 2019 to February 2022 in the Endocrinology Department of Sichuan Provincial People's Hospital were retrospectively analyzed

Results A total of 36 patients were included. T2DM patients with sepsis had bad blood glucose control, long hospital stays, poor nutritional status, severe infection, occult primary infection sites, and high detection rates of ESBL producing Escherichia coli and MRSA

Conclusion Multiple complex clinical factors made it difficult for T2DM patients with sepsis to be

cured or improved and raised great challenges for antibiotic therapy

关键字：Type 2 diabetes mellitus, sepsis, infection, drug resistance

医院内 MRSA 克隆传播和克隆变迁机制研究

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目的 甲氧西林耐药金黄色葡萄球菌（Methicillin-resistant Staphylococcus aureus，MRSA）是一种重要的人类病原体，在医院和社区引起从轻度到危及生命的广泛感染 1。MRSA 定植是公认的侵袭性、威胁生命感染的危险因素。医院环境中 MRSA 的定植可能导致患者的交叉感染。本研究旨在确定从重症监护病房(Intensive Care Unit，ICU) 病房和患者的常规筛查中分离的 MRSA 的分子流行病学，并重点关注涉及患者和 ICU 环境的传播事件 (transmission events，TEs)；此外，评估本研究中收集的 MRSA 流行克隆的特征。

方法 2019 年 9 月至 2021 年 7 月，定期从 ICU 病房床单位、水池等高接触物体表面以及患者身上采集样本，培养、鉴定获得 MRSA 菌株。通过抗菌药物敏感性试验（AST）、全基因组测序（whole genome sequencing，WGS）、cg MLST、构建系统发育树等方法分析患者和环境中分离的 MRSA 菌株之间的亲缘关系，研究 MRSA 的传播情况及主流克隆的基因组特征等。

结果 本研究在干预前阶段（I 期）和干预中阶段（II 期）共收集 169 株 MRSA 菌株，其中 143 株为定植菌株，26 株为患者的感染菌株。ST 型主要为 ST5（73.4%，124 / 169）、ST764（9.5%，16 / 169）、ST59（7.7%，13 / 169）等，其中 ST5 为主要克隆。cg MLST 结果显示存在潜在的 MRSA 克隆传播，涉及 ICU 环境内、患者间、环境与患者间，同时明确了 MRSA 在 ICU 中的时间上和空间上的传播模式。基于系统发育树结果，ST5 MRSA 菌株表现出成簇的微进化，处于 II 期分离的 ST5-B 和 ST5-C MRSA 菌株均携带消毒剂抗性基因 qacA，且表现为更高的多重耐药性，高度适应了大量使用抗生素和消毒剂的医院环境。

结论 WGS 确定了 ICU 环境内和环境与患者甚至医护人员之间可能存在的 MRSA 传播事件。ST5 作为 ICU 院内 MRSA 感染的优势克隆株，存在耐药和毒力基因差异的亚簇，尤其是消毒剂抗性基因。综上所述，积极监测 MRSA 定植情况，结合去定植和及时隔离治疗，有助于预防 MRSA 感染和传播。

关键字：MRSA，定植，克隆传播，消毒剂抗性

ST11-K64 Klebisella Pneumoniae, The Predominant Clone of Carbapenem-resistant Klebsiella Pneumoniae Co-exhibiting High Virulence in China.

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Objective We read with great interest the recent study conducted by the Northwestern University and Food and Drug Administration, delving into the intricate landscape of convergent Klebsiella pneumoniae strains in the United States. Their meticulous analysis of 2608 isolates, focusing on the convergence of antibiotic resistance and hypervirulence, revealed noteworthy insights into the complex interplay of these traits. In tandem with these findings, we wish to contribute unique perspectives drawn from our research in China. We aim to shed light on the distinct epidemiological patterns observed in China and offer critical reflections on certain limitations identified in the U.S. study. While the U.S. study significantly advances our understanding of convergent K. pneumoniae, a nuanced consideration of regional variations and potential biases is crucial for a comprehensive interpretation of global trends

Methods We conducted a two-phase retrospective, molecular epidemiological study on bloodstream infections caused by K.pneumoniae during 2018 and 2020

Results A total of 793 K. pneumoniae isolates (239 in 2018, 554 in 2020) analyzed in our study which were collected from 35 hospitals all over China exhibited a dominance of two multilocus sequence types (STs), ST11 (25%) and ST23 (12%). These STs were primarily capsule loci K64/K47 or K1 respectively, which varies differently from that discovered in the USA and shows a significant geographic difference. According to our data, 451 (57%) isolates harbored at least one hypervirulence gene (iucA, iroB, rmpA, and rmpA2), including 412 (52%) carried iucA, 378(48%) carried rmpA, 353 (45%) carried rmpA2 and 303 (38%) carried iroB. There were 218 strains resistant to carbapenem, and ST11 (89%, 189/218) was the predominant CRKP ST types, which were mainly capsule loci K64 and K47 (136 and 44 respectively). Among carbapenem resistant Klebsiella pneumoniae (CRKP), 58% (126/218) possessed at least one hypervirulence gene (iucA, iroB, rmpA, and rmpA2), including 123 (56%) contained rmpA2, 86 (39%) contained iroB, 76 (35%) contained rmpA and 40 (18%) contained iucA. We also noticed that 123 (56%) CRKPs simultaneously contained iucA/iroB and rmpA/rmpA2. ST11-K64 K. pneumoniae took up 90% (36/40) of the Hv-CRKP strains

that simultaneously possessed carbapenemase genes and at least one of the genes suggested to be the most predictive of hypervirulence[2] in 2018, and it still remained dominant in 2020 (77%, 66/86). Among strains defined as hypervirulent K. pneumoniae according to the previous published criteria[3], 96% (431/451) harbored rmpA and/or rmpA2, which increase capsule production. Among Hv-CRKP, 98% (124/126) strains harbored rmpA and/or rmpA2. All ST11-K64 Hv-CRKPs harbored rmpA and/or rmpA2 either in 2018 or in 2020. There was a significant relationship between harboring rmpA and/or rmpA2 and exhibiting hypervirulent according to the result we found in mouse infection models ($P < 0.05$, Fisher's Exact Test). More importantly, 85% (11/13) HvKP strains which carried rmpA/rmpA2 genes showed real hypervirulence phenotype in mouse infection models. Meanwhile, ST11-K64 Hv-CRKP strains expressing rmpA/rmpA2 showed high virulence comparable to typical hypervirulent strain K2044. Another important finding is that the 30-day survival rate for patients infected with ST11-K64 K. pneumoniae was significantly lower than that for other strains in 2020

Conclusion In conclusion, our study revealed the epidemiology of K. pneumoniae, especially Hv-CRKP in China. ST11-K64 took the most part in Hv-CRKP in China according to our data. Additionally, ST11-K64 strains also showed high virulence comparable with reference strain K.pneumoniae K2044 according to mouse infection models. This situation should be taken into serious consideration and need further investigation nationally and globally

关键字：ST11-K64，Klebisella pneumoniae，carbapenem-resistant，hypervirulence

细菌真菌感染的病原诊断技术

快速现场评价技术联合二代测序在呼吸道感染性疾病中的应用研究

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目的 探讨与研究快速现场评价（rapid on-site evaluation，ROSE）技术联合 NGS 在呼吸道感染性疾病中的应用价值。

方法 2021 年 10 月至 2022 年 5 月在我院接受治疗的 217 例复杂或疑难的肺部感染患者，将其标本送二代测序（NGS），并随机分为两组。观察组采用支气管镜进行肺泡灌洗获取标本，然后采用ROSE技术对标本进行快速评估，若 ROSE 结果阳性，则将该标本送 NGS，若 ROSE 结果阴性，则重新留取标本，直至 ROSE 结果阳性再送 NGS；在对照组中，仅用支气管镜进行肺泡灌洗获取标本并将其送 NGS。ROSE 结果阳性的标准：1.显微镜下看到细菌或菌丝；2.看到大量炎症细胞；3.看到上皮细胞反应性改变；3 个满足其中之一，均为阳性结果！比较两组间 NGS 检出有效致病微生物的阳性率、支气管镜引起的并发症（包括严重气道出血、胸腔积气、纵隔气肿等）、支气管镜操作时间、标本送检周期、支气管镜操作次数等的差异。

结果 观察组标本送检周期小于对照组，且肺泡灌洗液 NGS 检出致病微生物的阳性率大于对照组，但观察组支气管镜操作次数大于对照组，差异有统计学意义（$P<0.05$）。支气管镜操作时间及其并发症的发生率与对照组比较，差异无统计学意义（$P>0.05$）。

结论 在支气管镜下获得肺泡灌洗液后，使用 ROSE 技术评估标本并将其送 NGS，可以提高 NGS 的阳性率。同时，送检周期短，不增加支气管镜操作的时间和并发症。迅速为临床合理应用抗生素、精准抗感染治疗提供了强有力的依据，操作简单快捷、安全可靠，临床价值巨大，值得推广。

关键字：快速现场评价技术，肺泡灌洗液，二代测序，支气管镜，呼吸道感染

Development of A Duplex Real-time Multienzyme Isothermal Rapid Amplification Assay for Detection of The K1 and K2 Hypervirulent Klebsiella Pneumoniae in Spiked Blood Samples

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Objective Our study aimed to devise a rapid and precise detection approach for capsular serotypes K1 and K2 of hvKP in spiked blood samples, utilizing a duplex real-time multienzyme isothermal rapid amplification (real-time MIRA) assay

Methods The molecular diagnostics target for this study was the gene encoding the hvKP K1 and K2 genes. A duplex real-time MIRA assay was meticulously designed and optimized for the precise detection of hvKP in spiked blood samples. To assess its efficacy, the performance of the assay was systematically compared to real-time PCR, evaluating parameters such as analytical limit of detection, specificity, and clinical applicability

Results The real-time MIRA assay exhibited no cross-reactivity with other common pathogenic bacteria and had a limit of detection equivalent to real-time PCR (1×103 CFU per reaction, respectively) for detecting capsular serotypes K1 and K2 of hvKP. Analysis of clinical specimens (the spiked blood samples) demonstrated that the sensitivity and specificity of the duplex real-time MIRA assay were both 100%, compared with duplex real-time PCR

Conclusion The duplex real-time MIRA assay developed in our study exhibits numerous advantages over the currently available duplex real-time PCR diagnostic method, including a quicker time-to-result for a single sample and requiring minimal infrastructure and technical support

关键字：hypervirulent Klebsiella pneumoniae, duplex real-time MIRA, duplex real-time PCR, K1 and K2 genes, spiked blood samples

PCT, IL-6, and IL-10 Facilitate Early Diagnosis and Pathogens Classification of Bloodstream Infection

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Objective Inflammatory markers, including C-reactive protein (CRP), procalcitonin (PCT) and interleukin (IL), white blood cells count (WBC), neutrophil percentage (NE%), platelets count (PLT) and erythrocyte sedimentation rate (ESR) have been widely used in the diagnosis of bloodstream infection (BSI). However, the roles of those markers in identifying BSI from local bacterial infection (LBI) and distinguishing the classification of BSI pathogen remain unclear

Methods A historical cohort study with 102 patients with LBI and 242 patients with BSI was performed, and mouse models of BSI were used to verify the reliability of clinical data

Results Our results showed that the levels of inflammatory markers of CRP, PCT, IL-6, IL-10, WBC, NE%, PLT and ESR in patients with BSI were significantly higher than those with LBI ($p<0.05$). The analysis of receiver operating characteristic curve demonstrated that CRP, PCT, IL-6, IL-10, and NE% had excellent diagnostic efficacy for BSI. Furthermore, we found levels of CRP, PCT, IL-6 and IL-10 were significantly different between the patients with BSI caused by Gram-positive bacteria (GP-BSI) and Gram-negative bacteria (GN-BSI), but no significant difference were found in specific bacterial species. Finally, we found that the levels of PCT, IL-6 and IL-10 were increased remarkably in the mice with GN-BSI compared to mice with GP-BSI

Conclusion Our study confirmed that PCT, IL-6, and IL-10 were available biomarkers to differentiate BSI from LBI and were also used as the tools for the classification of BSI pathogens, which was extremely helpful for clinicians to initiate empiric antibiotic therapy and improve clinical prognosis of BSI

关键字：procalcitonin, interleukin-6, interleukin-10, bloodstream·infection pathogens classification

宏基因组学第二代测序技术快速诊断惠普尔养障体感染一例

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惠普尔病是由一种名为 Tropheryma Whipplei 的放线菌门革兰阳性需氧杆菌惠普尔养障体引起罕见的全身性感染疾病，由 1907 年惠普尔（Whipple）首次报道。该病多见于有接触土壤和动物的农民及免疫缺陷的人群。特征是同时累及多个器官与系统，包括消化系统、心血管系统、中枢神经系统、呼吸系统和关节，突出的症状是体重减轻、腹泻、腹痛、关节痛和发热。据报道，全球患病率约为 3/10 万，美国大多数患者为中年白种男性，在亚洲人群中非常罕见。本研究回顾分析 1 例罕见的术后感染惠普尔养障体的肺移植患者的临床资料、实验室检查结果和诊疗情况，结合最新文献复习，以提高对惠普尔病的认识。

1 例特发性肺纤维化的肺移植患者术后发生罕见感染，肺泡灌洗液宏基因组学第二代测序技术检测出惠普尔养障体序列。经过抗感染治疗，患者逐渐恢复。提示使用免疫抑制剂的器官移植患者需要警惕惠普尔养障体感染的可能性，宏基因组学第二

代测序技术在罕见病原学诊断中可能具有广阔的应用前景。

关键字：惠普尔，肺移植，宏基因组学第二代测序技术。

Value of Bronchoalveolar Lavage Fluid Metagenomic Next-generation Sequencing in Acute Exacerbation of Fibrosing Interstitial Lung Disease: An Individualized Treatment Protocol Based on Microbiological Evidence

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Objective Acute exacerbation of fibrosing interstitial lung diseases (AE-ILD) is a serious life-threatening event per year. Methylprednisolone and/or immunosuppressive agents (ISA) are a mainstay in any regimen, under the premise that pulmonary infection has been promptly identified and controlled. We investigated the value of bronchoalveolar lavage fluid (BALF) metagenomic next-generation sequencing (mNGS) on the treatment adjustment of AE-ILD

Methods We conducted a cross-sectional observational cohort study. All data were collected prospectively and retrospectively analyzed. We included fifty-six patients with AE-ILD and nineteen controls who underwent BALF mNGS at the beginning of admission

Results Patients with a variety of ILD classification were included. Connective–tissue disease related ILD (CTD-ILD) occupy the most common underlying non-idiopathic pulmonary fibrosis (non-IPF). The infection-triggered AE accounted for 39.29%, with the majority of cases being mixed infections. The microorganisms load in the AE-ILD group was significantly higher. After adjusted by mNGS, the therapy coverage number of pathogens was significantly higher compared to the initial treatment ($p< 0.001$). After treatment, the GGO score and the consolidation score were significantly lower during follow up in survivors (1.57 ± 0.53 vs 2.38 ± 0.83 with $p< 0.001$, 1.11 ± 0.24 vs 1.49 ± 0.47 with $p< 0.001$, respectively). Some detected pathogenic microorganisms, such as Tropheryma whipplei, Mycobacterium, Aspergillus, and mixed infections were difficult to be fully covered by empirical medication. BALF mNGS was also very helpful for excluding infections and early administration of methylprednisolone and/or ISA

Conclusion mNGS has been shown to be a useful tool to determine pathogens in patients with AE-ILD, the results should be fully analyzed. The comprehensive treatment protocol based on mNGS has been shown crucial in AE-ILD patients

关键字：Metagenomic next-generation sequencing; Fibrosing interstitial lung diseases; Acute exacerbation; Bronchoalveolar lavage fluid; Infection

Performance of Antimicrobial Susceptibility Testing Methods for Aztreonam in Combination with Avibactam Against Enterobacteriales

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Objective To evaluate the performance of broth disk elution (BDE) method and in-house developed disk diffusion method for aztreonam in combination with avibactam against Enterobacteriales

Methods The in vitro antibacterial activity of aztreonam with avibactam against 204 carbapenemase-producing Enterobacteriales was determined by BDE of two detection volumes (5 mL and 2 mL broth) and disk diffusion method, with broth microdilution method as a reference

Results For the BDE-5mL test, the categorical agreement (CA) of ATM+CZA tube (aztreonam/ceftazidime/avibactam: 6/6/4 mg/L) was 99.5%, with 0.5% major error (ME) and 0% very major error (VME); the CA of 2ATM+CZA tube (12/6/4 mg/L) was 100%, with no ME and VME. For the BDE-2mL test, the CA of ATM+2CZA tube (15/10/4 mg/L) was 98.5%, with 0% ME and 37.5% VME; the CA of 2ATM+2CZA tube (30/10/4 mg/L) was 97.1%, with 0% ME and 75% VME. The optimal S/R breakpoints for disk diffusion test of 30/20 μg and 10/4 μg disks calculated by the dBETs software using the model-based approaches, were ≥22/≤21 mm and ≥12/≤11 mm, respectively. And based on the estimated breakpoints, the CA for disk diffusion test of 30/20 μg and 10/4 μg aztreonam/avibactam disks were both 98.0%, with 0.5% ME and 37.5% VWE

Conclusion The BDE-5 mL test is an economical and practical method for clinical microbiology laboratories to determine the antibacterial susceptibility of aztreonam with avibactam against Enterobacteriales, especially the 2ATM+CZA tube with a final concentration of 12/6/4 mg/L of aztreonam/ceftazidime/avibactam

关键字：Enterobacteriales, Aztreonam, Avibactam, Antimicrobial susceptibility testing, Broth disk elution method

稍变家村氏菌致导管相关血流感染 1 例并文献复习

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目的 回顾性分析一例稍变冢村氏菌导致的导管相关血流感染儿童病例，并复习国内外相关文献，以提高临床和实验室人员对冢村氏菌的认识，为冢村氏菌感染的诊治提供借鉴。

方法 冢村氏菌是一种革兰氏阳性条件致病性细菌，可见于免疫功能低下或免疫抑制患者，且难以通过传统实验室技术手段鉴别。本文报道一例稍变冢村氏菌引起的急性淋巴细胞白血病患儿导管相关性血流感染，该患儿 5 月前因“间断发热 5 天，发现血常规异常 3 天”为代主诉入院，完善骨髓细胞学检查后确诊为急性淋巴细胞白血病。患儿化疗后合并骨髓抑制，第二次化疗结束后 15d 出现发热症状，为排查血流感染的可能，采集静脉血培养和 PICC 导管血培养同时送检。送检后 1d，PICC 导管血培养、血培养先后报阳，使用基质辅助激光解吸电离飞行质谱技术鉴定结果均为稍变冢村氏菌感染，患儿确诊为稍变冢村氏菌导致的导管相关性血流感染。经药学部会诊并查阅文献后给予口服复方磺胺甲噁唑片联合亚胺培南西司他丁钠抗感染治疗。

结果 患儿用药 7d 后复查血培养、PICC 导管血培养均为阴性，患儿继续口服复方磺胺甲噁唑片以巩固疗效。第三次化疗结束后患儿再次出现发热，外周血培养和 PICC 导管血培养结果均回示稍变冢村氏菌感染。查阅文献后结合上次病史及本次用药情况判断该菌株对多种抗菌药物耐药，对亚胺培南敏感，遂给予亚胺培南抗感染治疗，患儿用药 7d 后复查 PICC 管及静脉血培养均为阴性。用药 2 周后，停用亚胺培南，拔除 PICC 管后予以出院，口服复方磺胺甲恶唑片，2 月后随访未再复发。

结论 本案例为我国首例稍变冢村氏菌案例报道，也是世界第 2 例、我国首例儿童稍变冢村氏菌案例报道。近年来随着免疫力低下的患者逐渐增多，冢村氏菌机会性感染人体的风险也大大增加。当从血液中培养出革兰阳性杆菌时，临床医生通常会认为是污染菌而不进行干预，但对于接受中心静脉导管置管和化疗的恶性肿瘤患者，以及接受血液透析的慢性肾病、肾衰竭患者，临床医生应当意识到冢村氏菌致病的可能性。提升临床合格标本送检率和实验室的罕见菌鉴定能力对于早期精准抗感染治疗至关重要，当发现难以识别的罕见菌，实验室应及时采用质谱和测序等分子生物学技术进行菌种鉴定，以便临床制定最佳治疗方案和改善患者预后。

关键字：稍变冢村氏菌，冢村氏菌属，导管相关性血流感染，基质辅助激光解吸电离飞行时间质谱

Efficient Extraction and Biological Characterization of K. Pneumoniae-OMVs: A Comparison between Differential Centrifugation and Density Gradient Centrifugation

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Objective This study aims to compare the efficacy of differential centrifugation versus integrated differential density gradient centrifugation in isolating OMVs from virulent strains of Klebsiella pneumoniae. By meticulously examining the size, morphology, purity, and virulence attributes of the isolated OMVs, this research seeks to lay a solid foundation for their functional analysis

Methods We performed a comparative analysis of two isolation techniques for OMVs from virulent strains of K. pneumoniae: the established differential centrifugation (DC) and a novel combined differential-density gradient centrifugation (DDGC). DC entailed serial centrifugation to segregate cellular debris and enrich OMVs, while DDGC supplemented this with density gradient steps to augment OMV purity and maintain integrity. Size distribution and morphology of the OMVs were assessed using nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM), with protein quantification conducted via Bradford assay. OMV purity was evaluated by analyzing protein and lipopolysaccharide (LPS) content, while in vitro assays appraised biological activity by examining effects on host cell viability and pro-inflammatory cytokine production

Results TEM observations revealed that OMVs extracted by both DC and DDGC methods displayed spherical structures with typical lipid bilayers. However, OMVs extracted by the DDGC method showed a clearer background and more typical morphology.Compared to the DC method, the DDGC method extracted more OMVs with more uniform particle sizes and higher total protein content.OMVs extracted by the DDGC method contained higher LPS content.The greatest impact on the viability of A549 cells was observed at an OMV concentration of 20μg/mL.At a concentration of 20 μg/mL, although OMVs extracted by both DC and DDGC methods effectively induced the expression of inflammatory factors, those extracted by the DDGC method generally induced higher levels of inflammatory factor expression. Especially at an OMV concentration of 50 μg/mL, OMVs extracted by the DDGC method significantly surpassed those extracted by the DC method in inducing mRNA expression of pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β

Conclusion DDGC is a superior method for the extraction of K. pneumoniae-OMVs, offering advantages in terms of vesicle purity, protein content, and biological activity. This technique holds promise for advancing the study of bacterial OMVs, contributing to a deeper understanding of their role in pathogenesis and immune modulation. Future research should focus on optimizing extraction methods to improve yield and applicability in biomedical research, overcoming limitations noted in traditional approaches

关键字：Klebsiella pneumoniae，Outer Membrane Vesicles (OMVs)，Centrifugation Techniques，differential centrifugation， differential density gradient centrifugation

Nanopore Sequencing Ofinfectiousfluid Is A Promisingsupplement for Gold-standardculture in Real-worldclinical Scenario

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Objective Infectious diseases are major causes of morbidity and mortality worldwide, necessitating the rapid identfication and accurate diagnosis of pathogens. While unbiased metagenomic next-generation sequencing (mNGS) has been extensively utilized in clinical pathogen identification and scientific microbiome detection, there is limited research about the application of nanopore platform-based mNGS in the diagnostic performance of various infectious fuid samples

Methods In this study, we collected 297 suspected infectious fuids from 10 clinical centers and detected them with conventional microbiology culture and nanopore platform–based mNGS. The objective was to assess detective and diagnostic performance of nanopore-sequencing technology (NST) in realworld scenarios

Results Combined with gold-standard culture and clinical adjudication, nanopore sequencing demonstrated nearly 100% positive predictive agreements in microbial-colonized sites, such as the respiratory and urinary tracts. For samples collected from initially sterile body sites, the detected microorganisms were highly suspected pathogens, and the negative predictive agreements were relatively higher than those in the microbial-colonized sites, particularly with 100% in abscess and 95.7% in cerebrospinal fuid. Furthermore, consistent performance was also observed in the identification of antimicrobial resistance genes and drug susceptibility testing of pathogenic strains ofEscherichia coli, Staphylococcus aureus, and Acinetobacter baumannii

Conclusion Rapid NST is a promising clinical tool to supplement goldstandard culture, and it has the potential improve patient prognosis and facilitate clinical treatment of infectious diseases

关键字：metagenomic next-generation sequencing (mNGS), diagnosis, infectious diseases, infectious body fluids, nanopore sequencing technology (NST)

宏基因组二代测序在骨关节感染病原学诊断中的应用

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目的 探讨宏基因组二代测序（mNGS）在骨关节感染病原学诊断中的临床应用价值。

方法 回顾性分析从 2022 年 1 月-2023 年 5 月在广东省人民医院就诊的疑似骨关节感染患者临床资料，所有患者送检标本均进行 mNGS 检测、微生物培养，记录两种检测方法检出的病原菌种别，采用卡方检验进行统计学分析。

结果 研究共纳入 108 例疑似骨关节感染患者的 126 份标本。mNGS 检测的敏感性为 84.38%，高于微生物培养（48.44%）、影像学检查（62.50%）（c2=18.478，P<0.001），差异有统计学意义。mNGS 检测的阴性预测值为 85.51%，高于微生物培养（64.89%）、影像学检查（68.42%）（c2=9.075，P<0.05）。微生物培养特异性为 98.39%，高于 mNGS 检测（95.16%）、影像学检查（83.87%）（c2=8.811，P<0.05）。微生物培养阳性预测值为 96.88%，高于 mNGS 检测（94.74%）、影像学检查（81.63%）（c2=54.452，P<0.05）。mNGS 较微生物培养能检出更多的病原体，尤其是结核分枝杆菌（c2=5.742，P<0.05）。对其中 56 例高人源背景的标本同时进行去宿主及常规处理后测序，去宿主前后 mNGS 与临床诊断符合率分别为 87.50%（49/56）和 78.57%（44/56），差异无统计学意义（P = 0.125）。

结论 mNGS 诊断骨关节感染病原体的敏感性、特异性高、检测周期短，可检出更多的病原体，具有重要的临床应用价值。

关键字：宏基因组二代测序；骨关节感染；病原学诊断

降钙素原在不同病原体所致菌血症中的表达及其诊断临界值探讨

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目的 分析血清降钙素原（PCT）在不同病原体

所致菌血症中的表达情况，并探讨其诊断临界值。

方法 收集某院近几年菌血症确诊病例 401 例为试验组，并随机选取相同时期血培养阴性病例 100 例作为对照组，探究血清 PCT 在两组中的表达情况与诊断临界值。

结果 试验组内科（289 例，72.07%）、ICU（81 例，20.20%）、外科（31 例，7.73%）血清 PCT 浓度（ng/ml）的中位数与百分位数（P25，P75）分别为 0.77（0.18，4.73）、4.32（1.00，19.96)和 3.60（0.56，18.99)，不同科室间菌血症患者血清 PCT 浓度差异具有统计学意义（P＜0.05）。试验组与对照组总体血清 PCT 浓度分别为 1.21（0.23，7.66）和 0.24（0.06，0.74），具有统计学差异（P＜0.05）。另外，各类病原体菌血症患者组间血清 PCT 浓度无统计学差异（P＞0.05），PCT 鉴别菌血症患者的诊断临界值（Cut-off）为 0.51ng/ml。

结论 PCT 在不同病原体所致菌血症中均有高表达，可作为较敏感的指标，用于菌血症诊断。

关键字：降钙素原；菌血症；临界值；特异性；灵敏度

基于表面增强拉曼散射技术快速鉴别肠球菌敏感性

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目的 研究基于表面增强拉曼散射(surface-enhanced Raman scattering，SERS)技术在肠球菌耐药株快速鉴别中的应用价值。

方法 收集某三甲医院临床分离的肠球菌，根据药敏情况把实验菌株分为万古霉素敏感株和万古霉素耐药株，利用非标记法 SERS，以带正电荷的纳米银颗粒（AgNPs+）为增强底物采集 SERS 指纹图谱，对获取到的 SERS 指纹图谱进行处理，利用正交偏最小二乘回归（Orthogonal Partial Least Squares Discriminant Analysis,OPLS-DA）法对处理后的光谱数据进行深度分析。

结果 本试验合成应用的带正电荷纳米银颗粒（AgNPs+）大小均匀，拉曼增强效果明显，可与实验菌有效结合，且均有稳定的拉曼响应度。肠球菌万古霉素敏感株和耐药株的拉曼光谱数据在 OPLS-DA 法分析下得到很好的区分，鉴别精确度为 100% ，验证了表面增强拉曼散射技术用于肠球菌耐药性鉴别上的可行性。

结论 表面增强拉曼散射技术在肠球菌敏感株和耐药株的的快速鉴别领域具有极大的应用价值和潜力。本研究验证了一种操作简单、价格低廉、适应性强的操作方法，与传统细菌耐药性鉴别方法相比，周期大大缩短，为临床常见耐药菌的快速鉴别上提供了思路和借鉴。

关键字：肠球菌；万古霉素耐药；表面增强拉曼散射；快速检测

基于 Multi-AS-PCR 的 CRISPR/Cas12a 检测 10 种基因突变——以结核分枝杆菌为例

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目的 单核苷酸多态性（SNP）检测对于传染病、肿瘤和遗传病的诊断及治疗至关重要。目前实时荧光定量 PCR（qPCR）和二代测序技术为常用 SNP 检测方法，但 qPCR 通量低、DNA 测序成本高且操作复杂。自从珍妮弗·杜德娜发现 CRISPR/Cas 系统以来，基于 CRISPR/Cas 系统检测 SNP 的方法日益流行，但通常只能检测单个 SNP。本研究联合 CRISPR/Cas12a 系统与巢式多重等位特异性 PCR（Multi-AS-PCR），开发出一种可以同时检测 10 个 SNPs 的方法，预计可解决传染病、肿瘤和遗传病领域同时检测多个 SNPs 的难点问题。为评估其在真实临床背景下的应用价值，将该方法用于利福平耐药结核病的诊断。

方法 本研究首先采用巢氏 PCR-Cas12a 方法检测 rpoB 基因鉴定 MTB。随后，建立并优化了巢氏 Multi-AS-PCR-Cas12a 方法，用于并行检测多个 rpoB 基因 SNPs。最后，评估了该方法的灵敏度和特异性，并将其与“金标准”测序技术进行了比对。

结果 巢氏 PCR-Cas12a 和巢氏 Multi-AS-PCR-Cas12a 的检测下限分别为 105 拷贝/μL、104 拷贝/μL，可鉴定 MTB，区分 MTB 的野生型及其耐药性突变型且与其他细菌 DNA 无交叉反应。方法的灵敏度、特异性、阳性预测值和阴性预测值分别达到了 100%、93.33%、90.00%及 100%。此外，我们发现等位特异性引物错配越靠近 3′端，对扩增的抑制作用越强，且不同类型的错配也决定了抑制效率，依次递减为 A-C< A-A< C-C < T-C <A-G。由于同一位点存在多个引物竞争结合 DNA 模板，所以退火温度的优化对于 Multi-AS-PCR 至关重要。不同引物之间的组合及其比例会显著影响扩增效率和特异性。

结论 综上所述，巢氏 Multi-AS-PCR-Cas12a 可对 10 种 rpoB 基因 SNPs 并行检测，通过设计一个通用反向引物和 10 个正向等位特异性引物，最大限度地减少了引物二聚体的形成。该方法在传染病和肿瘤耐药基因突变检测及特定遗传性疾病筛查方面

具有巨大潜力，后续可通过引入通用的标签序列消除引物二聚体的影响，进一步扩大突变检测数量。

关键字：CRISPR-Cas12a，Muiti-AS-PCR，结核分枝杆菌，rpoB，SNP

艰难拟梭菌分子检测新方法的建立与评估

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目的 艰难拟梭菌是引起抗生素相关性腹泻最常见的病原体之一，近年来，我国艰难拟梭菌感染（CDI）的发病率和多位点序列分型（MLST）1 型（ST1）高产毒艰难拟梭菌的流行率呈上升趋势。现有检测艰难拟梭菌的方法存在繁琐、特异性低和成本过高等缺点。我国老龄人口基数大，慢性病患者众多，抗生素使用和管理制度不完善，面临着较大的 CDI 防治压力。本研究旨在建立一种准确快速，经济有效的艰难拟梭菌分子检测新方法，以促进我国 CDI 的临床诊治和流行病学研究。

方法 通过膜蛋白基因组和蛋白组学比较寻找 ST1 型高产毒艰难拟梭菌的特异性膜蛋白，通过序列比对明确 ST1 的 4 型菌毛蛋白基因 pilW 的 SNP 位点，用于区分 ST1 和非 ST1 型艰难拟梭菌。基于 SNP 位点，组合 hsp (heat shock protein，内参基因)，tcdB 和 cdtB 三个基因，构建了一种四重 TaqMan 实时荧光定量 PCR（pilW_4-plex qPCR）检测方法，用于检测粪便标本中的艰难拟梭菌毒素基因并鉴定是否为 ST1 型高产毒艰难拟梭菌。用 403 株艰难拟梭菌临床分离株和 180 例腹泻患者的粪便样本验证该检测方法的灵敏度和特异性，并与现有的传统 PCR 方法进行了比较。

结果 1.ST1 型艰难拟梭菌的特异膜蛋白基因 pilW 的第 165 位碱基发生了 C>T 的突变，该位点被选作为鉴定 ST1 的靶点。2.利用 pilW_4-plex qPCR 从分离株和粪便样本中分别检出 21 株和 9 株 ST1 型艰难拟梭菌，经 MLST 确证无误。3. 利用 pilW_4-plex qPCR 从分离株和粪便样本中分别检出 333 株和 78 株产毒型艰难拟梭菌，与传统 PCR 方法相比，我们的方法鉴定 403 株艰难拟梭菌的灵敏度和特异性均为 100%，鉴定 180 份粪便标本中艰难拟梭菌的灵敏度和特异性分别为 94.7%和 93.3%。4. pilW_4-plex qPCR 检测耗时约 2 小时，远快于传统 PCR 方法，成本约 35 元每样本，远低于现有检测方法。

结论 我们建立的 pilW_4-plex qPCR 是一种准确快速，经济有效的艰难拟梭菌分子检测新方法，适用于我国 CDI 的临床诊断和流行病学研究。

关键字：艰难拟梭菌，鉴定，ST1，膜蛋白

CRISPR/ Cas13a 助力耐碳青霉烯肺炎克雷伯菌（CRKP）检测

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目的 耐碳青霉烯类肺炎克雷伯菌(Carbapenem-resistant Klebsiella pneumoniae, CRKP)可引起严重的社区和医院获得性感染。然而，目前 CRKP 的鉴定复杂且效率低下。在本研究中，我们建立了一种基于 CRISPR-cas13 系统并结合 PCR 或重组聚合酶等温扩增技术（RAA）的检测方法，检测 KPC，NDM 碳青霉烯酶基因和肺炎克雷伯菌（KP）基因助力 CRKP 的检测。

方法 首先，通过比对 KPC、NDM 和部分 KP 基因序列获得保守区域，并在区域内设计 KPC、NDM 和 KP 基因的质粒、检测 crRNA 以及相应的 PCR、RAA 引物。我们通过 PCR 或 RAA 扩增检测模板，并将扩增产物加入 CRISPR-Cas13a 系统进行反应；其次评价该方法的灵敏性、特异性；最后，我们收集来自北京佑安医院保存的 61 株临床菌株，同时使用 qPCR，RAA-CRISPR 荧光读出法，RAA-CRISPR 横向测流试纸条读出法，NG-Test CARBA 5，mCIM/eCIM 进行检测。

结果 建立了基于 PCR/RAA-CRISPR 的 CRKP 检测方法，采用 PCR-CRISPR 检测系统，梯度稀释的质粒 LOD 可达到 1 拷贝/微升。采用 RAA-CRISPR 检测系统，荧光法和横向测流试纸条读出系统 LOD 均可达到 10 拷贝/微升。灵敏度高于 qPCR；使用 PCR/RAA-CRISPR 检测 61 株临床样本，CRKP 检出率均可达到为 92.16%。

结论 本次研究将 PCR/RAA 扩增技术与 CRISPR-cas13 技术相结合，建立了一种快速准确廉价的助力 CRKP 检测的方法。该方法在耐药监测，感染控制临床以及治疗指导方面有广泛的应用前景。

关键字：肺炎克雷伯菌，碳青霉烯类耐药，CRISPR/Cas13a 技术，灵敏度，准确度，感染控制

Fully Integrated Microfluidic Biosensor Combining Immunomagnetic Separation and Loop-mediated Isothermal Amplification for Rapid Detection of Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae

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Objective Carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKP) can cause liver abscess, bacteremia, pneumonia and soft tissue infection. It is widely resistant to a variety of antibiotics and seriously threatens human health. It is urgent to establish a rapid and accurate detection method to reduce its harm

Methods In this study, a portable microfluidic biosensor based on immunomagnetic separation, loop-mediated isothermal amplification and smartphone image processing was developed to detect CR-hvKP. The chip is assembled by three functional areas:immunomagnetic separation, nucleic acid extraction and signal detection.First, the target bacteria were isolated from clinical specimens using antibody-modified magnetic nanoparticles (MNPs). Then the captured bacteria were lysed to extract DNA. Based on the loop-mediated isothermal amplification reaction, the target genes kpc-2 and peg-344 were amplified and detected by fluorescence. Under a 3d printed detection device, a smartphone app is used to collect and analyze fluorescent images

Results This method has good detection performance in blood and cerebrospinal fluid, and achieves specific detection of the isolated CR-hvKP. The limit of detection was 101 CFU / mL in PBS and cerebrospinal fluid, 102 CFU / mL in blood, and the linear range was 101-106 CFU / mL

Conclusion Overall, the biosensor achieved ' sample input and response ' detection of CR-hvKP, shortening the detection time (within 2h) and eliminating the need for large and skilled personnel

关键字：Carbapenem-resistant hypervirulent Klebsiella pneumoniae; immunomagnetic separation; LAMP; Microfluidic Biosensor

基因芯片技术直接检测临床样本中结核分枝杆菌及耐药基因的应用价值研究

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目的 探讨基因芯片技术在结核分枝杆菌快速鉴定及耐药分析中的应用价值。

方法 收集我院 2022 年 10 月~2023 年 2 月收治疑似结核病患者的临床样本，包括痰液、肺泡灌洗液、脓液或分泌物、穿刺液（含胸腹水和脑脊液）等，同时进行 MGIT960 接种培养、药敏试验和基因芯片直接检测法，对两种方法的检测效能进行比对分析。

结果 （1）以 MGIT960 培养鉴定为参考标准，基因芯片法检测结核分枝杆菌的敏感度为 83.33%、特异度为 92.86%、阳性预测值为 90.91%、阴性预测值为 86.67%、一致性为 88.46%、Kappa 值为 0.766。基因芯片法检测痰液样本中结核分枝杆菌的敏感度为91.18%、特异度为91.67%、阳性预测值为91.18%、阴性预测值为 91.67%、一致性为 91.43%、Kappa 值为 0.828。（2）以 MGIT960 药敏试验为参考标准，基因芯片法检测结核分枝杆菌利福平耐药的敏感度为81.82%、特异度为94.87%、阳性预测值为81.82%、阴性预测值为 94.87%、一致性为 92.00%、Kappa 值为 0.767；检测异烟肼耐药的敏感度为 75.00%、特异度为 92.86%、阳性预测值为 66.67%、阴性预测值为 95.12%、一致性为 90.00%、Kappa 值为 0.755。

结论 以 MGIT960 培养法及药敏试验为参考标准，基因芯片技术直接检测临床原始标本的敏感度、特异度高，有较好的一致性。应用基因芯片直接检测法有助于结核病的早期诊断及治疗。

关键字：结核分枝杆菌 基因芯片技术 耐药结核病 利福平 异烟肼

An Evaluation of Mp1p Antigen Screening for Talaromycosis in HIV-infected Antiretroviral Therapy-naïve Population in Guangdong, China

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Objective Southern China is one of the major endemic regions of T. marneffei, thus the prevention and control of talaromycosis are urgently needed. Screening is recommended by World Health Organization (WHO) as the important component for guiding resources in a public health approach for identifying major opportunistic infections (OIs). A number of diagnostic methods for T. marneffei infection have been developed, but researches on assessing their diagnostic utility in screening for talaromycosis are insufficient. The gold standard for the diagnosis of T. marneffei infection is microbiological culture. But its characteristic of time-consuming makes early clinical diagnosis and effective treatment difficult. Therefore, the lack of screening remains a major obstacle to improve the treatment of T. marneffei-infected patients. To address the knowledge gaps, we performed this study to evaluate the prevalence of talaromycosis based on the Mp1p antigen detection, a T. marneffei-specific protein which located throughout the cell wall of T. marneffei yeast and is abundantly secreted, and to assess the utility of Mp1p antigen screening among HIV-infected ART-naïve population in

Guangdong, China

Methods We performed a cross-sectional study of HIV-infected antiretroviral therapy (ART)-naïve adult patients who were seen in 2018 at Guangzhou Eighth People's Hospital, Guangzhou Medical University. Serum samples collected from all the 784 enrolled patients were tested for Mp1p antigen using double-antibody sandwich enzyme-linked immunosorbent assay. Receiver operating characteristic (ROC) curve analysis and Youden's index (J) were used to determine the optimal cut-off of CD4+ count for classifying the existence of Mp1p antigen. A culture of pathogen was conducted in 350 clinically suspected patients to confirm talaromycosis, and to evalute the screening efficacy of Mp1p antigen by comparing this result with that of the Mp1p antigen test

Results Among the 784 enrolled patients, the median age was 37.0 years, 87.8% (688/784) were male, and 78.6% (616/784) were infected with HIV by sexual intercourse. The median CD4+ count was 151 Nr/μl (IQR, 35–289 Nr/μl), and the median CD4+/CD8+ ratio was 0.20 (IQR, 0.09–0.36). Totally 89 of the 784 (11.4%) patients had detectable Mp1p antigen in serum samples. Compared to the Mp1p negative group, the Mp1p positive group present with more advanced HIV disease, characterized by significantly lower CD4+ counts (12 Nr/μl [IQR, 6-38 Nr/μl] vs. 179 Nr/μl [IQR, 61-315 Nr/μl], P<0.001), lower CD4+/CD8+ ratio (0.05 [IQR, 0.03-0.10] vs. 0.22 [IQR, 0.10-0.38], P<0.001), higher proportion of HIV/AIDS stage IV (78.7% vs. 11. 2%, P<0.001), higher proportion of other known OIs (86.5% vs. 34.2%, P<0.001) and higher risk of hospitalization (83.2% vs. 40.3%, P<0.001). The CD4+ count was stratified according to the cut-off values commonly used in clinical practice by ≤50 Nr/μl, 51-100 Nr/μl, 101-200 Nr/μl, 201-350 Nr/μl, and >350 Nr/μl. The overall prevalence of talaromycosis based on the Mp1p antigen detection was 11.4% (89/784) and peaked at 32.2% (75/233) in patients with CD4+ ≤50 Nr/μl. Logistic regression analysis found Mp1p antigen positive rate decreased with the increase in CD4+ counts (OR 0.982, 95% CI 0.977-0.987, P<0.01). ROC curve analysis revealed the ability of CD4+ count to discriminate between patients who were Mp1p antigen positive or negative with the area under ROC curve [AUC] = 0.870 (95% CI, 0.835–0.906, P<0.001). Analyses to determine an optimal CD4+ count cutoff to classify patients with or without Mp1p antigen using the Youden index (J) indicated the optimal cutoff is 50 Nr/μl or less, yielding a sensitivity of 84.3% and specificity of 77.7%. Among the 350 patients received both fungal culture and Mp1p antigen detection, whose CD4+ counts showed the similar trend with those of the total of 784 participants, 95/350 (27.1%) patients were culture-positive for a Talaromyces marneffei, 75/350 (21.4%) patients were Mp1p antigen positive. The Mp1p antigen assay showed a good agreement to the culture of pathogen, and the sensitivity, specificity, positive predictive value, negative predictive value and kappa value was 71.6% (68/95), 97.3% (248/255), 90.7% (68/75), 90.2% (248/275), and 0.737, respectively. The screening accuracy of the Mp1p antigen assay in patients with CD4+ counts of ≤50 Nr/μl was superior to that in those with higher CD4+ counts with a sensitivity of 73.6%, a specificity of 96.5%, a PPV of 94.1% and a NPV of 82.8% and a higher Kappa value (0.720 vs. 0.509)

Conclusion Mp1p antigen screening can be an effective tool for more efficient diagnosis of Talaromycosis, especially in HIV/AIDS patients with low CD4+ counts. Future validation studies are needed

关键字： Mp1p antigen, HIV, talaromycosis, screening, ART-naïve

Four Thermostatic Steps: A Novel CRISPR-Cas12-based System for The Rapid At-home Detection of Respiratory Pathogens

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Objective The outbreak of coronavirus disease 2019 (COVID-19) in 2019 has severely damaged the world's economy and public health and made people pay more attention to respiratory infectious diseases. However, traditional quantitative real-time polymerase chain reaction (qRT-PCR) nucleic acid detection kits require RNA extraction, reverse transcription, and amplification, as well as the support of large-scale equipment to enrich and purify nucleic acids and precise temperature control. Therefore, novel, fast, convenient, sensitive and specific detection methods are urgently being developed and moving to proof of concept test. In this study, we developed a new nucleic acid detection system, referred to as 4 Thermostatic steps (4TS), which innovatively allows all the detection processes to be completed in a constant temperature device, which performs extraction, amplification, cutting of targets, and detection within 40 min. The assay can specifically and sensitively detect five respiratory pathogens, namely SARS-CoV-2, Mycoplasma felis (MF), Chlamydia felis (CF), Feline calicivirus (FCV), and Feline herpes virus (FHV). In addition, a cost-effective and practical small-scale reaction device was designed and developed to maintain stable reaction conditions. The results of the detection of the five viruses show that the sensitivity of the system is greater than 94%, and specificity is 100%. The 4TS system does not require complex equipment, which makes it convenient and fast to operate, and allows immediate testing for suspected infectious agents at home or in small clinics. Therefore, the assay system has diagnostic value and significant potential for further reducing the

cost of early screening of infectious diseases and expanding its application

Methods Preparation of viral plasmids and clinical samples

Extraction of RNA from virus

Design of primers, CRISPR RNAs (crRNAs) and reporter genes

Amplification of DNA fragments

Measurement of fluorescence intensity values

Lateral flow assay (LFA)

Kit Reagents

Kit Reagents

Results Establishment of 4TS

Optimization of 4TS

Specificity of the 4TS system and its lower limit of detection

Clinical validation of the 4TS system

Design of a 4TS system simulation device

The stability of the 4TS system simulation device

Conclusion Due to the global COVID-19 pandemic and the continuous emergence of new pathogens, it is urgent to rapidly detect respiratory infectious pathogens. Based on the large potential of CRISPR-Cas systems, our newly developed 4TS system is highly scalable and could be used for home testing and infection surveillance. Our innovation importantly lays the foundation for fast and inexpensive POCT in the future

关键字：CRISPR-Cas12, Point-of-Care Testing, Respiratory pathogens, SARS-CoV-2

评估 BD 和梅里埃血培养检测系统的检测能力及对抗菌药物的吸附能力

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目的 比较不同培养系统的报阳时长以抗生素吸附能力，为临床诊断提供参考依据。

方法 通过体外模拟不同菌种血流感染的血培养，评估不同血培养瓶和血培养仪的 TTD 差异，通过体外模拟抗生素峰浓度下采集血培养，评估三种血培养瓶对各类抗损伤的吸附能力。

结果 在所有受试组中，BacT/Alert VIRTUO 配套使用 BacT/Alert-PF plus 和 Bactec FX 系统配套 Bactec-PF 相比 BacT/Alert 3D 配套使用 BacT/Alert-PF 的中位 TTD 分别缩短了 5.63 和 3.77 小时，BacT/Alert-PF plus 比 BacT/Alert-PF 中位 TTD 缩短 3.33 小时，BacT/Alert VIRTUO 比 BacT/Alert 3D 中位 TTD 缩短 2.3 小时，BacT/Alert VIRTUO 配套使用 BacT/Alert-PF plus 比 Bactec FX 系统配套 Bactec-PF 中位 TTD 缩短 1.86 小时，但上述检测方案在念珠菌中未见明显差异。在抗生素吸附性能试验中，Bactec-PF（51.3%）和 BacT/Alert-PF plus（46.1%）相比 BacT/Alert-PF（51.3%）的检出率高； Bactec-PF 相比 BacT/Alert-PF plus 在不同抗生素菌种组合中的检出率各有高低，整体检出率略高，但 TTD 更长；Bactec-PF 和 BacT/Alert-PF plus 的检出率随细菌耐药程度相应升高，三种血培养瓶在阿米卡星组的检出率均为 100%，在头孢曲松和美罗培南组检出率均为 0%。新型血培养仪和新型血培养瓶的使用可为临床更早提供血培养阳性报告，同时新型血培养瓶的使用可通过吸附抗菌药物提高血培养的阳性率。

结论 快速准确的血培养阳性报告（包括鉴定和药敏）对临床抗菌药物的合理选择和使用有指导意义，新型血培养仪和血培养瓶的使用可为病人及时从经验治疗转为病原学治疗提供可靠依据，避免广谱抗生素对病人的附加损害，同时减缓细菌耐药的发生。

关键字：脓毒症，血培养，抗生素，血流感染；

结核病患者外周血淋巴细胞亚群联合血浆 12 项细胞因子流式检测分析

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目的 对结核病患者外周血淋巴细胞亚群和血浆 12 项细胞因子进行流式检测分析，探讨淋巴细胞亚群联合细胞因子在结核病患者中的差异性变化及在结核病中的诊断效能。

方法 筛选 2022 年 1 月至 2023 年 12 月在解放军总医院第八医学中心就诊的有病原学证据或临床确诊的结核病患者 128 例作为研究对象，其中肺结核 83 例，肺外结核 45 例，另选择性别和年龄相匹配的健康体检者 100 例作为对照组。采用流式细胞术检测三组患者外周血淋巴细胞亚群和血浆 12 项细胞因子（IL-5、IFN-α、IL-2、IL-6、IL-1β、IFN-γ、IL-8、IL-17、IL-12p70、TNF-α、IL-4 和 IL-10），分析差异性变化，采用相关性分析比较结核病患者各指标之间的相关性，二元 Logistic 回归筛选结核病相关因素，受试者工作曲线（ROC）评价结核病相关因素的诊断效能。

结果 与对照组相比，肺结核组和肺外结核组 CD3+T 淋巴细胞、CD3+CD8+T 淋巴细胞、CD3+CD4+T 淋巴细胞、NK 细胞和 B 细胞绝对数均显著下降（P＜0.05），肺结核组 11 项细胞因子（IL-1β 除外）均不同程度升高（P＜0.01），肺外结核组

IL-6、IFN-γ、IL-17、TNF-α、IL-4 和 IL-10 共 6 项细胞因子呈不同程度升高（P＜0.05）。与肺外结核组相比，肺结核组 IL-8 升高且差异具有统计学意义（P=0.026），IL-1β 在三组间比较均无统计学意义（P＞0.05）。spearman 相关性分析结果显示：IL-6、IFN-γ、IL-8 和 IL-10 与淋巴细胞亚群绝对数呈不同程度弱负相关（-0.37≤R2≤-0.13）；二元 Logistic 回归分析显示：IL-6、IFN-γ、IL-8、IL-10 是结核病重要相关因素，4 项细胞因子联合诊断结核病 AUC 为 0.845。

结论 肺结核和肺外结核患者的淋巴细胞亚群绝对数和细胞因子水平显示其免疫功能处于低下状态，促炎因子（IL-6、IFN-γ、IL-8）和抑炎因子（IL-10）明显升高紊乱，4 项细胞因子联合检测具有较高的诊断效能，其中，IL-8 有望成为肺结核和肺外结核鉴别诊断的关键标志物。

关键字：肺结核； 肺外结核； 淋巴细胞亚群； 细胞因子； 流式细胞术；鉴别诊断

306 例细菌性肝脓肿的临床特点及病原学分析

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目的 通过对细菌性肝脓肿(BLA)患者的病原学特征、临床表现、治疗及易发因素进行分析，以进一步提高对 BLA 的诊疗水平。

方法 回顾性分析我院住院治疗的 306 例 BLA 的临床资料，包括基础疾病、临床表现、实验室检查、影像学检查、病原学检查、治疗措施及转归等。

结果 共收集 306 例 BLA 患者，其中男 213 例，女 93 例，男女比例为 2.29:1。平均年龄 57.33±13.84 岁，发病高峰年龄段为 50～69 岁。基础疾病以糖尿病（140 例，45.75%）最多见，其次为胆道疾病（105 例，34.31%）。临床表现以发热（271 例，88.56%）最常见，其次分别是畏冷、寒战（177 例，57.84%），腹痛（118 例，38.56%），典型发热、寒战、腹痛三联征仅占 85 例（27.78%）。脓液培养阳性率高于血培养（65.18% vs 33.59%，P＜0.001）。其中，肺炎克雷伯菌占 64.74%（123/190），大肠埃希菌占 8.95%（17/190），两者产 ESBLs 菌的比例分别为 3.25%（6/123）和 23.53%（4/17）。123 株肺炎克雷伯菌中，经典肺炎克雷伯菌 101 株，高毒力肺炎克雷伯菌 22 株，两者产 ESBLs 菌分别为 6 株和 0 株，两者间比较无统计学意义（P＞0.05）。大肠埃希菌对氨曲南、头孢他啶、环丙沙星、头孢吡肟、头孢噻肟、左氧氟沙星、四环素、哌拉西林、氨苄西林舒巴坦、复方磺胺的耐药率高于肺炎克雷伯菌（均 P＜0.05）。单因素及多因素 Logistic 回归分析提示糖尿病（OR=4.468，P＜0.001）、胆道结石（OR=0.374，P=0.019）、直接胆红素（OR=0.971，P=0.032）与 BLA 患者易出现肺炎克雷伯菌感染有关。基于以上三者构建回归模型 Logit（P）=1.497×糖尿病－0.984×胆道结石－0.030×DBIL－2.735，该模型预测 BLA 患者为肺炎克雷伯菌感染的曲线下面积（AUC）为 0.816（95% CI：0.760-0.864），敏感性和特异性分别为 73.17%和 75.47%。218 例（71.24%）患者选择抗生素+经皮穿刺置管引流术。306 例患者总的有效率为 90.45%，院内死亡率为 2.94%，最常见的并发症为呼吸道感染（80 例，26.14%）。在 123 例的肺炎克雷伯菌肝脓肿中，发生侵袭性综合征的有 20 例（16.26%）。

结论 BLA 好发于中老年人，男性多见，多伴有糖尿病。临床表现以发热最常见，典型发热、寒战、腹痛三联征少见。肺炎克雷伯菌是 BLA 的主要致病菌，而糖尿病则是肺炎克雷伯菌感染的独立危险因素。

关键字：细菌性肝脓肿，临床特点，肺炎克雷伯菌，侵袭性综合征

Interpretation of Positive Reports Improves The Infection Diagnostic Precision of Metagenomic Sequencing in Hematological Disorder Patients

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Objective Metagenomic next-generation sequencing (mNGS) is increasingly being applied in clinical settings due to its rapid, culture-independent, and unbiased nature. In the context of diagnosing infections in patients with hematologic disorders, mNGS offers advantages such as high sensitivity, broad pathogen detection, and reduced impact from antimicrobial drugs. Nonetheless, due to the lack of standardized interpretation criteria for mNGS results, clinicians still approach mNGS findings cautiously. The mNGS detection exhibits a high positive rate; however, not all identified microorganisms are pathogenic, emphasizing the crucial need for interpreting the results. To date, neither has there been research on how to interpret microorganisms detected by mNGS, nor a unified standard for determining whether they are pathogens. The purpose of this study is to understand the interpretation challenges clinicians face with positive mNGS reports. Additionally, the study aims to assess the accuracy and clinical value

of mNGS results interpretations, provided by microbiologists who are informed about the clinical information of the patients at the time of mNGS test

Methods This study employed a survey questionnaire to understand the common challenges faced by clinicians when interpreting positive mNGS reports. After recognizing the concerns expressed by clinicians, microbiologists began offering interpretation services for positive reports - termed 'Report Interpretation Cards (RIC). The Interpret includes a list of positive microorganisms detected in the mNGS report, pathogen interpretation, and detailed information about the microorganisms. The pathogen interpretation consists of 1. Suspected Pathogen; 2. Indeterminate; 3. Non-Pathogen. The accuracy of the interpretations was evaluated by a clinical expert panel. This study conducted a clinical assessment of 300 RICs provided to clinicians from October 2022 to March 2023. Out of these, 281 RICs were included in the final analysis

Results More than 80.0% of clinicians had confusion when dealing with positive mNGS reports, yet their satisfaction with the interpretation services reaches 97.8%. The most common concern was that when mNGS detects microorganisms with low reads, clinicians cannot determine whether they have clinical significance (64.1%, 59/92)

In the 281 infection cases, the detection rates for bacteria, fungi, viruses, and parasites were 42.7% (120/281), 26.7% (75/281), 86.1% (242/281), and 1.1% (3/281), respectively . In terms of interpretation, 97.5% (117/120) of bacteria, 100% (75/75) of fungi, and 24.4% (59/242) of viruses were interpreted as suspected pathogens. Regarding assessment, the percentages of bacteria, fungi, and viruses assessed as suspected pathogens were 92.5% (111/120), 97.3% (73/75), and 26.4% (64/242).

Out of all cases, 72.2% (203/281) detected multiple microorganisms . In these cases where multiple microorganisms were detected, Only 37.9% (77/203) and 37.4% (76/203) were respectively interpreted and assessed as having mixed infections with multiple pathogens.

In 26.3% of the 281 cases, no suspected pathogen was detected after clinical assessment.

Among the cases, a total of 728 microorganisms were detected, including bacteria (n=164), fungi (n=92), DNA viruses (n=451), RNA viruses (n=18), and parasite (n=3). Among these, 45.5% (331/728) were interpreted as suspected pathogens, 14.4% (105/728) as indeterminate, and 40.1% (292/728) as non-pathogens. Within the microorganisms interpreted as suspected pathogens, the concordance rate of clinical assessment also being suspected as pathogens is 91.5% (definite-30.5%; probable-42.0%; possible-19.0%). In the interpretation of microorganisms not considered as pathogens, 92.9% (369/397) are assessed as non-pathogenic.

Bacteria, fungi, and viruses were interpreted as suspected pathogens in 97.0% (159/164), 100.0% (92/92), and 16.4% (77/469) of cases, respectively. Meanwhile, 92.1% (151/164), 95.7% (88/92), and 19.0% (89/469) were assessed as suspected pathogens. In virology, different types of viruses have significant clinical implications. RNA viruses, such as SARS-CoV-2 and Human respirovirus, were all interpreted/assessed as suspected pathogens. In contrast, for DNA viruses like CMV, EBV, and HSV, the proportion interpreted and assessed as suspected pathogens is less than 20%. Analysis of consistency and error rates in interpretation and assessment revealed concordance rates of 93.9%, 95.7%, and 72.3% for bacterial, fungal, and viral interpretations, respectively.

In 281 cases, mNGS positively influenced pathogen diagnosis in 68.7% (193/281) and facilitated antimicrobial therapy adjustment in 40.9% (115/281) of the cases. The positive impact was more significant in cases with suspected pathogens than in cases with indeterminate pathogens or non-suspected (87.7% vs. 15.9% vs. 3.8%, $P<0.001$) . In cases of detecting bacteria, fungi, and viruses, the positive impact percentages were 87.5% (105/120), 96.0% (72/75), and 18.6% (45/242), respectively. Additionally, in cases where viruses were detected, the positive impact of mNGS was greater in cases where the virus was interpreted as a suspected pathogen compared to those where it was not (55.9% vs. 6.6%, $P<0.001$).

Conclusion Although mNGS has become one of the important tools for clinicians in diagnosing infections, however having questions about the positive mNGS reports is a common phenomenon among clinicians[19,22–24]. For the first time, this study augmented mNGS results with interpretations conducted by microbiologists informed about clinical information. Additionally, the accuracy and clinical impact of these interpretations were evaluated. The study results showed that there was a high consistency between report interpretation and clinical assessment, and the report interpretation was appreciated by clinicians, contributing to the better application of mNGS

The positive mNGS reports interpretation has a positive impact on addressing clinicians' doubts with positive mNGS reports. This service assists clinicians in promptly and accurately identifying infectious pathogens, particularly for hematologic patients with less evident infection characteristics. However, in assessing the practical utility of the 'RIC' service in clinical practice, larger-scale studies are still needed to obtain more comprehensive data support.

关键字：Metagenomic Next Generation Sequencing (mNGS), Hematological disorders; Infection, Interpretation

2D Film-Like Magnetic SERS Tag with Enhanced Capture and Detection Abilities for Immunochromatographic Diagnosis of Multiple Bacteria

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Objective The accurate identification of pathogens in the early stages of infections is key for guiding timely treatment and saving lives. Given that several common pathogens, including Staphylococcus aureus (S. aureus), Pseudomonas aeruginosa (P. aeruginosa), and Salmonella typhimurium (S. typhi), cause more than 50% of deaths from bacterial diseases, a rapid, simple, and sensitive method needs to be urgently developed for the simultaneous detection of these major pathogens

Methods Herein, we report the design and fabrication of a 2D film-like magnetic surface-enhanced Raman scattering (SERS) tag (named GFe–DAu–D/M) and demonstrate its potential to facilitate SERS-based immunochromatography (ICA) for the ultrasensitive and simultaneous monitoring of three pathogens. The novel GFe–DAu nanosheet with a well-defined 2D flexible structure, excellent magnetic performance, large reaction interface and superior SERS activity was prepared through a PEI-mediated assembly. A combination of 4-mercaptophenylboronic acid (MPBA) and 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB) was simultaneously modified onto the GFe–DAu surface to generate strong SERS signals for bacterial sensing and provide boronic acid groups for effective broad-spectrum bacterial capture

Results The developed technology can directly and simultaneously diagnose three major pathogens (S. aureus, P. aeruginosa, and S. typhi) within 25 min with detection limits down to the level of 10 cells/mL, and had increased by at least 100 times compared with that of the AuNP-based ICA. The good performance of the proposed method in the detection of real clinical samples (37 urinary tract infection specimens) was also demonstrated, suggesting the great potential of the GFe–DAu–D/M–ICA platform for the highly sensitive and on-site monitoring of bacterial infections or contamination

Conclusion The concept and material of film-like magnetic SERS tags were proposed and introduced into an ICA platform for the first time. This approach effectively eliminated sample matrix interference and improved the colorimetric and SERS signals on test strips. The GFe–DAu–D/M–ICA method is a promising candidate for application in the clinical and POCT fields for the rapid and sensitive monitoring of multiple pathogens

关键字：film-like magnetic SERS tag, pathogenic bacteria, SERS–ICA

One-step and One-tube LAMP/CRISPR-Cas12b Detection Platform on TcdA and TcdB Genes in Clostridioides Difficile

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Objective Clostridioides difficile infection (CDI) is a gastrointestinal infection caused by toxigenic Clostridioides difficile, which is the primary cause of hospital-acquired infectious diarrhea. Rapid and accurate detection of its virulence factors is momentous to diagnosis and subsequent treatment of infection

Methods In this study, two one-step platforms have been developed by combining loop-mediated isothermal amplification (LAMP) and CRISPR-Cas12b system to detect the coding genes of two major toxins, tcdA and tcdB, respectively. The convenience of the one-step detection platforms was evaluated by visual testing. The sensitivity was evaluated by determining the limit of detection (LoD). The clinical strains of toxigenic Clostridioides difficile and some human intestinal bacteria were collected to analyze the specificity. Fresh stool samples of patients with suspected CDI were collected from Huashan Hospital, Fudan University between August 2023 and February 2024. To evaluate the efficacy of the one-step platforms for clinical sample detection, fecal genes were extracted and used as templates in both one-step platforms and qPCR. Meanwhile, the results of tcdB detection were also compared to those of the Xpert C. difficile nucleic acid test in medical history. The results obtained from the above were summarized and statistically analyzed

Results The reactions were performed at a constant temperature for about 40 minutes, and the results could be interpreted either through the fluorescence intensity changes measured by a fluorescence reader or via the color changes observed by the naked eye under ultraviolet light. By targeting tcdA and tcdB, the analytical limit of detection (LoD) for LAMP/CRISPR-Cas12b assays could reach 3 to 14 copies per test. When using the one-step platforms to detect C. difficile clinical strains and other common pathogenic bacteria, there was no cross-reactivity. Moreover, 55 fecal samples from patients with suspected infection were collected for clinical validation. Referring to the results of qPCR, the newly established system targeting tcdA exhibited

the sensitivity of 86.4% (19/22), the specificity of 84.8% (28/33), and the Kappa value of 0.701, while the system targeting tcdB exhibited the sensitivity of 96.6% (28/29), the specificity of 100% (26/26), and the Kappa value of 0.964. Compared to the results of Xpert C. difficile assay, the system targeting tcdB exhibited the Kappa value of 0.838

Conclusion In conclusion, the detection results obtained by LAMP/CRISPR-Cas12b platforms were comparable to those of the reference methods. Accordingly, due to the properties of celerity, handiness, low cost, high sensitivity, and high specificity, such one-step assays have the potential to be conducted in clinical practice and point-of-care testing

关键字：Clostridioides difficile, LAMP, CRISPR-Cas12b, nucleic acid detection

高毒力肺炎克雷伯菌的耐药性、毒力分子特征与鉴别诊断标记物的研究

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目的 掌握高毒力肺炎克雷伯菌(Hypervirulent Klebsiella pneumonia, hvKP)的临床分布、耐药现状、毒力特征及潜在的鉴别鉴别诊断标志物。

方法 收集 2015 年-2020 年首次分离的 569 株肺炎克雷伯菌(Klebsiella pneumonia，KP)，对菌种进行鉴定及药敏分析；对菌株的临床分布、标本来源进行回顾性研究。通过拉丝实验初步分选其中的 hvKP 和 cKP 菌株，并采用 PCR 对 18 种毒力基因和 6 种荚膜血清型基因进行检测，比对 cKP 菌株与 hvKP 菌株的基因检测情况。运用 logistics 回归分析构建鉴别诊断 hvKP 的预测模型，采用 ROC 曲线分析评价预测模型的鉴别诊断价值，探讨 hvKP 鉴别诊断价值较高的标志物组合。

结果 共收集 569 株 KP，包括 369 株 hvKP 和 200 株 cKP。药敏结果显示，cKP 对受试抗生素的耐药率普遍高于 hvKP；hvKP 对环丙沙星耐药率为 16.6%，对其余 12 种抗生素耐药率均＜10.0%。荚膜血清分型显示，hvKP 菌株主要以 K1、K2 型为主；cKP 菌株主要以 K47 型为主。毒力基因检测显示：hvKP 携带的毒力基因检出率普遍比 cKP 的高。其中，9 种基因(wcaG、rmpA/A2、iucA、iutA、iroB/N、allS 和 peg-344)的检出率均＞55.0%，明显比 cKP(＞9.0%)高。在 24 种鉴别诊断标志物中，7 种毒力基因(peg-344、iroB/N、iutA、iucA 和 rmpA/A2)在鉴定 hvKP 方面具有较高的鉴别诊断价值(灵敏度和特异度均＞80.0%)，尤其是 peg-344 基因。2 个血清型基因(K1 和 K2)基因鉴定 hvKP 的准确率一般(灵敏度和特异度均＞50.0%)。结合标志物的鉴别诊断价值，将单因素分析有显著统计学意义(P＜0.05)的毒力基因(peg-344、iroB、iroN、iutA 和 iucA)和血清型基因(K1 和 K2)纳入 logistics 回归分析。由“peg-344+iroB+iroN+iutA+iucA”建立的预测模型是鉴别诊断 hvKP 较为可靠的模型；由“peg-344+iutA”建立的模型是鉴别诊断 hvKP 菌株最佳的鉴别诊断模型。两个模型的灵敏度和特异度均＞90.0%。

结论 hvKP 菌株多分离自呼吸科和神经外科，在痰液和脓液标本中多见，耐药率较低，荚膜血清型多以 K1 和 K2 为主。临床上可选择联合 peg-344 和 iutA 作为鉴定 hvKP 的快速筛选方法；联合 peg-344、iroB、iroN、iutA 和 iucA 的能够更加准确鉴定 hvKP 菌株。

关键字：高毒力肺炎克雷伯菌，耐药性，毒力，鉴别诊断标志物

细菌真菌感染的治疗

Rare Occurrence of Pulmonary Coinfection Involving Aspergillus Fumigatus and Nocardia Cyriacigeorgica in Immunocompetent Patients Based on NGS A Case Report and Literature Review

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Objective In our search on PubMed, we found that reports of co-infections involving Aspergillus fumigatus and Nocardia cyriacigeorgica in the literature are notably scarce. It aims to improve the level of awareness and efficacy of treatment for these diseases. Aspergillus fumigatus and Nocardia cyriacigeorgica are widely distributed in the natural environment, and both are opportunistic pathogens. Their spores or hyphae are inhaled through the human respiratory tract, invading the lungs and leading to pulmonary infections known as pulmonary aspergillosis and pulmonary nocardiosis, respectively. The clinical symptoms and radiological presentations of pulmonary infectious pathogens lack specificity, rendering these types of cases prone to misdiagnosis and underdiagnosis. Accurate differentiation necessitates laboratory techniques combined with clinical diagnostic progress to exclude all potential alternative diseases. A literature review revealed that cases of mixed infection involving these 2 pathogens are infrequent and are mostly observed in patients with compromised immune functions or underlying pulmonary conditions. In contrast, our patient did not present with any of these risk factors. Furthermore, there have been no recent incidents such as near-drowning or other accidents in the patient history. To the best of our knowledge, no similar cases have been reported before

Methods Most cases have been documented in patients with compromised immune systems or underlying pulmonary conditions. In contrast, our patient did not present with any of these risk factors. Furthermore, there have been no recent incidents such as near-drowning or other accidents in the patient history. To the best of our knowledge, this case represents a hitherto unreported clinical scenario. To enhance comprehension, we conducted a comprehensive literature review by compiling a total of 20 case reports (spanning from 1984 to 2023) on co-infections involving Aspergillus and Nocardia species, retrieved from PubMed.Upon admission (Day 1), a preliminary clinical diagnosis of pulmonary infection was retained, and empirical symptomatic treatment was initiated using a combination of piperacillin sodium tazobactam and etimicin sulphate. To clarify the etiology, a bronchoscopy was performed (Day 5). Bronchoscopy revealed mucosal congestion and edema in the apical segment of the right upper lobe of the lung. The filamentous substance can be seen on the surface of the bronchial. Two spherical polypoid new organisms could be seen, which obstructed the opening of the subsegment of the bronchus and moved along with the respiratory activity . The pathological examination of new organisms disclosed evidence of severe chronic inflammation, accompanied by neovascularization and localized fibrosis. Notably, the presence of Aspergillus fungi was observed within the tissue . Next-Generation Sequencing was performed on the bronchoalveolar lavage fluid sample sample (Day 6). The results revealed the presence of A fumigatus (1 × 10^3 copies/ mL) and N cyriacigeorgica (1 × 10^2 copies/mL). While there have been limited reports of mixed infections involving both pathogens in immunocompetent patients, it is noteworthy that our patient had a history of occupational exposure and significant risk factors for airborne infections. We promptly communicated the NGS results to the microbiology laboratory, allowing for an extended culture duration to yield more clinically meaningful pathogenic results. After 9 days of antibiotic treatment, a follow-up chest CT scan (Day 9) displayed exacerbation of patchy and nodular high-density opacities in both lungs, and the treatment regimens were considered to have poor efficacy. After 5 days of culturing BALF, A fumigatus, and Nocardia spp were discovered on Columbia blood agar plates(Day 11). Aspergillus fumigatus presented as cottony colonies with a greenish color, while Nocardia spp presented as millet grain size. Extending the cultivation time of Nocardia, the colony appears chalky, lacking luster, irregular, and wrinkled in shape, with edges trapped in the culture medium. Sputum samples were centrifuged and sediment was taken for acid-fast staining. Under high magnification microscopy, weak positive acid-fast staining was found, with slender filaments and branching Nocardia genus. Examination of the Aspergillus hyphal wet mount revealed flask-shaped vesicles and single-layered conidia. In light of the patient clinical presentation, treatment course, occupational exposure history, changes observed in the chest CT scan, microbiological findings, and pathological results, we have arrived at the diagnosis of pulmonary aspergillosis and pulmonary nocardiosis in the patient. Based on the aforementioned diagnosis, we adjusted the treatment regimen. Voriconazole (200mg q12h) was administered for the treatment of the A fumigatus infection, while sulfamethoxazole-trimethoprim(SMZ-TMP) tablets (1 tablet qid) were employed to address the N cyriacigeorgica infection. After 6 days of this protocol (Day 18), the patient's ESR decreased significantly (ESR 90.00mm/h), and improvements were noted in his anemia and hypoproteinaemia (HB 116.20g/L, ALB 37.15g/L) compared to the values at baseline. The patient had no adverse reactions to sulfonamides, and this allowed for an increase in the dosage of SMZ-TMP tablets to 2 tablets qid. After adjusting the treatment plan to voriconazole and SMZ-

TMP for 11 days, the chest CT scan (Day 20) shows a reduction in the size of the localized lesion compared to previous antibiotic treatment (Day 9) . Bronchoscopy (Day 22) shows reduced congestion and edema in the mucosa of the opening of the apical segment of the upper lobe of the right lung, with a reduction in the filamentous material on the surface of the mucosa

Results After 2 weeks of treatment (Day 26), the patient body temperature normalized, with no cough or sputum, and an overall assessment indicated effective treatment. In accordance with the patient and family's wishes, discharge was arranged. Following discharge, the patient continued oral administration of voriconazole and sulfamethoxazole-trimethoprim. A telephone follow-up at 6 months, the patient reported no clinical symptoms, stopped taking the medication voluntarily 1 month ago, and refused to be reviewed

Conclusion Regarding treatment for pulmonary aspergillosis, voriconazole is a lipophilic drug that is widely distributed in lung tissue, alveoli, and epithelial cell lining fluid and is the primary choice for medical treatment. For pulmonary nocardiosis, sulfamethoxazole-trimethoprim has been a longstanding preferred therapeutic option. Originating from a search on PubMed, a retrospective analysis was conducted on case reports, and a total of 20 instances of mixed infections involving both Aspergillus and Nocardia were found from 1984 to 2023. Among these, patients aged 50 and above constituted half of the cases (50%), with the majority being male (75%). Each case report in the table presented multiple predisposing factors contributing to these mixed infections and we tabulated and assessed the most significant Predisposing factors of literature . Revealing a predominance of immunocompromised hosts. The instances encompassed cases of immunosuppressive drug therapy,[hematologic malignancies, organ transplantation, chronic granulomatous disease, and systemic lupus erythematosus, and a case of tooth extraction in a mildly immunosuppressed patient. Such cases were also observed in nonimmunosuppressed hosts, including patients with diabetes, allergic disorders, bronchial thermoplasty therapy ulcerative colitis during golimumab therapy, and even accidental drowning incidents. Pulmonary involvement was universal across all patients, while infection was also identified in subcutaneous tissues, lymph nodes, and intracranial and central nervous system sites. A majority (60%) of the patients demonstrated a substantial recovery post-treatment. In our search on PubMed, we found that reports of co-infections involving A fumigatus and N cyriacigeorgica in the literature are notably scarce. Most cases have been documented in patients with compromised immune systems or underlying pulmonary conditions. In contrast, our patient did not present with any of these risk factors. Furthermore, there have been no recent incidents such as near-drowning or other accidents in the patient history. Clinical practitioners are effectively leveraging the notable advantages and value of NGS in detecting rare and mixed pathogens associated with pulmonary infections. By integrating traditional microbiological culture results and clinical manifestations, timely diagnosis and treatment were achieved, leading to the successful recovery of the patient. This case report holds significant educational and research value, aiming to enhance clinical awareness of such rare bacterial mixed pulmonary infections

关键字：Aspergillus fumigatus, immunocompetent patient, Next-Generation Sequencing (NGS), Nocardia cyriacigeorgica, pulmonary co-infection

Fluconazole Combined with Fire Needle Therapy Against Chromoblastomycosis: A Case Report and Literature Review

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Objective Chromoblastomycosis (CBM), or chromomycosis, is a chronic, progressive subcutaneous fungal infection characterized by pigmented muriform cells in the tissue. Untreated, CBM can increase the patient'srisk for getting secondary bacterial infections and developing skin fibrosis or even skin cancer. Treatment of CBM is not standardized and can be difficult. Itraconazole, terbinafine, posaconazole, amphotericin B, 5-fluorocytosine and fluconazole have all been used, sometimes unsuccessfully, to treat CBM. Surgical excision, cryotherapy, electrical cautery, laser vaporization and photodynamic therapy have been used as adjuvants to antifungal therapy to treat CBM.In China, fire needle therapy, a type of acupuncture where the needle is heated until red-hot and then quickly inserted into the affected area, has been used to treat various skin conditions, such as scaly hyperplastic skin lesions and infectious exudative skin lesions. Fire needle therapy characterized by"giving equal weight to needling and scorching, stressing warming and unblocking";"rapid needle insertion and withdrawal"and"needling based on pattern differentiation"; have the double function of acupuncture and moxibustion. This technique is thought to regulate immunity, control inflammation, drain pus and reduce swelling, dissipating the nodule.Fire needle diameters may be thick, average or thin. The thickness of the average needle is 0.8mm and this is the most commonly used needle for acupuncture

We report here a case of Chromoblastomycosis (CBM) treated using fluconazole and fire needle therapy. We also review the literature regarding the treatment of CBM.

Methods A 67-year-old farmer presented to our

institution with a 4 month history of progressively enlarging lesions on the dorsum of his right hand. The skin lesions initially started as a 1×2cm nodule on the dorsum of his right hand.The nodule was incised and drained at a local clinic but after this the lesion continued to expand to 5×6 cm and developed black discoloration and raised edges, became painful, had an unpleasant odor and caused limited range of motion of the hand. He denied having fever. He was treated with topical fluticasone propionate ointment, moxifloxacin ointment, compound polymyxin B ointment, naproxenone conazole cream and oral clarithromycin and ciprofloxacin, all without improvement. His risk exposure history was significant only for working on a farm

His past medical history was significant for essential hypertension, type 2 diabetes mellitus, chronic kidney disease, a cerebral hemorrhage and psoriasis, but for psoriasis he was not taking immunosuppressant medication . He had no history of weight loss.

On physical examination the patient's vital signs were normal and he was afebrile. The dorsum of the right hand had a 7×6 cm lesion that was black, firm, minimally mobile and had a foul smell. He was unable to flex the right hand due to stiffness. There were no other skin lesions. He had no lymphadenopathy in the right arm. The rest of the physical examination, including the liver and spleen, was normal .A complete blood count showed a white blood cell count of 7.4×109/l with 68.6% neutrophils, 19.4% lymphocytes and 7.5% monocytes. His erythrocyte sedimentation rate was 49mm/hour, his c-reactive protein was <0 . 80mg/l and his procalcitonin level was 0.16ng/ml. His estimated glomerular filtration rate was 16 ml/min/1.73m2 . His liver function testing was normal and coagulation studies were normal.

An acid-fast stain of a swab obtained from the skin lesion was negative for acid fast bacilli. He had a negative tuberculin skin test. A fungal culture of the lesion yielded Candida, which was assumed to be a commensal organism. A bacterial culture of the lesion yielded both Klebsiella pneumoniae and Enterococcus faecalis. Metagenomic sequencing of a swab obtained from the lesion identified Candida, Enterococcus faecalis, Klebsiella pneumoniae and Bacteroides fragilis.

A biopsy of the lesion showed epidermal papillomatous growth with marked hyperkeratosis, focal incomplete coagulation, micro-abscesses and an old hemorrhage. Part of the biopsy specimen had colony-like structures with collagen proliferation, dermal fibrosis, hyperplasia, dilation of the small blood vessels, perivascular infiltration with lymphocytes, plasma cells, scattered neutrophils, isolated eosinophils and occasional multinucleated giant cells. Hematoxylin-eosin staining showed collagen proliferation, papillomatous growth, micro-abscesses, inflammatory cell infiltration, hyperkeratosis, fibrosis and multinucleated giant cells. Fungal culture and metagenomic sequencing analysis of the pus did not detect the presence of pathogenic fungi.

The patient was then diagnosed with having CBM with a secondary bacterial infection and the presence of underlying essential hypertension, type 2 diabetes mellitus, chronic kidney disease, a history of cerebral hemorrhage and psoriasis.

The patient was treated with intravenous fluconazole (200mg/day), meropenem (1,000mg/day) and linezolid (600 mg/day) for one month. He was also treated with fire needle therapy with the needles placed in the skin lesion to a dept of 0.2-0.3cm and repeated 20-30 times for each area penetrated. The treatments were spaced 0.5 cm apart and given every other day for 1 month. With this treatment, the inflammation decreased, the odor improved and the lesion decreased in size until the patient was discharged from the hospital. He was continued on treatment as an outpatient with oral fluconazole (200mg / day), linezolid (600 mg/day) and fire needle therapy for an additional month.

Results We successfully treated this patient with dermal CBM using fluconazole and fire needle therapy in a relatively short period without serious complications or recurrence. The patient's CBM lesion resolved completely without evidence of recurrence for one year of follow-up

Conclusion The combination of the fire needle therapy with antifungal therapy in this reported patient resulted in a relatively shorter treatment course of 2 months as compared to monotherapy with an antifungal medication to treat CBM which can take up to 12 months with itraconazole or terbinafine or up to 8 months with fluconazole. A shorter treatment course should result in better treatment adherence

We conclude this combination may be an effective treatment option. Further studies are needed to determine the efficacy of this combination to treat other CBM patients.

关键字：chromoblastomycosis, fluconazole, fire needle, adjuvant therapy

Polymyxin B in The Treatment of Infections Caused by Multidrug-resistant Gram-negative Bacteria in Children: A Retrospective Case Series and A Literature Review

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Objective Multidrug-resistant Gram-negative bacteria (MRGN) pose a significant threat and require priority attention. According to the World Health Organization (WHO) classification of drug-resistant bacteria

based on threat severity, Multidrug-resistant Gram-negative Bacteria (MRGN), including Carbapenem-resistant Enterobacteriaceae (CRE), Carbapenem-resistant Acinetobacter baumannii (CRAB), Carbapenem-resistant Pseudomonas aeruginosa (CRPA), represent the most critical threats deserving priority attention. Polymyxin B (PMB) stands out, making it potentially the preferred choice for MRGN infections in children. To assess the effectiveness and safety of PMB in treating MRGN infections in Chinese children, a retrospective study was conducted at a specialized tertiary hospital for women and children in Southwest China. Additionally, a comprehensive literature review was undertaken to provide valuable references for the judicious clinical utilization of PMB

Methods The paediatric patients aged 0-18 years were enrolled in the study who were hospitalized in West China Second University Hospital of Sichuan University, a tertiary teaching hospital special for women and children, Children's National Regional Medical Center in Southwest China, from October 1, 2019, to November 30, 2022. Demographic data, medication information and laboratory test results were collected through Hospital Information System. All enrolled patients obtained approval for the use of PMB as part of the pre-authorization management within paediatric antimicrobial stewardship programs. The patients who did not use PMB finally were excluded even though the approval form was submitted, and the cases who received PMB treatment for less than 3 days because of the difficulty in effectiveness evaluation were excluded as well. Refer to the U.S. Food and Drug Administration (FDA) guidelines for the evaluation of clinical research on anti-infective drugs, and the American Society of infectious diseases (IDSA) guidelines for the evaluation of infectious diseases, the therapeutic effect of PMB was divided into “effective” and “ineffective”. In the assessment of adverse drug events associated with PMB, a thorough data cleaning was conducted for relevant symptoms, physical signs, and laboratory examination results documented in the patient's medical records. Special attention was given to the potential nephrotoxic effects of PMB. These cases were then compared with those identified in a literature review that was conducted to collect clinical studies focusing on the use of PMB in the treatment of infections caused by MRGN in paediatric patients. In logistic regression, three independent variables (whether a loading dose was used, whether it was co-administered with carbapenems, and whether it was co-administered with tigecycline) were used for analyzing clinical effectiveness, and two independent variables (whether a loading dose was used, whether it was co-administered with nephrotoxic drugs) for nephrotoxicity

Results A cohort of 54 children was included in study and 24 eligible literature of 259 children were included in literature review. Out of the 54 patients, 53.7% showed favorable clinical responses, while 13.0% died during their hospitalization, and 3.7% died within 30 days after discharge. AKI was observed in 25.9% patients with 11.1% risk stage, 7.4% injury stage and 7.4% failure stage. Among the 54 individuals, 13.0% (7/54) died during their hospital stay, and 3.7% (2/54) died within 30 days after discharge. By individually including each of the three independent variables, the results of logistic regression analysis showed that co-administration with carbapenems was associated with significantly higher effectiveness (odds rate [OR] = 3.16, 95% confidence interval [CI]: 1.02 – 9.86, P = 0.05). But the loading dose (OR = 0.55, 95% CI: 0.18 – 1.72, P = 0.31) and co-administration with tigecycline (OR = 0.83, 95% CI: 0.21 – 3.29, P = 0.79) did not have significantly impact on effectiveness. After simultaneously including all three independent variables, none of them, including loading dose (OR = 0.60, 95% CI: 0.18 – 2.02, P = 0.41), co-administration with tigecycline (OR = 0.67, 95% CI: 0.15 – 2.91, P = 0.59), and co-administration with carbapenems (OR = 3.07, 95% CI: 0.97 – 9.75, P = 0.06), showed significant differences. No patients adjusted the dose of PMB due to AKI. Renal function recovery was observed in 71.42% patients before PMB was discontinued, and one patient recovered renal function one day after PMB was discontinued. Three patients who had progressed to renal failure experienced further deterioration and were eventually discharged, with no additional records available. By individually including each of the two independent variables, the results of logistic regression analysis showed that co-administration with potent diuretic (furosemide) may be a contributing factor that increased the risk of AKI (OR = 4.91, 95% CI: 0.96 – 24.98, P = 0.05) and loading dose was not a contributing factor to AKI (OR = 0.97, 95% CI: 0.27 – 3.47, P = 0.96). When both factors were included in the model for analysis, the results showed that neither of them had a significant impact on AKI (loading dose: OR = 0.93, 95% CI: 0.25 – 3.47, P = 0.92; co-administration with potent diuretic: OR = 4.44, 95% CI: 0.87 – 22.61, P = 0.07). One patient developed erythema after using PMB, and no instances of neurological toxicity was observed. The most reported pathogen in literature was K. pneumoniae (159 cases), followed by the A. baumannii (73 cases), P. aeruginosa (37 cases). The intravenous administration dosage range for PMB was 1.5 – 4.0 mg/kg, while the intrathecal injection range was 0.2 – 0.5 mg/kg. Excluding studies with only one case, the mortality rate in the remaining studies ranged from 6.3% to 42.9%, clinical effectiveness rate ranged from 47.8% to 93.7%, and pathogen clearance rate ranged from 30.8% to 100.0%. Correspondingly, the safety outcomes of nephrotoxicity ranged from 0.0% to 82.4%, neurotoxicity ranged from 0.0% to 17.6%, pigmentation ranged from 0.0% to 7.7%. Other adverse events reported in literature include increased eosinophil count, erythema and papule, and skin desquamation

Conclusion Our study highlighted the importance of PMB in managing MRGN infections in paediatric patients by demonstrating favourable clinical responses and pathogen clearance rates. AKI was also a safety issue that cannot be ignored. Combining PMB with carbapenems may increase clinical effectiveness but combining it with potent diuretics may increase the risk of AKI

关键字：Polymyxin B, Multidrug-resistant Gram-negative Bacteria, Children, Effectiveness, Acute Kidney Injury

Exploring Calcium Channel Blocker As A Candidate Drug for Pseudomonas Aeruginosa Through Network Pharmacology and Experimental Validation

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Objective The network pharmacology was employed to investigate the potential targets and mechanisms of CCB, such as nifedipine, verapamil and diltiazem to inhibit PA, and molecular docking was applied to determine the binding activity between CCB and targets. The possible mechanism of CCB inhibiting PA was revealed at the multi-component, multi-target and multi-channel levels. The experimental results indicated that CCB could inhibit the growth of PA in vitro

Methods The accurate chemical structures of these three drugs were sourced by searching the DrugBank website (Wishart et al., 2018) (https://go.drugbank.com/) and PubChem website (Wang et al., 2010) (https://pubchem.ncbi.nlm.nih.gov/). The chemical structure of the drug 2D was plotted using ChemDraw 20.0 software (Cousins, 2011). The potential channel proteins, efflux pump proteins and ion channel proteins of CCB against bacteria were derived from the literature. Through the Discovery Studio 2019 Client software, the target macromolecules were hydrogenated and the water molecules and ligands were removed. Molecular docking simulation of protein modification was performed by the CB-DOCK platform (Liu et al., 2020) (https://clab.labshare.cn/cb-dock/php/). These proteins were collected through the PDB and Uniprot platform. The binding mode of the docking complexes was simulated by the CB-Dock platform and Discovery Studio 2019 Client software. The PPI network was constructed by the String platform and Cytoscape 3.8.2 platform. GO was explained by the PANTHER platform. The pathway diagram was drawn with the Pathway Builder Tool 2.0 software. The inhibitory effect of CCB on PA was verified through antibacterial experiments

Results Finally, the DrugBank website (https://go.drugbank.com/) and PubChem website (https://pubchem.ncbi.nlm.nih.gov/), the chemical and molecular structural formulas of the three drugs were accurately found and drawn by using the ChemDraw 20.0. The RSCB PDB protein library (https://www.rcsb.org/), UniProt protein database (https://www.uniprot.org/), the membrane channel proteins of PA, proteins related to iron uptake, proteins related to other ion uptake and drug efflux pump proteins of drug-resistant bacteria were found, and the 3D structure of these proteins was downloaded. The 76 proteins were obtained: the iron channel protein of PA demonstrated a good docking relationship with all three CCBs, and the optimum binding energy was approximately -9.0 kcal/mol. GO analysis (biological process [BP], cellular component [CC] and molecular function [MF]) of protein genes showed a good docking relationship (optimum binding energy <-8.0 kcal/mol). The MF annotation results indicated that the target of CCB may be present on the PA membrane protein. The ion channel protein PPI enrichment p-value was 6.65e-08, and PfeA showed the strongest correlation. The experimental results suggested that CCB could inhibit the growth of PA

Conclusion In this paper, network pharmacology and molecular docking technology were employed to predict the potential targets and mechanism of CCB in inhibiting PA. CCB can work on iron channel proteins, drug-efflux channel proteins and OM regulatory proteins of PA, among which the iron-channel protein PfeA is likely to be the receptor protein of CCB in PA. Meanwhile, the inhibitory effect of CCB on PA was further verified by antibacterial experiments. This study provides a theoretical basis for further study on the mechanism of CCB in microorganisms and in exploring new antibacterial strategies

关键字：Calcium channel blocker； experimental verification； network pharmacology； Pseudomonas aeruginosa.

Cryptococcus Neoformans Bloodstream Infection Complicated with Meningitis: A Case Report

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Cryptococcosis is an invasive and opportunistic fungal infection caused by species within the Cryptococcus genus. Despite growing clinical awareness of cryptococcosis, significant challenges persist in its treatment and prevention. This article detailedly describes a case involving Cryptococcus neoformans that caused disseminated infection throughout the body. The patient, a 47-year-old male, was admitted with a complaint of "headache for 18 days, worsening over the past week". Based on blood and cerebrospinal fluid cultures, the patient was diagnosed with Cryptococcus neoformans bloodstream infection, complicated with cryptococcal meningitis. Treatment involved a combination of amphotericin B and 5-fluorocytosine for antifungal therapy, along with potassium supplementation, intracranial pressure reduction, and nutritional support. Following 22 days of treatment, the patient exhibited improvement and was subsequently discharged. Early identification and diagnosis of Cryptococcus infections are crucial, and healthcare providers should remain vigilant for infections in patients without predisposing factors and present with nonspecific symptoms. Early intervention significantly enhances patient prognosis.

1 INTRODUCTION

Cryptococcus is extensively distributed worldwide and can survive in various environments, including soil, air, water, decaying wood, and bird excrement [1]. Cryptococcosis is an invasive and opportunistic fungal infection arising from pathogenic species within the Cryptococcus genus. The primary manifestation is cryptococcal meningitis, followed by pulmonary and bloodstream infections [2-3]. Symptoms of cryptococcal meningitis involve neurological manifestations such as headaches, nausea, and vomiting, imposing a significant burden on the affected individuals. Additionally, pulmonary infections may present with respiratory symptoms, including cough, shortness of breath, and chest pain. And bloodstream infections involve multiple organ systems, eliciting systemic symptoms such as high fever, weakness, and weight loss. Cryptococcosis is highly correlated to the status of the immune system, making immunocompromised patients more susceptible to infection. Nevertheless, individuals with normal immune function can also get infected. Therefore, a profound understanding of the diverse manifestations and potential risk factors associated with Cryptococcus infection is crucial for a comprehensive grasp of the disease and for providing enhanced medical care. This article meticulously details a case of a non-immunocompromised patient involving Cryptococcus neoformans bloodstream infection complicated with meningitis. After undergoing a regimen of combined antifungal therapy, the patient's condition significantly improved. The purpose of reporting this case is to enhance the diagnostic and therapeutic proficiency of healthcare professionals in managing such diseases and to fortify the overall comprehension of cryptococcosis.

2 CASE REPORT

The Patient is a 47-year-old male admitted for "headache for 18 days, worsening over the past week." The headache, which started without an apparent cause 18 days ago, presented as a continuous dull pain in the crown, forehead, and occipital region, accompanied by nausea and vomiting. There were no associated symptoms of fever, altered consciousness, seizures, or abnormal behavior. One week before admission, the symptoms intensified, characterized by explosive-like pain throughout the entire brain. A previous brain MRI conducted at a local hospital a week ago revealed no significant abnormalities. Despite symptomatic treatment, there was no notable improvement. For further diagnosis and treatment, the patient was admitted with a provisional diagnosis of "intracranial infection." The patient had a history of a left femoral fracture owing to a car accident ten years ago, which was managed with internal fixation surgery.

Upon admission, the patient presented with a body temperature of 37.4°C, a respiratory rate of 20 breaths per minute, a pulse rate of 59 beats per minute, and a blood pressure of 131/81 mmHg. Physical examination of the heart, lungs, chest, and abdomen revealed no abnormalities. Neurological examination showed positive tendon reflexes, neck stiffness, and a positive Kernig sign, with no other abnormalities noted. Complete blood count results were as follows: white blood cell count 8.81 × 10^9/L, hemoglobin concentration 140 g/L, platelet count 168 × 10^9/L. Clinical biochemistry results included potassium 3.40 mmol/L, sodium 126.5 mmol/L, chloride 93.4 mmol/L, urea 3.55 mmol/L, creatinine 38.97 μmol/L. The concentration of C-reactive protein was 6.4 mg/L, procalcitonin was 0.09 ng/mL, and the HIV test was negative. Cerebrospinal fluid analysis revealed a white blood cell count of 90.00 × 10^6/L, with 37.0% polymorphonuclear cells and 63.0% lymphocytes. The Pandy test showed weakly positive results. Biochemical analysis of cerebrospinal fluid showed glucose at 0.31 mmol/L, chloride at 112.3 mmol/L, and total protein concentration at 669 mg/L. Cerebrospinal fluid smear revealed encapsulated spores through India ink staining (Figure 1A). The cerebrospinal fluid pressure exceeded 330 mm of water. Brain MRI results showed slight punctate hemorrhages in both frontal lobes.

关键字：Cryptococcus neoformans; Bloodstream infection; Cryptococcal meningitis; Clinical prognosis

1 例鹦鹉热衣原体重症肺炎患者的病例分析

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目的 旨在通过回顾性分析 1 例鹦鹉热衣原体肺炎患者的诊治过程，为临床早期诊断和治疗提供思路。

方法 患者 65 岁男性，2023 年 6 月 30 日以“发热 9 天”收住呼吸与危重症医学科，入院时诊断重症肺炎，经验性用药：美罗培南 1.0g Q8H 联合莫西沙星 0.4g Qd 静脉点滴，后 BALF NGS 回报鹦鹉热衣原体（序列数 252），临床药师建议调整抗生素为米诺环素 100mg Q12H 口服联合莫西沙星 0.4g Qd 静脉点滴，临床予以采纳。

结果 调整抗感染药物为米诺环素联合莫西沙星联合治疗后患者体温降至正常，PCT、CRP 等感染指标、氧合情况好转，2023 年 7 月 4 日患者出院。

结论 目前鹦鹉热衣原体未纳入常规临床实验室筛查，容易误诊漏诊。因此，建议对 CAP 患者进行更频繁的检测，尤其是有鸟类接触史等高危因素时，以减少诊断缺陷和确定性不足。

关键字：鹦鹉热衣原体；重症肺炎；病例分析

Successful Treatment of Pulmonary Mucormycosis with Amphotericin B Deoxycholate, Isavuconazole, and Surgical Debridement

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Abstract Mucormycosis is a severe infectious disease caused by fungi of the order Mucorales, with pulmonary mucormycosis being the most common and destructive form. Herein, we present the case of a 41-year-old male patient with diabetes mellitus complicated by pulmonary mucormycosis. After initial treatment failure with mucor-targeted therapy, a successful salvage treatment was achieved through the combination of liposomal amphotericin B, deoxycholate, and isavuconazole, along with surgical debridement. The purpose of this report is to discuss the formulation and adjustment of salvage treatment strategies in cases where initial treatment fails due to multiple contributing factors. His favorable outcome not only provides a method for improving drug tolerance but also serves as an experiential reference for the combined use of polyenes and triazoles in antifungal therapy.

Categories: Internal Medicine, Infectious Disease

Introduction Mucormycosis, caused by fungi of the order Mucorales, is a severe infectious disease characterized by tissue destruction. It commonly occurs in immunocompromised patients, such as those with diabetes, undergoing chemotherapy or immunotherapy for malignant tumors, solid organ transplantation, or neutropenia. The disease is highly dangerous and progresses rapidly, with a mortality rate ranging from 40% to 80%. Pathogenic fungi of the order Mucorales primarily include Rhizopus, Lichtheimia, and Mucor species, with Rhizopus arrhizus being the most common . Opportunistic pathogens, these fungi possess spores that exhibit potent vascular invasiveness. They can directly infect the skin, respiratory tract, gastrointestinal tract, and other sites through inhalation, ingestion, or trauma. Furthermore, they can disseminate and affect the bones, central nervous system, etc. Among the infections caused by Mucorales, pulmonary mucormycosis (PM) and rhino-orbital-cerebral mucormycosis (ROCM) are the most common and destructive

The treatment principles for mucormycosis include actively managing underlying diseases, systemic antifungal therapy, and early surgical intervention when conditions permit. Systemic antifungal therapy can be further divided into first-line monotherapy, first-line combination therapy, sequential therapy when initial treatment is effective, and salvage therapy when initial treatment fails . Particularly, the development of a safe and effective salvage treatment plan presents a significant challenge for clinicians in cases of initial treatment failure.

Here, we report a case of a patient with newly diagnosed diabetes who developed pulmonary mucormycosis infection. We focus on exploring salvage antifungal treatment strategies for patients who experience initial treatment failure due to factors such as drug intolerance and refractory mucormycosis infection.

Conclusions In light of the above, we present a successful case of treating PM, where complete control of the infection in the patient may be attributed to early diagnosis, prompt initiation of antifungal therapy, timely and effective salvage treatment, and complete surgical excision. In this case, an innovative salvage treatment plan was formulated based on clinical response titration, given the unknown cause of initial treatment failure in PM. Two exploratory interventions were conducted during the course of treatment to improve outcomes. For cases of primary treatment failure due to drug intolerance, it may be possible to enhance drug tolerance by modifying drug formulations, routes of administration, or even combining systemic and local administration of the same drug. Moreover, for refractory or breakthrough fungal infections leading to initial

treatment failure, the experience of safely and effectively combining polyenes with azoles provides a new perspective for subsequent decisions on salvage therapy

关键字：pulmonary mucormycosis, amphotericin B, isavuconazole, rhizopus arrhizus, mucormycosis

Investigating The Mechanism of Action of Novel Copper-containing Ferrite Nanoparticles Against Methicillin-resistant Staphylococcus Aureus Through Proteomics and Transcriptomics

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Objective The treatment of methicillin-resistant Staphylococcus aureus (MRSA) infection is posing a significant challenge to global public health. Metallic nanoparticles have opened up new avenues for enhancing antimicrobial efficacy and reducing resistance rates. This study aimed to investigate the antimicrobial activity and mechanism of action of novel copper-containing ferrite nanoparticles (Cu@Fe NPs) against MRSA

Methods The kinetics of the antibacterial activity of Cu@Fe NPs in combination with the conventional antibiotics ampicillin (Amp) and gentamicin (Gen) were tested using checkerboard assay and time-kill curves, and the antibacterial activity of Cu@Fe NPs synergized with Amp or Gen was verified by propidium iodide (PI)/SYTO9 bacterial dead/alive stained fluorescent pictures. Activity

Bone Marrow-Derived Macrophage (BMDM) cells from C57BL/6 mice were cultured in vitro, and the cells were infected with FITC fluorescently labeled MRSA strains and given different concentrations of Cu@Fe NPs, and fluorescence co-localization was detected by confocal laser scanning microscopy, and the droplet dish was tested for bacterial loading of CFUs. RT-qPCR detected inflammatory cytokine changes after cell collection.

4D-Label-free quantitative proteomics and prokaryotic transcriptomics were applied to analyze the effects of sub-MIC (0.5 ug/ml) Cu@Fe NPs treatment on MRSA.

Results Low doses of Cu@Fe NPs could re-sensitize MRSA to Amp and Gen. The combination of 1/8 MIC Cu@Fe NP and 1/4 MIC Amp, and 1/8 MIC Cu@Fe NP and 1/4 MIC Gen could significantly inhibit the growth of MRSA, which provided new ideas for the treatment of MRSA infection

After using Cu@Fe NPs to remove MRSA cells from the supernatants of the BMDM infection model, the number of viable bacteria in macrophages decreased significantly with time. In addition, Cu@Fe NPs decreased the expression of inflammatory cytokines TNF-α, IL-1β, TGF-β, and chemokine MCP-1 mRNA transcripts in MRSA-treated BMDM, effectively attenuating MRSA's inflammatory infiltration into BMDM.

A total of 2436 proteins were identified by MRSA proteomics before and after treatment with Cu@Fe NPs. A total of 553 proteins were significantly differentially regulated by MRSA. Of these, 281 (50.8%) were upregulated and 272 (49.2%) were downregulated. Transcriptome analysis identified a total of 2,731 genes, and 847 genes were significantly differentially expressed, of which, 420 genes were up-regulated and 427 genes were down-regulated. Functional analyses showed that Cu@Fe NPs were able to interfere with multiple targets, promote oxidative stress disrupt metal-iron ion homeostasis in bacteria, and disrupt nucleotide, amino acid, carbohydrate, and energy metabolism leading to MRSA cell death.

Conclusion Overall, Cu@Fe NPs are important for the clinical development of novel antimicrobials and for slowing down the spread of drug-resistant bacteria

关键字：MRSA，Cu@Fe NPs，antibiotic synergy，antimicrobial mechanism，proteomics，transcriptomics

Real-world Study of Effectiveness and Safety Compared Among Isavuconazole, Amphotericin B, and Voriconazole in Invasive Mold Disease Patients

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Objective Isavuconazole (ISA) emerges as a novel triazole, exhibiting a broad spectrum of antifungal activity. Within the antifungal arsenal, Amphotericin B (AMB) and voriconazole (VCZ) stand as pivotal components. However, a comprehensive assessment of the effectiveness and safety of these three drugs in invasive mold disease (IMD) remains elusive

Methods A real-world investigation into the comparative effectiveness and safety of ISA, AMB, and VCZ in patients with IMD transpired from October 2019 to March 2022 at the First Affiliated Hospital of Guangzhou Medical University. This study encompassed IMD patients subjected to treatment with ISA, AMB, or VCZ. The scrutiny involved testing the non-inferiority of the primary efficacy endpoint—comprising all-cause mortality from the initial dose of the study drug to day 42. The Wilcoxon and Kruskal–Wallis rank-

sum tests were also used. Concurrently, safety evaluations were conducted in patients who received the inaugural dose of the study drugs

Results A total of 299 IMD patients were included, including 40 patients in the ISA group, 33 patients in the AMB group, and 226 patients in the VCZ group(Table 1, Figure 1). The 42-day all-cause mortality was 5% in the ISA group, 24% in the AMB group, and 13% in the VCZ group (ISA vs. AMB: treatment difference 19.24% [95% CI 2.36 to 36.12%]; p<0.001. ISA vs. VCZ: treatment difference 7.83% [95% CI –5.47 to 21.13%]; p=0.004. VCZ vs. AMB: treatment difference 11.41% [95% CI 1.02 to 21.8%]; p<0.001)(Table 2, Figure 2). These three groups exhibited significant differences in 42-day and 84-day all-cause mortality in the Kruskal–Wallis rank-sum test (P=0.033 and P=0.048, respectively) (Table 3). Patients who had lower adverse event rates of renal and urinary disorders (8%) and liver disorders (8%) received ISA(Figure 3)

Conclusions ISA and VCZ were superior to AMB in IMD patients, whereas ISA was non-inferior to VCZ in IMD patients. ISA produced a positive therapeutic response and had an acceptable safety profile

关键字：invasive mold disease， isavuconazole，amphotericin B，voriconazole，noninferior; effectiveness and safety

CD5L 在念珠菌血症患者血清中的水平升高并加重模型小鼠的病情

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目的 检测 CD5L 水平在念珠菌血症患者中的变化，并研究 CD5L 对念珠菌血症疾病发展的作用。

方法 选取健康对照者 20 例，细菌血症患者 27 例和念珠菌血症患者 35 例，ELISA 检测各组血清中的 CD5L 水平。分析 CD5L 水平与患者血清中感染及肾损伤指标之间的相关性。尾静脉注射白色念珠菌至 C57BL/6 小鼠，构建念珠菌血症小鼠模型。腹腔注射 CD5L 蛋白，利用组织病理及血清学检测分析小鼠模型肾损伤，检测肾脏菌载量，统计小鼠生存率，分析 CD5L 处理对念珠菌血症小鼠病情的影响。ELISA 检测 CD5L 处理对念珠菌血症小鼠血清 IL-6 及 IL-8 水平的影响。

结果 与健康对照及细菌感染患者相比，念珠菌血症患者血清 CD5L 水平显著升高（P<0.01），且 CD5L 水平与白细胞数（WBC）、1, 3-β-D-葡聚糖（BDG）、肌酐（Scr）和降钙素原（PCT） 水平呈正相关。与正常小鼠相比，念珠菌血症小鼠血清及肾脏 CD5L 水平显著升高（P<0.01）。腹腔注射 CD5L 蛋白可以显著上 调念珠菌血症小鼠肾组织菌载量，促进小鼠表达炎症因子 IL-6 和 IL-8，加重小鼠肾脏损伤，降低小鼠生存率（P<0.05）。

结论 血清 CD5L 水平在念珠菌血症患者中升高，CD5L 加重念珠菌血症小鼠病情。

关键字：念珠菌血症；CD5L；炎症；肾损伤

CYB2- Knockout Saccharomyces Cerevisiae with Broad-spectrum Antimicrobial Activity Via Lactic Acid Accumulation

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Bacterial infectious diseases seriously threaten human health, and the rational use of antibiotics is an effective means of treating and controlling such diseases. However, countries around the world are facing the threat of a marked increase in drug resistance among pathogenic bacteria. Probiotics have attracted widespread interest in recent years as a treatment for pathogenic bacterial infectious diseases. In this study, we determined that CYB2-knockout (CYB2-KO) Saccharomyces cerevisiae can exert effective antibacterial activity. The MIC, growth curve, bacteriostatic spectrum and co-culture experiment all showed an effectively inhibitory effect on the growth of pathogens. Meanwhile, it can effectively inhibit the formation of Escherichia coli and Staphylococcus aureus biofilms. In addition, it exhibits low hemolytic activity, acid resistance, resistance to high bile salt concentrations, high Auto-aggregation capacity, and high Co-aggregation capacity with pathogenic bacteria. Moreover, the survival time of infected larvae was significantly prolonged under the treatment of CYB2-KO S. cerevisiae in Galleria mellonella-E. coli (in vivo) and G. mellonella-S. aureus (in vivo) infection models. The mouse model of urinary tract infection suggested that CYB2-KO S. cerevisiae reduced the bacterial load in the bladder of mice. In addition, the mouse enteritis model also showed that CYB2-KO S. cerevisiae could alleviate systemic symptoms and prolong the survival time of mice by reducing the bacterial load in the intestinal tract. Further, mechanism research revealed that CYB2-KO S. cerevisiae produced lactic acid by metabolism, which reduced the pH of the environment and thus inhibited the growth of pathogenic bacteria. In a word, this study showed the potential probiotic effects of CYB2-KO S. cerevisiae with broad-spectrum antibacterial activity in vitro and in vivo and low toxicity, which provides a probiotic candidate, CYB2-KO S. cerevisiae, for clinical prevention and control of bacterial infection.

关键字：Probiotic，Saccharomyces cerevisiae，Multidrug resistant pathogens，Broad-spectrum antibacterial activity，Antimicrobial metabolites

慢性肾脏病合并耶氏肺孢子菌肺炎患者的临床及预后特征

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目的 探讨慢性肾脏病合并耶氏肺孢子菌肺炎（Pneumocystis jirovecii pneumonia，PJP）患者临床及预后特征，为该类感染诊治提供依据

方法 对 22 例病原宏基因组二代测序（Metagenomic next-generation sequencing，mNGS）检出耶氏肺孢子菌并临床诊断为耶氏肺孢子菌肺炎的病例进行回顾性分析

结果 2019 年 10 月-2023 年 10 月共 22 例患者检出耶氏肺孢子菌的同时临床诊断为耶氏肺孢子菌肺炎，其中男性 6 例（27.3%），女性 16 例（72.7%），平均年龄为 57 岁，主要基础疾病为膜性肾病，IgA 肾病，狼疮性肾炎，ANCA 相关性肾炎。15 例（68.2%）患者 PJP 发生在肾病确诊后 1 年内。16 例（72.7%）患者发生I型呼吸衰竭。所有患者在感染前 3 个月内使用糖皮质激素或免疫抑制剂。肺部 CT 表现包括主要表现为磨玻璃为主的混合型和斑片/结节型（81.8%）。所有患者乳酸脱氢酶均升高。18 例（81.8%）患者（1,3）-β-葡聚糖（BG）检测阳性。16 例（72.7%）患者淋巴细胞绝对值偏低。CD4 细胞计数均值为 292.3 个/μl，其中 60.0%患者 CD4 细胞计数<200 个/μl。入院血肌酐均值 232.0μmol/L，其中 15 例（68.2%）患者发生急性肾损伤，需要透析 12 例（54.5%）。血浆是最常见的耶氏肺孢子菌检出的样本类型，其次为肺泡灌洗液和痰。92.3%的标本检测出多种病原微生物。常见检出合并病原菌为巨细胞病毒和细菌。22 例均进行了抗 PJP 治疗，16 例（72.7%）患者因 mNGS 结果调整了治疗用药。复方磺胺甲恶唑平均剂量为 11.0 mg·kg-1·d-1（以甲氧苄啶计）。10 例（45.5%）需要机械通气，14 例（63.6%）治愈，8 例（36.4%）死亡。与治愈组相比，死亡组入院时口服激素剂量较大（28.6mg vs 18.1mg，P=0.039），需要透析（87.5% vs 35.7%，P=0.031），需要机械通气（87.5% vs 21.4%，P=0.006）人数较多。

结论 肾病患者耶氏肺孢子菌的临床感染诊断需结合临床症状、影像及实验室检查，病原宏基因组二代测序可为该类感染提供病原学证据支持以辅助指导肺孢子菌肺炎的治疗。长期口服激素剂量大，需要透析、需要机械通气是 PJP 患者预后不佳的危险因素。

关键字：耶氏肺孢子菌；宏基因组二代测序；肾病；免疫抑制剂

新型 β-内酰胺酶抑制剂 FL058 提高亚胺培南对脓肿分枝杆菌的体外抗菌活性

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目的 脓肿分枝杆菌复合群（MABC）感染治疗极具挑战性，β-内酰胺类药物是抗 MABC 治疗的关键。然而，MABC 通过生成 A 类广谱 β-内酰胺酶（BlaMab）来水解 β-内酰胺类药物，从而产生耐药性。二氮杂双环辛烷类 β-内酰胺酶抑制剂（DBO BLIs）可以有效抑制 BlaMab，FL058 是一种新型 DBO BLI，其与 β-内酰胺类药物联用对 MABC 的活性尚不清楚。

方法 采用肉汤微量稀释法测定 10 种 β-内酰胺类药物（亚胺培南、美罗培南、法罗培南、替比培南、头孢西丁、头孢吡肟、头孢他啶、头孢地尼、头孢呋辛和阿莫西林）与 3 种 DBO BLIs（FL058、阿维巴坦和瑞来巴坦）联合对 MABC 标准菌株的抗菌活性。同时评估了亚胺培南与 FL058、阿维巴坦或瑞来巴坦联用对 193 株 MABC 临床菌株的抗菌活性。通过测定杀菌时间曲线和巨噬细胞内增殖情况，对亚胺培南、亚胺培南-FL058、亚胺培南-阿维巴坦和亚胺培南-瑞来巴坦之间的活性进行比较。

结果 FL058、阿维巴坦和瑞来巴坦显著提高 β-内酰胺类（尤其是亚胺培南）对 MABC 标准菌株的抗菌活性。加入 4mg/L 的 FL058 后，亚胺培南对临床菌株的 MIC50 从 32mg/L 降至 4mg/L。亚胺培南-FL058 的抗菌活性（MIC50=4mg/L，MIC90=16mg/L）优于亚胺培南-阿维巴坦（MIC50=4mg/L，MIC90=32mg/L）和亚胺培南-瑞来巴坦（MIC50=8mg/L，MIC90=64mg/L）。细胞内存活实验表明，FL058 提高了亚胺培南的细胞内抗菌活性。

结论 FL058 明显提高亚胺培南对 MABC 的体外抗菌活性，亚胺培南-FL058 可能是治疗 MABC 感染的候选新药。

关键字：FL058，二氮杂双环辛烷类 β-内酰胺酶抑制剂，脓肿分枝杆菌复合群，β-内酰胺类

Polymyxin B Combined with Cefepime-avibactam Against PolymyxinB-resistant and

Carbapenem-resistant Klebsiella Pneumoniae : Assessment of In Vitro and In Vivo Efficacy

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Objective Therapeutic options for infections caused by polymyxin B-resistant and carbapenem-resistant Klebsiella pneumoniae (CRKP) are currently suboptimal. Combination regimens with novel β-lactam–β-lactamase inhibitor combinations and a polymyxin are emerging given the proven synergistic potential. The current study was performed to evaluate the in vitro and in vivo efficacy of polymyxin B and cefepime-avibactam alone and in combination against polymyxin B-resistant CRKP

Methods Five polymyxin B-resistant CRKP clinical isolates were used for all experiments. The mutated sites of polymyxins resistance genes phoP, phoQ, pmrA, pmrB and mgrB were confirmed by PCR-sanger sequencing method. The in vitro dynamic PK/PD model and the the galleria mellonella larvae infection model were used to examine the activity of polymyxin B, cefepime-avibactam and in combination

Results The mutation sites of polymyxin-B resistant genes in the test isolates were the missense mutations G53C of pmrA and T157P of pmrB, and the insertion sequences of mgrB gene ISKpn14, IS903B and ISKpn26. The results of in vitro dynamic pharmacokinetic/pharmacodynamic (PK/PD) model study showed that polymyxin B combined with cefepime-avibactam showed a good synergistic bactericidal effect. Regarding the in vivo galleria mellonella larvae infection model, the co-administration of polymyxins B and cefepime-avibactam (intermediate concentration) could significantly improve the survival rate of the larvae infected with strains CSPZ-01 and 1128-76 ($p<0.05$)

Conclusion Polymyxin B in combination with cefepime-avibactam could be a potential clinical option for clinical treatment of infections caused by polymyxin B -resistant CRKP

关键字：Polymyxin B; Cefepime-avibactam; Polymyxin B-resistant CRKP; combination;in vitro; in vivo

Machine Learning and Deep Learning Based Prediction of 28-Day Mortality in Sepsis Patients with Gram-Negative Bacteria Infection: Evaluating The Impact of Antimicrobial De-escalation Therapy

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Objective This study employs machine learning to develop predictive models for assessing the impact of antimicrobial de-escalation (ADE) therapy on 28-day mortality

Methods We included adult sepsis patients with Gram-negative bacteria(GNB) infection from MIMIC-III and MIMIC-IV, excluding short-stay or incomplete data cases

Results A total of 2,628 patients were included in this study. Random Forest (RF) and Logistic Regression (LR) achieved an area under receiver operating characteristic curves(AUC) of 0.80, while XGBoost(XGB) and Multi-Layer Perceptron (MLP) showed robust performance with an AUC of 0.81. Across the entire dataset (MIMIC-III and MIMIC-IV), RF consistently outperformed other models with AUC of 0.916 (sensitivity 0.919, specificity 0.912). Calibration, assessed by Brier's Score and Calibration Curve, revealed favorable calibration for LR (Brier's Score = 0.150), slight deviation for XGB (Brier's Score = 0.155), and reasonable calibration for RF (Brier's Score = 0.153) and MLP (Brier's Score = 0.151). Clinical decision curve analysis highlighted RF's consistently superior clinical utility

Conclusion In conclusion, our study not only developed robust machine learning models for predicting 28-day mortality in sepsis patients with GNB infection but also provided valuable insights into assessing the impact of ADE therapy on 28-day mortality

关键字：sepsis, antimicrobial de-escalation, Gram-negative bacteria infection, 28-day mortality,machine learning

香芹酚抑制高毒力肺炎克雷伯菌生物被膜形成机制的研究

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目的 为探究香芹酚抑制高毒力肺炎克雷伯菌生物被膜形成的潜在作用机制。

方法 采用结晶紫染色法评价亚抑菌浓度的香芹酚对高毒力肺炎克雷伯菌生物被膜形成的影响；SEM观察香芹酚对高毒力肺炎克雷伯菌生物被膜形态学的影响；刚果红吸附试验与间羟基联苯比色法测定香芹酚对高毒力肺炎克雷伯菌胞外多糖及荚膜

多糖含量的改变；荧光定量 PCR 分析香芹酚干预后生物膜相关基因 rmpA2、magA、mrkA、mrkB、treC 表达量变化。

结果 香芹酚对高毒力肺炎克雷伯菌的最小抑菌浓度为 512ug·mL-1，且对该菌生物被膜形成有明显的抑制作用，其效应呈浓度依赖性；扫描电镜下观察到香芹酚干预状态下生物被膜结构松散、细胞之间连接不致密；刚果红吸附试验与间羟基联苯比色法测定表明香芹酚可降低高毒力肺炎克雷伯菌荚膜多糖含量而不影响胞外多糖总含量；荧光定量 PCR 显示亚抑菌浓度香芹酚作用下，有关荚膜多糖合成、糖转运系统以及菌毛粘附相关基因表达量变化明显下降。

结论 香芹酚对高毒力肺炎克雷伯菌生物被膜形成具有明显的抑制作用，其机制可能与降低细菌荚膜多糖合成、糖转运系统以及菌毛粘附等生物被膜相关基因的表达有关。

关键字：香芹酚；高毒力肺炎克雷伯菌；生物被膜；荧光定量

伏立康唑与奈玛特韦/利托那韦相互作用的临床回顾性分析

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目的 本文通过伏立康唑 TDM 探索奈玛特韦/利托那韦对伏立康唑谷浓度的影响，以指导两药联用时的方案调整。

方法 收集 2023 年 1 月-2023 年 8 月我院收治的联用伏立康唑和奈玛特韦/利托那韦且进行伏立康唑 TDM 的病例，汇总患者的一般资料、伏立康唑给药方案、其他合并用药及伏立康唑 TDM 结果。

结果 共纳入 10 例病例，5 例同时联用伏立康唑与奈玛特韦/利托那韦，5 例先后使用两药，两组谷浓度达标率均为 60%，且谷浓度分布没有差异。联用组中，3 例患者在联用/停用奈玛特韦/利托那韦前后分别测定伏立康唑谷浓度，谷浓度未发生明显变化。

结论 联用伏立康唑和奈玛特韦/利托那韦未对伏立康唑谷浓度产生明显影响，两药可在伏立康唑 TDM 下联合使用。

关键字：伏立康唑；奈玛特韦/利托那韦；治疗药物监测；药物相互作用

Anti-virulence and Bactericidal Activities of Stattic Against Shigella Sonnei

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Objective The purpose of this study is to screen and develop new antivirulent compounds that can inhibit the virulence of Shigella sonnei

Methods The biofilm assay was used for screening the compounds which can inhibit pathogenic phenotype of Shigella sonnei

Results We discovered that Stattic a potent signal transducer and activator of transcription 3 inhibitor, displayed strong antimicrobial activity against S. sonnei. Our results showed that Stattic has dual antibacterial mechanisms. At low concentrations, Stattic binds to GalU of S. sonnei, inhibits its enzyme activity, and then reduces biofilm formation and extracellular polysaccharide production, which ultimately attenuates S. sonnei virulence in human cell lines. At high concentrations, Stattic could kill bacteria by disrupting the integrity of the bacterial cell membrane, causing space collapse and the outflow of contents. Furthermore, Stattic showed excellent synergistic effects with antibiotics against S. sonnei

Conclusion In this study, we demonstrated that Stattic employs two antibacterial mechanisms against S. sonnei. It exerted both anti-virulence activity and bactericidal activity against S. sonnei, suggesting that it shows advantages over traditional antibiotics. Moreover, Stattic showed excellent synergistic effects with ampicillin against S. sonnei. Our findings suggested that Stattic has promising potential for development as a new antibiotic or as an adjuvant to antibiotics for infections caused by S. sonnei

关键字：Shigella sonnei, Stattic, biofilm, antibiotic, virulence

尼可地尔拮抗多粘菌素 E 抗菌活性机制的初步探究

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目的 目前细菌耐药问题越来越严重，多粘菌素 E 被认为是治疗耐药菌感染的最后一道防线。本研究旨在探究尼可地尔拮抗多粘菌素 E 杀伤多重耐药肺炎克雷伯菌的作用机制。本研究提示治疗被多重耐药肺炎克雷伯菌感染的心血管病患者时，若该患者服用尼可地尔，应慎用多粘菌素 E。

方法 （1）使用飞行时间质谱系统 Clin-TOF-II 鉴定 40 株多重耐药的肺炎克雷伯菌菌株；（2）用微量肉汤稀释法测多粘菌素 E 对肺炎克雷伯菌的最

低抑菌浓度（MIC）；（3）用快速时间-杀菌实验及生长曲线测定实验验证多粘菌素 E 和尼可地尔联合使用的效果；（4）实时荧光定量 PCR（qRT-PCR）检测介导氧化应激的调控基因，两个超氧化物歧化酶编码基因 sodA、sodC 和两个过氧化氢酶编码基因 katE、katG 的相对表达水平，并分析其表达情况；（5）通过检测 ROS 累积情况，验证多粘菌素 E 联合尼可地尔的抗菌机制；（6）构建肺炎克雷伯菌诱导的小鼠肺感染损伤模型，证明尼可地尔-多粘菌素 E 对肺炎克雷伯菌的联合杀菌效果。

结果 （1）多粘菌素 E 联合尼可地尔杀菌时，40 株多重耐药肺炎克雷伯菌中的 11 株在快速时间-杀菌实验中尼可地尔增加了肺炎克雷伯菌的生长，菌株 GN191034 中尼可地尔的拮抗效果最明显，并用生长曲线测定实验进行了验证；（2）qRT-PCR 实验，结果表明其 sodA、sodC、katE、katG 的表达水平显著下调；（3）通过 RNS 检测表明尼可地尔通过释放 NO 拮抗多粘菌素 E 的抗菌活性；（4）ROS 检测发现多粘菌素 E 单独作用时肺炎克雷伯菌胞内 ROS 的积累显著增加，联合尼可地尔共同作用时 ROS 的积累显著减少；（5）构建肺炎克雷伯菌小鼠肺炎模型实验，通过小鼠肺部肺炎克雷伯菌感染组织细菌负荷情况和病理学结果验证尼可地尔-多粘菌素 E 治疗可加剧肺炎克雷伯菌引起的肺部炎症。

结论 尼可地尔对多粘菌素 E 对肺炎克雷伯菌的抗菌活性有显著影响，可能是其通过释放一氧化氮产生芬顿反应可显著抑制多粘菌素 E 的氧化应激作用，进而拮抗多粘菌素 E 对肺炎克雷伯菌的抗菌活性。

关键字：肺炎克雷伯菌；耐药性；多粘菌素 E；一氧化氮供体药物；氧化应激

Effectiveness of Combination Therapy with Intrathecal Or Intraventricular Administration of Polymyxin B for Hospital-acquired Central Nervous System Infections Caused by Carbapenem-resistant Acinetobacter Baumannii: A Retrospective Study

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Objectives To evaluate the therapeutic regimen, efficacy and safety of intrathecal or intraventricular (ITH/IVT) administration of polymyxin B for hospital-acquired central nervous system (CNS) infections caused by carbapenem-resistant Acinetobacter baumannii (CRAB)

Methods A retrospective study was performed on patients with CNS infections caused by CRAB treated with ITH/IVT combination therapy. The primary study outcome was the clinical efficacy after treatment. Secondary outcomes were bacterial clearance rate and safety of therapy

Results In total, 35 episodes who received ITH (13 [37.1%]) or IVT (22 [62.9%]) polymyxin B as combination therapy were included. The median duration of ITH/IVT polymyxin B therapy was 9 days (interquartile ranges, 7-11). The overall clinical cure and bacterial clearance rate was 77.1% and 85.7%, respectively. No adverse effects deemed related with ITH/IVT polymyxin B were recorded. Clinical failure was independently associated with the initial Acute Physiology and Chronic Health Evaluation II (≥ 15) (odds ratio [OR], 1.24; 95% confidence interval [CI]: 1.05-1.42; P = 0.038) and Glasgow Coma Scale scores (≤ 8) (OR, 0.69; 95% CI: 0.49-0.88; P = 0.029). Early administration (within 4 days) of ITH/IVT polymyxin B therapy can support significantly higher clinical cure rate (OR, 0.65; 95% CI: 0.49-1.12; P < 0.001), and potentially reduce the length of treatment and the adverse effects

Conclusions ITH/IVT administration of polymyxin B is a valid alternative for the treatment of CNS infections caused by CRAB. Early use of ITH/IVT polymyxin B can lead to higher clinical success

关键字：polymyxin B; intracranial infection; intrathecal; intraventricular; carbapenem-resistant Acinetobacter baumannii

3-Diethylaminopropyl Isothiocyanate Modified Glycol Chitosan for Constructing Mild-acid Sensitive Electrospinning Antibacterial Nanofiber Membrane

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Objective Bacterial infections would cause pathological inflammation and even generate chronic wound

Methods Herein, a ciprofloxacin (Cip)-loaded mild acid-responsive electrospinning nanofiber membrane (NFM) containing 3-diethylaminopropyl isothiocyanate material grafted glycol chitosan (GC-DEAP) was fabricated to prevent bacterial infection against hemostatic and inflammatory phases of wounds

Results The presence of Cip and GC-DEAP in the objective NFM (PCL/GC-DEAP/Cip) was confirmed through XRD and FTIR. Meanwhile, PCL/GC-

DEAP/Cip NFM exhibited high mechanical profiles, suitable water absorption and water vapour transmission ratio. The nonprotonated amphiphilic GC-DEAP under pH 7.4 facilitated the formation of uniform and smooth nanofibers with polycaprolactone (PCL) and Cip. However, the GC-DEAP was demonstrated to sharply respond to the mildacid environment of the wound and effectively be protonated, and thus improved the swelling ability of NFM and triggered burst release of Cip. Due to the combination between protonated GC-DEAP and Cip, PCL/GC-DEAP/Cip NFM achieved attractive antibacterial activity in the mild-acid environment in vitro, and induced more efficient prevention of wound infection and faster wound healing compared with the commercial chitosan dressing

Conclusion The designed NFM is expected to be a potential smart wound dressing against hemostatic and inflammatory phases with mild-acid specifically strengthened antibacterial features and satisfactory biocompatibility

关键字：Electrospinning，3-Diethylaminopropyl isothiocyanate，pH-responsive，Ciprofloxacin，Antibacterial wound dressing

按蚊伊丽莎白菌相关性脑膜炎患儿的药学分析与监护

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目的 按蚊伊丽莎白菌从属于伊丽莎白菌属，在 2011 年才首先报道从冈比亚按蚊中分离出来，为一类需氧、非发酵革兰阴性杆菌，从此以后便不断有文献报道该细菌会导致脑膜炎、脓毒血症等严重感染。由于按蚊伊丽莎白菌所致感染临床并不常见，少有文献报道，但却可致严重感染，因此本文旨在探讨按蚊伊丽莎白菌相关性脑膜炎治疗方案的制定与药学监护，为相关疾病的治疗和药学服务提供经验

方法 临床药师回顾参与 1 例 11 岁 7 月的神经外科术后患儿，在美罗培南使用期间再次出现高热，脑脊液性状及常规提示脑膜炎，脑脊液及血细菌培养提示为按蚊伊丽莎白菌，由于目前缺乏该细菌的药物敏感性试验参考标准，因此本中心未做药物敏感性试验。临床药师通过查阅文献发现按蚊伊丽莎白菌对多数 β-内酰胺类药物敏感性低，对米诺环素、左氧氟沙星、头孢哌酮-舒巴坦以及万古霉素敏感性较高。该病例患者为儿童，以上药物最常用于治疗儿童脑膜炎的为万古霉素。因此，临床药师建议医师经验性加用万古霉素 60mg/（kg·d）分 3 次静滴联合美罗培南抗感染，因为不排除合并有其他格兰阴性菌的感染，用药满 48 小时后监测万古霉素血药谷浓度，血药浓度建议维持在 10-15mg/L。

结果 加用万古霉素治疗 3 天后，患儿体温热峰较前明显下降，复查脑脊液常规白细胞亦较前明显降低。监测到万古霉素血药浓度为 7.26μg/ml，低于目标血药浓度 10-15μg/ml，将万古霉素用法用量上调为 80mg/（kg·d） 分 4 次。使用万古霉素 5 天后患儿未再发热，复查脑脊液及血细菌培养转阴，停用美罗培南。万古霉素剂量调整 2 天后复查血药谷浓度为 14.1μg/ml。万古霉素治疗 33 天后，患儿病情明显好转予以办理出院，治疗过程中无药物相关不良反应发生。

结论 伊丽莎白菌属相关感染性疾病临床并不常见，但可引起免疫力低下患者、新生儿出现危及生命的重症感染，目前认为按蚊伊丽莎白菌为主要致病菌种，该细菌具有多重耐药的特性，万古霉素可以有效治疗按蚊伊丽莎白菌所致的感染。万古霉素治疗重症患者、儿童患者应做好治疗监测。

关键字：药学监护，儿童，按蚊伊丽莎白菌，万古霉素，脑膜炎

替格瑞洛增强粘菌素对肺炎克雷伯菌的抗菌活性的机制探究

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目的 肺炎克雷伯菌作为临床重点关注的病原体，由于其耐药性居高不下，迫切需要更有效的治疗方案。多粘菌素 E 被认为是治疗耐药菌感染的最后一道防线，然而多粘菌素耐药菌的出现已经成为一个新棘手问题。本研究旨在探究替格瑞洛联合多粘菌素 E 杀伤多重耐药细菌的作用机制。本研究提示替格瑞洛作为新型粘菌素佐剂改善细菌感染的治疗结果的潜力。

方法 （1）使用飞行时间质谱系统 Clin-TOF-II 鉴定 20 株多重耐药的肺炎克雷伯菌菌株和 20 多株碳青霉烯耐药的肺炎克雷伯菌以及 20 多株临床收集的铜绿假单胞菌；（2）用微量肉汤稀释法测多粘菌素 E 对肺炎克雷伯菌的最低抑菌浓度（MIC）；（3）用生长曲线测定实验验证多粘菌素 E 和替格瑞洛联合使用的效果；（4）通过检测 ROS 累积情况，验证多粘菌素 E 联合替格瑞洛的抗菌机制；（5）构建肺炎克雷伯菌诱导的小鼠肺感染损伤模型和血流感染模型，证明替格瑞洛--多粘菌素 E 对肺炎克雷伯菌的联合杀菌效果。

结果 （1）多粘菌素 E 联合替格瑞洛杀菌时，20 株多重耐药肺炎克雷伯菌和 20 株碳青霉烯耐药的肺炎克雷伯菌以在平板稀释实验中替格瑞洛减少

了肺炎克雷伯菌的生长，并且菌株 GN191034 和 ATCC 43816 使用生长曲线测定实验进行了验证；（2）ROS 检测发现多粘菌素 E 单独作用时肺炎克雷伯菌胞内 ROS 的积累增加，联合替格瑞洛共同作用时 ROS 的积累显著增加；（3）构建肺炎克雷伯菌小鼠肺炎模型实验，通过小鼠肺部肺炎克雷伯菌感染组织细菌负荷情况和病理学结果验证替格瑞洛-多粘菌素 E 治疗可减轻肺炎克雷伯菌引起的肺部炎症。

结论 我们的研究表明替格瑞洛和粘菌素对肺炎克雷伯菌的抗菌活性有显著影响，揭示了替格瑞洛作为一种新型粘菌素辅助剂的潜力，联合使用可以改善细菌感染的治疗效果。

关键字：多重耐药菌；肺炎克雷伯菌；多粘菌素 E；替格瑞洛

Ceftazidime–avibactam Versus Polymyxins in Treating Patients with Carbapenem-resistant Enterobacteriaceae Infections: A Systematic Review and Meta-analysis

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Objective Carbapenem-resistant Enterobacteriaceae (CRE) pose a significant threat to human health and have emerged as a major public health concern. We aimed to compare the efficacy and the safety of ceftazidime–avibactam (CAZ–AVI) and polymyxin in the treatment of CRE infections

Methods A systematic review and meta-analysis was performed by searching the databases of EMBASE, PubMed, and the Cochrane Library. Published studies on the use of CAZ–AVI and polymyxin in the treatment of CRE infections were collected from the inception of the database until March 2023. Two investigators independently screened the literature according to the inclusion and exclusion criteria, evaluated the methodological quality of the included studies and extracted the data. The meta-analysis was performed using RevMan 5.4 software

Results Ten articles with 833 patients were included (CAZ–AVI 325 patients vs Polymyxin 508 patients). Compared with the patients who received polymyxin-based therapy, the patients who received CAZ–AVI therapy had significantly lower 30-days mortality (RR = 0.49; 95% CI 0.01–2.34; I 2 = 22%; P < 0.00001), higher clinical cure rate (RR = 2.70; 95% CI 1.67–4.38;I 2 = 40%; P < 0.00001), and higher microbial clearance rate (RR = 2.70; 95% CI 2.09–3.49; I 2 = 0%; P < 0.00001). However, there was no statistically difference in the incidence of acute kidney injury between patients who received CAZ–AVI and polymyxin therapy (RR = 1.38; 95% CI 0.69–2.77; I 2 = 22%; P = 0.36). In addition, among patients with CRE bloodstream infection, those who received CAZ–AVI therapy had significantly lower mortality than those who received polymyxin therapy (RR = 0.44; 95% CI 0.27–0.69, I 2 = 26%, P < 0.00004)

Conclusions Compared to polymyxin, CAZ–AVI demonstrated superior clinical efficacy in the treatment of CRE infections, suggesting that CAZ–AVI may be a superior option for CRE infections

关键字：Carbapenem-resistant Enterobacteriaceae, CRE, Ceftazidime–Avibactam, Polymyxins, Meta-analysis

Efficacy of Short-course Antibiotic Therapy for Staphylococcus Aureus Bacteremia in Patients with Hematological Diseases: A Retrospective Comparative Study

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Objective Data regarding duration of antibiotic therapy for Staphylococcus aureus bacteremia (SAB) in hematological patients were limited. Current guideline recommended at least 14 days of antibiotic therapy with limited evidence.The objective of this study was to evaluate the effect of antibiotic treatment duration on clinical outcomes for hematological patients with SAB

Methods We performed a retrospective single-center cohort study including hematological adult patients (≥14) with SAB. Logistic regression models fitted with inverse probability of treatment weighting were used to assess the association between the clinical outcomes and treatment duration

Results Between January 2013 and December 2023, a total of 236 hematological patients were included (short course, ≤10 days, n=103; long course, >10 days, n=133). The recurrent SAB or mortality within 90 days of the initial positive blood culture occurred in 11 (10.7%) patients in the short-course group and in 21 (15.8%) in the long-course group. The recurrent fever within 7 days of discontinuing antibiotic therapy occurred in 13 (12.6%) patients in the short-course group and in 12 (9.0%) in the long-course group. In the weighted cohort, the multivariate logistic analysis indicated that short course of antibiotic therapy had similar outcomes with the long course (90-day mortality and relapse: p= .259; 7-day recurrent fever: p= .353). Additionally, in patients with neutropenic fever, empirical

treatment without the use of agents active against aerobic gram-positive cocci, despite the indications of suspected catheter-related infection or skin or soft-tissue infection, was neither associated with the risk of recurrent SAB or mortality within 90 days of the first positive blood culture (p= .684), nor with the increased recurrent fever rates within 7 days of discontinuing antibiotic therapy (p= .845)

Conclusion For hematological patients infected with SAB, short-course antibiotic therapy was non-inferior to long-course therapy in terms of clinical outcomes. And for patients with neutropenic fever, empirical treatment without the use of agents active against aerobic gram-positive cocci, did not result in an increased rate of poor clinical outcome

关键字：Staphylococcus aureus bacteremia, hematological patients

基于肺炎克雷伯菌型菌毛的抗毒力化合物筛选

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目的 肺炎克雷伯菌（Klebsiella pneumoniae）是重要的条件致病菌和医源性感染菌，可导致肺炎、肝脓肿和泌尿系统感染等多种感染性疾病。2022 年，K. pneumoniae 高居临床分离菌种的第二位。与以往数据相比，K. pneumoniae 的耐药种类愈加丰富，耐药率也普遍提高，而 K. pneumoniae 的生物膜是其抵抗抗生素的重要原因。鉴于 K. pneumoniae 感染的严重性、广泛性、高耐药性以及高毒力，开发新型抗菌方法迫在眉睫。K. pneumoniae 的菌毛是重要的毒力因子，可促进其粘附在宿主细胞表面并定殖，且与生物膜形成密切相关，是筛选抗毒力化合物的理想靶标之一。通过筛选不影响细菌生长，只抑制细菌的粘附和毒力的小分子化合物，避免细菌进化耐药性，为治疗 K. pneumoniae 感染提供一种新型治疗思路。

方法 构建菌毛报告系统，快速筛选可抑制菌毛基因表达的候选化合物。

结果 通过报告系统，我们从 2000 多种天然化合物中筛选得到 7 个化合物可以显著降低 K. pneumoniae 菌毛基因的转录表达水平。然后，我们进一步检测了候选活性化合物对细菌生物被膜、侵袭力和铁载体等致病表型的影响。结果表明，黄酮类化合物 W7 不影响细菌正常生长，可以显著抑制生物被膜形成、对细胞的侵袭力和降低铁载体产量，最终抑制致病毒力。

结论 随着多药耐药 K. pneumoniae 感染人数的全球激增和大流行，现有的抗生素疗法已经无法满足治疗需求，急需寻找替代治疗手段来增加对 K. pneumoniae 的治疗方案。粘附是细菌定植感染的前提，我们通过靶向粘附相关基因的表达，筛选可抑制致病表型和毒力的化合物。该类化合物不影响细菌的正常生长，从而避免产生耐药性，是一项行之有效的治疗方案。

关键字：肺炎克雷伯菌，抗毒力，耐药，粘附

A Fresh PH-responsive Imipenem-loaded Nanocarrier Against Acinetobacter Baumannii with A Synergetic Effect

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Objective In the face of the abundant production of various types of carbapenemases, the antibacterial efficiency of imipenem seen as “the last line of defence” is weakening. Following, the incidence of carbapenem-resistant Acinetobacter baumannii (CRAB), which can generate antibiotic-resistant biofilms, is increasing. Based on the superior antimicrobial activity for silver nanoparticles against multifarious bacterial strains compared with common antibiotics, we constructed the silver nanocomposite whose core was silver nanoparticle to tackle the current dilemma, and silver nanocomposite was able to function as a novel smart pH-sensitive nanodrug system

Methods Preparation of silver nanoparticles; Characterization and the release characteristics of silver nanocomposite; Assay for antibacterial effects and research on antibiofilm activity of silver nanocomposite in vitro; Assessing influence on CRAB-infection MLE-12 cells by counting, apoptosis evaluation and CLSM; A series of cell experiments to verify toxicity and biocompatibility in vitro; Constructing mice model of carbapenem-resistant A. baumannii pneumonia and studying therapy in vivo; Experiments of toxicity research in vivo; Statistical analysis

Results we have constructed a new pH-responsive antibacterial nano-delivery system (Imi@ZIF-8) for the antibacterial treatment of Acinetobacter baumannii. Due to its pH-sensitive characteristics, the nano-delivery system offers an improved release of the loaded imipenem antibiotic at the acidic infection site. Based on the high loading capacity and positive charge of the modified ZIF-8 nanoparticles, they are excellent carriers and are suitable for imipenem loading. The Imi@ZIF-8 nanosystem features synergistic antibacterial effects, combining ZIF-8 and imipenem to eliminate A. baumannii through different antibacterial mechanisms. When the loaded imipenem concentration reaches 20ug/ml, Imi@ZIF-8 is highly effective against

Acinetobacter baumannii in vitro. Imi@ZIF-8 not only inhibits the biofilm formation of A. baumannii but also has a potent killing effect. Furthermore, in mice with celiac disease, the Imi@ZIF-8 nanosystem demonstrates excellent therapeutic efficacy against A. baumannii at imipenem concentrations of 10 mg/kg, and it can inhibit inflammatory reaction and local leukocyte infiltration. Due to its biocompatibility and biosafety, this nano-delivery system is a promising therapeutic strategy in the clinical treatment of A. baumannii infections, providing a new direction for the treatment of antibacterial infections

Conclusion The above experimental studies demonstrated the promising potential of our novel antimicrobial nano-delivery system (Imi@ZIF-8) in the treatment of A. baumannii infections, showing good biocompatibility, high biosafety, pH acid responsiveness and efficient antimicrobial action. Due to its response to acidic pH, the Imi@ZIF-8 nano-delivery system features an improved release of the loaded imipenem at the acidic bacterial infection sites. Therefore, a synergistic antibacterial effect is achieved between the ZIF-8 and imipenem in the nano-delivery system, further enhancing its antibacterial activity against A. baumannii. When the loaded imipenem concentration reaches 20ug/ml, Imi@ZIF-8 is highly effective against Acinetobacter baumannii in vitro. Moreover, Imi@ZIF-8 exerts excellent therapeutic efficacy against A. baumannii at imipenem concentrations of 10 mg/kg and facilitates the inhibition of inflammatory response and leukocyte infiltration in mice with peritonitis, which promotes tissue recovery after bacterial infection. Overall, the Imi@ZIF-8 nano-delivery system provides a new clinical treatment strategy for the antimicrobial treatment of A. baumannii and provides a strong foundation for nano-antimicrobial therapy. More studies on the preventive effect of this nanomaterial on bacterial infections can be conducted in the future

关键字：Acinetobacter baumannii，Imi@ZIF-8，antibacterial infection，synergistic effect，anti-biofilm

头孢他啶阿维巴坦治疗多重耐药革兰阴性菌感染的真实世界研究

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目的 描述与评价头孢他啶阿维巴坦（ceftazidime-avibactam，CZA）治疗多重耐药革兰阴性菌（multidrug - resistant gram-negative bacteria，MDR-GNB）感染患者的临床特征、治疗管理与临床结局。

方法 选取 2019 年 9 月至 2021 年 12 月在徐州医科大学附属医院住院治疗的患者进行回顾性的队列研究。连续接受 CZA 治疗≥72 h 的成人患者符合纳入条件。主要结局是临床失败，定义为 30 d 全因死亡、微生物学疗效失败和/或在接受 CZA 治疗期间未能解决或改善感染迹象和症状的综合因素。

结果 共计对 198 例 MDR-GNB 感染患者的数据进行描述与评估，其中耐碳青霉烯类肠杆菌科细菌（carbapenem-resistant Enterobatceriaceae，CRE）队列 132 例，假单胞菌属（Pseudomonas spp.）队列 66 例。主要感染部位以肺部感 染（92.42%）、腹 腔 感 染（10.61%）、颅 内 感 染（10.61%）最为常见，血培养阳性 63 例（31.82%）。临床结局失败 61 例（30.81%），30 d 全因死亡 33 例（16.67%），30 d 微生物疗效失败 11 例（5.56%）。体质量指数（BMI）、急性生理学及慢性健康状况

评分（APACHE II）、多种病原微生物感染与临床结局失败呈正相关（矫正 OR 1.109，95%CI 1.017，1.209；矫正 OR 1.071，95%CI 1.015，1.129；矫正 OR 2.844，95%CI 1.391，5.814）。入院后 48 h 内启动 CZA 治疗与临床结局失败呈负相关（矫正 OR 0.424，95%CI 0.205，0.879）。共 15 例患者出现了与 CZA 可能相关的不良反应，其中皮疹 2 例，恶心呕吐 6 例，抗生素相关性腹泻 7 例。

结论 CZA 能够用于治疗一系列 MDR-GNB 导致的感染，包括 Pseudomonas spp.和 CRE。

关键字：头孢他啶阿维巴坦；多重耐药革兰阴性 菌；耐碳青霉烯类肠杆菌科细菌；假单胞菌属

280 例细菌性肝脓肿病原学和抗菌药物使用情况分析

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目的 分析成人细菌性肝脓肿（Pyogenic Liver Abscess, PLA）患者的一般情况、病原学特征、抗菌药物的使用情况、治疗及预后，以提高对 PLA 的诊疗水平。

方法 回顾性分析自 2019 年 12 月至 2022 年 12 月于天津医科大学总医院住院且诊断为细菌性肝脓肿的成人患者资料，包括一般情况、病原菌培养和药敏结果、治疗情况及预后情况，分析 PLA 的病原学特点和目前临床抗感染用药情况。

结果 本研究共收录 280 例成人 PLA 患者，其中男性 161 例，女性 119 例，男女比例 1.35:1，平均

年龄 63.05±13.58 岁，发病高峰集中在 50-80 岁。最常见感染途径为隐源性感染(55.71%)。最常见的基础疾病是糖尿病（41.07%）。血培养阳性率为 28.39%，脓液培养阳性率为 80.34%。肺炎克雷伯菌（Klebsiella pneumoniae, K.p）和大肠埃希菌（Escherichia coli, E.coli）是血培养及脓液培养最常见的细菌。共培养出耐药菌 14 株，其中产超广谱 β-内酰胺酶（Extended-spectrum β-lactamase, ESBLs）肺炎克雷伯菌 3 株，产 ESBLs 大肠埃希菌 3 株，耐碳青霉烯肺炎克雷伯菌 1 株，耐碳青霉烯大肠埃希菌 1 株，耐甲氧西林葡萄球菌 2 株，耐高浓度氨苄西林及氨基糖苷肠球菌 3 株，耐万古霉素肠球菌 1 株。相比较而言，培养出的革兰阴性菌对左氧氟沙星的敏感性最低（82.30%），对亚胺培南敏感性最高（98.23%），整体对头孢菌素/β-内酰胺酶抑制剂合剂、青霉素类/β-内酰胺酶抑制剂合剂、氨基糖苷类、甘氨酰环素类、头霉素类、碳青霉烯类以及磺胺类药物敏感性较好。PLA 初始经验性治疗以头孢菌素/β-内酰胺酶抑制剂应用最多。

结论 PLA 好发于男性，发病年龄高峰在 50-80 岁之间，多伴有糖尿病。主要致病菌为肺炎克雷伯菌，对常见抗生素敏感性较好。经验性治疗以头孢菌素/酶抑制剂为主，碳青霉烯类药物的使用较多，存在不必要的联合用药情况，特殊使用级抗生素送检率偏低，在应用抗菌药物中尚有不规范之处，需要予以重视。

关键字：细菌性肝脓肿，肺炎克雷伯菌，糖尿病，临床特点，病原学，抗菌药物

成团泛菌感染的临床特征及耐药性分析

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目的 分析成团泛菌感染的临床特征及耐药性，为临床合理使用抗菌药物提供相应的参考依据。

方法 回顾性分析某综合医院 2016-2023 年成团泛菌感染患者的临床特征及治疗转归，并对成团泛菌的耐药性进行分析。

结果 2016-2023 年 22 例成团泛菌感染患者，男性 16 例（72.7%），女性 6 例（27.3%），60 岁以上中老年患者是主要感染人群（72.7%），多数患者伴有基础疾病或合并多系统疾病（86.4%），其中以呼吸系统疾病、泌尿系统疾病及肿瘤患者最为常见（77.2%），且术后发生感染机率较高（54.5%），易发生医院感染（72.7%）。22 株成团泛菌中，除 1 株为产 ESBLs 耐药菌株，其余对抗菌药物均有很好的敏感性，哌拉西林/他唑巴坦、厄他培南、阿米卡星和头孢哌酮/舒巴坦敏感率为 100%，头孢他啶、头孢吡肟、左氧氟沙星和甲氧苄啶/磺胺甲恶唑敏感率为 94.1%，氨曲南敏感率为 93.3%，庆大霉素和妥布霉素敏感率为 92.9%，头孢曲松敏感率为 81.3%，头孢唑林和阿莫西林/克拉维酸敏感率为 75%，氨苄西林敏感率为 66.7%。

结论 成团泛菌引起的感染多为院内感染，与患者年龄、疾病种类、感染部位、手术、合并症及手术等相关；目前，成团泛菌对多数抗菌药物敏感，但部分菌株对抗菌药物产生耐药，临床治疗中应加强成团泛菌的防控，根据药敏试验结果合理使用抗菌药物。

关键字：成团泛菌；临床特征；耐药性

河北省某三甲综合医院神经型布鲁菌病 20 例临床特征分析

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目的 总结河北省某三甲综合医院 20 例神经型布鲁菌病（neurobrucellosis, NB）患者的流行病学、临床特征、治疗及预后情况。

方法 回顾性分析河北医科大学第三医院 2018-2023 年间收治的 NB 患者的流行病学、临床表现、实验室与影像学检查及治疗与预后等资料。

结果 20 例 NB 患者中男性 16 例（80%），女性 4 例（20%），年龄 20-76 岁（中位年龄 44 岁）。13 例（65%）患者报告有牲畜或畜牧产品接触史。诊断脑膜炎/脑炎共 17 例（85%），脑脓肿 2 例（10%），脊髓炎 1 例（5%），其中合并脊柱炎 2 例（10%）。非神经系统症状起病患者，发病至出现神经系统症状的中位时间间隔为 22 天，发病至确诊 NB 的中位时间间隔为 60 天。临床表现常包括：发热（70%，14/20 例）、头痛（65%，13/20 例）、恶心呕吐（65%，13/20 例）、颈项强直（25%，5/20 例）、复视（25%，5/20 例）、肌力下降（20%，4/20 例）等。65%（13/20 例）患者以发热和（或）头痛起病，25%（5/20 例）患者发病时即有神经系统受累症状，表现为肢体麻木 2 例、复视 2 例，行走不稳、听力下降及谵妄各 1 例。所有 20 例 NB 患者的布鲁菌血清凝集试验检

查阳性，仅 1 例血培养阳性。17 例患者进行腰椎穿刺术，脑脊液检查结果示：16 例患者（93.75%）的脑脊液蛋白升高（中位数 2.14 g/L; 0.61-24.85 g/L），14 例患者（82.4%）脑脊液白细胞增多（中位数 144/mm3；15-1380/mm3），脑脊液细菌培养均为阴性。共 12 名患者送检脑脊液病原体宏基因组二代测序（NGS），10 例（83%）回报布鲁菌序列阳性（中位数 46 序列数；5-8293 序列数）。70%（14/20）的患者存在影像学异常改变，脑叶异常信号 7 例（50%），脑室或脑室周围白质病变 5 例（35.7%），多发缺血灶 2 例（14.3%），可疑静脉窦血栓及马尾前侧异常团块影各 1 例。治疗以利福平+多西环素+头孢曲松为基础方案，选择性联合复方新诺明或左氧氟沙星。经治疗，95%（19/20）患者症状改善，2 例患者治疗 5 个月时仍有间断头痛。

结论 NB 的临床表现缺乏特异性，发病早期多表现为发热伴头痛，脑膜炎/脑炎最为常见，尤其有牲畜或畜牧产品接触史患者需高度警惕。NB 的脑脊液细菌培养阳性率低，脑脊液 NGS 可作为 NB 病原学诊断的重要检测手段。

关键字：布鲁菌，脑膜炎，神经，脑膜炎

Colistin Sulfate Is Effective and Safe in The Treatment of Severe Pneumonia Patients with CRE Resistance: A Retrospective Cohort Study

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Objective Severe pneumonia is difficult to treat and have a high mortality rate. The increasing drug resistance problem increasing the difficulties to the treatment of clinical doctors and the prognosis of patients. In this study, we estimated whether colistin sulfate reduces the mortality of severe pneumonia patients with suspicious CRO infection

Methods Our retrospective cohort study was conducted on the medical record of patients who consecutively admitted for pneumonia to the Second Affiliated Hospital of Chongqing Medical University from Jan 2022 to Feb 2023

Results We found that the 28-day mortality after discharge of severe pneumonia patients with suspected MDR bacterial infections in our cohort study is also high (42/84, 50%). The 28-day mortality of discharge in tigecycline (TC) group is a bit significantly lower than that of colistin combined with other antibiotics (OC) group (18/46, 39.1% vs. 24/38, 63.2%, P=0.048). Further multivariate analysis revealed that positive sputum culture was significantly associated with the 28-day discharge mortality rate of patients with different treatment regimens (OR 0.073, 95% CI 0.006-0.882, P=0.040). And no significant differences were founded before and after the use of colistin sulfate for the white blood count (WBC), neutrophil count, lymphocyte count, platelet count, level of CRP, PCT, ALT, AST, and creatinine

Conclusion Colistin sulfate is effective and safe in the treatment of severe pneumonia patients with CRE resistance.

关键字：Colistin sulfate，multiple drug resistance, efficiency, safety

Ceftazidime-avibactam-based Combination Therapy for Carbapenem-resistant Klebsiella Pneumoniae Infections Following Liver Transplantation

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Objective Infections caused by carbapenem-resistant Klebsiella pneumoniae (CRKP) are associated with significant mortality rates and high hospital costs, owing to limited antibiotic treatment options. Experience of ceftazidime-avibactam (CZA) for CRKP infection in recipients after liver transplantation (LT) is relatively limited. We aimed to assess its efficacy in a single-center cohort study

Methods A retrospective observational study was conducted on LT recipients receiving CZA therapy for CRKP infection. The primary outcomes were the clinical efficacy and 30-day mortality, and secondary outcomes included microbiological responses and adverse events related to CZA. Multivariate regression analysis was used to identify variables independently associated with 30-day mortality and clinical failure

Results In total, 58 liver transplantation patients with hospital-acquired CRKP infections who received treatment of CZA for ≥ 72 hours were enrolled. The median interval from operation to infection onset was 5.0 days (IQR 1.0–8.8) and the most common infections (62.1%) were intra-abdominal infections (IAIs). A significant portion of patients (43.1%) were residing in the intensive care unit with a median APACHE II score of 11.0 (IQR 8.0–12.8) and a median SOFA score of 15.5 (IQR 8.0–20.0). A total of 48 cases were treated with CZA-based combination therapies, while the remaining ten were treated with CZA alone. At the end of treatment, the overall clinical efficacy rate was observed to be 69.0%

(40/58), with a bacterial clearance rate of 70.7% (41/58) and an all-cause mortality rate of 29.3% (17/58). In multivariate analysis, clinical failure was still linked to a higher MELD score (P=.02), higher APACHE II score (P=.01), chronic kidney disease (P=.10), and the duration of CZA therapy (P=.045). The independent predictors of 30-day mortality included APACHE II score (P=.004), and chronic kidney disease (P=.015). According to Cox multivariate regression analysis, patients with chronic kidney disease had a lower overall survival rate compared to those without

Conclusion CZA-based combination therapy may be an alternative and promising regimen for CRKP infection in liver transplant recipients

关键字：Infections following liver transplantation; Ceftazidime-avibactam; Carbapenem-resistant Klebsiella pneumoniae; Clinical efficacy

A Pharmacovigilance Study on The Association of Vancomycin Plus Piperacillin with Acute Kidney Injury: True Nephrotoxicity Or Pseudo-injury?

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Objective Although dozens of studies have associated vancomycin+piperacillin (VP) with increased acute kidney injury (AKI) risk, it is unclear whether the association represents true injury or a pseudotoxicity characterized by isolated effects on creatinine secretion. We tested this hypothesis by detecting signals for different AKI-related adverse events with the VP combination

Methods The FDA Adverse Event Reporting System (FAERS) was mined between 2004Q1 and 2023Q3 to analyze the association between VP and adverse events (AEs) involving AKI. Standardized Medical Dictionary for Regulatory Activities (MedDRA) Queries (SMQs) with “broad” and “narrow” preferred terms (PTs) relevant to AKI was applied to systematically search demented AE reports. The Reporting Odds Ratio (ROR) was used to calculate the disproportionality

Results We filtered the query for drug and identified 79,600 vancomycin-associated reports in FAERS during the analytical period. Among all the reports, piperacilin (regardless of the presence of an associated b-lactamase inhibitor) was listed as suspected or concomitant/interacting drug in 16,231 cases. The ROR for broad AKI associated with VP was 1.27 (95%CI 1.22-1.33). A safety signal was detected for VP with changes in creatinine (ROR 1.30, 95%CI 1.17-1.45), while no significantly elevated reporting rates of other biomarkers and clinical outcomes related to AKI was evident with VP (urea changes: ROR 0.94, 95%CI 0.74-1.18; severe AKI: ROR 0.98, 95%CI 0.91-1.05; renal replacement therapy (RRT initiation): ROR 1.11, 95%CI 0.94-1.32)

Conclusion The co-administration of vancomycin and piperacillin has been linked to a heightened likelihood of creatinine-defined AKI. However, this association does not extend to alterations in other kidney function biomarkers or subsequent clinical outcomes following true AKI. This observation aligns with the idea that creatinine-defined AKI in the context of vancomycin and piperacillin co-administration might signify pseudotoxicity

关键字：vancomycin, piperacillin, pseudo acute kidney injury, true nephrotoxicity

187 例单一屎肠球菌和粪肠球菌血流感染者临床特征及预后因素

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目的 分析单一肠球菌血流感染（ BSI）者的临床特征、耐药性及 30 d 内死亡危险因素

方法 收集 2018 年 1 月至 2023 年 2 月清华大学附属北京清华长庚医院收治的 187 例单一屎肠球菌或粪肠球菌 BSI 患者的临床资料，入组患者分为屎肠球菌 BSI 组（ 133 例）和粪肠球菌 BSI 组（ 54 例），比较两组患者的临床特征和耐药性差异，应用多因素 Logistic 回归分析两类肠球菌 BSI 患者 30 d 内死亡的危险因素

结果 单一肠球菌BSI患者中159例（85.03%）为医院获得性感染，原发感染灶以肝胆（91 例、48.66%）、胃肠（ 39 例、 20.86%）及泌尿生殖系统（ 30 例、16.04%）为主。与粪肠球菌 BSI 组患者比较，屎肠球菌 BSI 组患者既往 90 d 内住院比例（78.95% vs. 62.96%： P＝0.023）和降钙素原（PCT）水平(P＝0.035)均显著升高，而原发感染灶为泌尿生殖系统来源比例及感染后继发呼吸衰竭占比低（ 12.03% vs. 25.93%：P＝0.027，28.57% vs. 46.30%：P＝0.020），差异均有统计学意义。两组患者 30 d 病死率差异无统计学意义（ 29.32% vs. 33.33%： P＝0.589）。屎肠球菌对青霉素、氨苄西林和左氧氟沙星耐药率均＞ 90%，显著高于粪肠球菌（ P ＜ 0.001）；其中分离耐万古霉素的屎肠球菌（VRE） 5 株（2.67%）。多因素 Logistic 回归分析显示：合并肿瘤（OR＝6.569、95%CI：1.625～26.556、P＝0.008）、白蛋白（ ALB）＜ 30 g/L（ OR＝5.173、 95%CI：1.640～16.317、 P＝0.005）及感染后继发心功能不全（ OR＝10.361、 95%CI： 2.710～39.612、 P＝0.001）均为屎肠球菌 BSI 患者 30 d 内死亡的独立危险因素，针对性用药为保护因素（OR ＝ 0.106、

95%CI： 0.021～0.531、 P＝0.006）。感染后继发呼吸衰竭（ OR = 32.844、 95%CI：1.946～554.441、P＝0.015）和肾功能不全（ OR＝14.492、 95%CI：1.422～147.683、 P = 0.024）为粪肠球菌 BSI 患者 30d 内死亡的独立危险因素。

结论 肠球菌 BSI 多为院内感染，以屎肠球菌为主，耐药率高，早期识别预后危险因素、积极抗感染治疗及加强脏器功能支持有助于改善患者预后。

关键字：肠球菌；血流感染；预后分析；危险因素

丁酸通过 p62-Keap1-Nrf2 轴减轻肺炎克雷伯菌感染诱导的氧化应激损伤

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目的 探究肠道菌群代谢物产物丁酸在肺炎克雷伯菌肺炎中发挥的作用及其机制。

方法 1、构建肺炎克雷伯菌（K. pneumoniae）感染的小鼠肺炎模型，观察感染后不同时间点对照组(补充 PBS 组）及实验组(补充丁酸组）小鼠生存率、肺组织细菌负荷、肺组织病理变化。2、体外利用巨噬细胞与 K. pneumoniae 共培养，通过细胞转录组学方法分析丁酸发挥功能的主要途径及关键分子。3、构建 p62 基因敲除细胞系，利用流式细胞术及 Western blot 探究野生型及敲除组巨噬细胞感染 K. pneumoniae 后细胞 ROS 水平、细胞凋亡水平。4、利用 Western blot 或细胞免疫荧光方法检测对照组及实验组感染 K. pneumoniae 后 P62、p-P62（Ser349）、Nrf2、Keap1、LC3B、Beclin-1 蛋白表达；RT-qPCR 检测 Nqo1、Ho-1、p62、LC3、Nrf2、Keap-1、Gstm2、Tnf-α、Il-1β、Il-6 基因表达。5、利用谷胱甘肽及 SOD 检测试剂盒检测肺组织及细胞 GSH、SOD 水平。6、构建 p62 基因敲除小鼠，观察对照组及实验组感染 K. pneumoniae 后不同时间点对照组及实验组小鼠生存率、肺组织细菌负荷、肺组织病理变化；利用流式细胞术检测小鼠感染 K. pneumoniae 后肺巨噬细胞凋亡水平。

结果 1、补充丁酸可以延长肺炎克雷伯菌感染小鼠生存率，降低肺组织细菌负荷，减轻肺组织病理损伤及炎症浸润。2、丁酸上调巨噬细胞 p62 基因表达及抗氧化应激通路。3、巨噬细胞感染 K. pneumoniae 后胞内 ROS 水平升高，细胞凋亡水平增加，NAC 处理抑制 K. pneumoniae 诱导的细胞凋亡。4、丁酸通过 p62 依赖途径抑制 K. pneumoniae 诱导的巨噬细胞凋亡。5、丁酸通过 p62 依赖途径促进转录因子 Nrf2 入核及抗氧化应激基因转录。6、p62 基因敲除小鼠感染 K. pneumoniae 生存率降低，肺组织细菌负荷增加，肺组织病理损伤加重及炎性浸润增加，肺巨噬细胞凋亡水平增加。

结论 丁酸通过上调抗氧化应激通路，减轻 K. pneumoniae 感染诱导的氧化应激损伤，在 K. pneumoniae 肺炎中发挥保护作用。

关键字：肺炎克雷伯菌；氧化应激；丁酸；p62

Novel RamR Point Mutations Modulated Host-bacteria Interaction in Clinical Isolates of Klebsiella Pneumoniae

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Objective Carbapenemase-resistant hypervirulent Klebsiella pnuemoniae (CR-hvKP) has been leading to life-threatening infections. Eravacycline, a new powerful antibiotic, is especially effective against multidrug-resistant gram-negative bacteria. However, the resistance mechanism is unclear. Here, we reported two novel ramR point mutations, L58P and F165l, which led to eravacycline resistance while simultaneously decreased virulence in clinical CR-hvKP

Methods and Results In this study, we screened 119 clinical K. pneumoniae isolates from 5 hospitals in China with different eravacycline MICs ranging from 0.0625 to 16 mg/L

In 97.6% of strains with MIC of >0.5.mg/L, efflux pump inhibitors phenyl-arginine-β-naphthylamide (PAβN, Sigma) could restore their eravacycline susceptibility. Up-regulated ramA, oqxB, and acrB were obtained in the eravacycline-resistant group compared to the eravacycline-susceptible group (P<0.001). Significant mutation patterns were observed in strains overexpressing AcrAB-TolC/ OqxAB and exhibiting high eravacycline MICs (4-8mg/L). Point mutations L58P, I141T, F165L in ramR as well as M1I in acrR were statistically linked to eravacycline resistance, and strains containing these mutations showed high levels of resistance (MIC up to 8mg/L). Adapting a CRISPR-Cas9 system, we constructed 4 mutants based on a CR-hvKP strain AZJ65. Higher drug-resistance levels were reached due to overexpression of AcrAB and OqxAB mediated by ramA in ramR L58P/ F165L mutants. And enhanced biofilm formation ability was also found in ramR L58P/ F165L mutants.Compared with the wild-type, decreased mortality rates were observed in mice infected with ramR L58P/ F165L mutants, and a lower bacteria burden in spleen, kidney and lung was also found. The elevated expression level of lipid A modification and biosynthesis genes (lpxL, LpxM, LpxP, LpxC, LpxT) were observed by qRT-PCR. A structure modification was confirmed in ramR L58P/ F165L mutants by MALDI-TOF. The numbers of ramR L58P/

F165L mutants that survived after incubation with whole blood and serum were lower than the wild type. Four mutants showed lower inflammation-related cytokine cytokines levels compared with the wild type. Although lipid A is linked to bacteria growth, no fitness cost was detected in 4 mutants.

Conclusion In conclusion, ramA, oqxB, and acrB contribute to eravacycline and several commonly used antibiotic agents' resistance in K. pneumoniae by up-regulating the AcrAB-TolC/ OqxAB efflux pumps. Importantly, this study, for the first time, reveals the dual function of point mutations ramR L58P and F165L in contributing to high resistance and decreased host immune response in K. pneumoniae

关键字：lipid A, Klebsiella pnuemoniae, drug-resistance, ramR, AcrAB-TolC/ OqxAB

细菌真菌耐药监测与耐药机制

Distribution and Antibiotic Resistance Analysis of Blood Culture Pathogens in A Tertiary Care Hospital in China in The Past Four Years

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Objective This study aimed to investigate the antibiotic resistance patterns and clinical distribution of blood culture-positive isolates at Suining Central Hospital between 2018 and 2021. The findings of this study can provide a basis for ensuring rational and effective use of antibiotic therapy in clinical settings

Bloodstream infection(BSI) is a serious and potentially life-threatening systemic infectious disease caused by pathogenic microorganisms invading the bloodstream and releasing toxins and metabolites that can lead to infection, poisoning, and a systemic inflammatory response1. Although molecular approaches have been explored for pathogen diagnosis, blood culture (BC) remains the gold standard tool for identifying BSI and sepsis2.It provides an accurate and reliable basis for clinical diagnosis and rational antibiotic administration3.The pathogenic spectrum and pattern of antibiotic resistance of BSI vary among affected regions due to distinct epidemiological and geographic factors4,5.Monitoring data from Dalian, China, from 2015 to 2019 showed that Gram-positive cocci were the most prevalent BSI pathogens in blood cultures6.In contrast, antibiotic resistance surveillance data from Korea and Europe revealed that E. coli and S. aureus were the most common pathogens of , BSI7,8.According to studies, incorrect empiric antibiotic therapy is an independent risk factor for increased mortality, particularly in individuals with S. aureus or Enterobacter spp,In addition relevant studies have shown that bloodstream infections are associated with various risk factors, such as advanced age, comorbidities, previous infections, neutropenia, long-term use of immunosuppressive medications, and the presence of indwelling venous catheters9,10. Therefore, to provide clinicians with a reference for rational antibiotic use in treating BSI, this retrospective study aimed to examine the main pathogenic species and resistance patterns in blood cultures of inpatients at Suining Central Hospital between 2018 and 2021. In summary, bloodstream infection is severe, and blood culture remains the most reliable diagnostic tool. Antimicrobial resistance patterns vary across regions, highlighting the need for region-specific surveillance and treatment guidelines. This study investigates the pathogenic species and resistance patterns of BSI in Suining Central Hospital, aiming to guide the rational use of antibiotics in the treatment of BSI.

Methods This retrospective study analyzed the data of 3660 non-repeating strains that tested positive for clinical blood culture, collected from the microbiology laboratory of Suining Central Hospital between January 2018 and December 2021. The identification of bacterial species and their antibiotic resistance patterns were analyzed

Results The study found that 76.7% of the bacterial strains identified were Gram-negative bacteria, while 23.3% were Gram-positive bacteria. Escherichia coli (44.8%), Klebsiella spp. (19.2%), Staphylococcus aureus (9.2%), Enterococcus spp. (5.3%), and Enterobacter spp. were the top five bacterial ratios observed. These bacteria were detected most frequently in the Digestion Center, intensive care unit (ICU), Neurology Center, Urology Department, and Hematology Department. Among the Staphylococcus spp., methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCNS) were detected at rates of 39.3% and 71.8%, respectively. However, no vancomycin- or linezolid-resistant staphylococci were identified. Enterococcus faecalis showed higher susceptibility to most antibiotic than Enterococcus faecium, except for tetracycline. The resistance rates of E. coli and Klebsiella spp. to meropenem and imipenem were low, but the resistance rates for other antibiotic were above 40%

Conclusion The results of this study show a rising incidence of bacterial antibiotic resistance in positive blood culture specimens at Suining Central Hospital. Clinicians should carefully consider the importance of blood culture antibiotic susceptibility testing to ensure effective treatment. The Department of Microbiology at Suining Central Hospital should regularly analyze the distribution of pathogenic bacteria and antibiotic resistance in blood cultures to ensure the most effective treatment possible. Keywords: blood stream infection, antibiotic resistance, antibacterial drugs

关键字：blood stream infection, antibiotic resistance, antibacterial drugs

肺炎克雷伯菌临床分离株分子分群和流行病学特征

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目的 分析临汾市中心医院肺炎克雷伯菌临床分离株的分子分群和流行病学特征（荚膜血清型、耐药基因和毒力基因），为临床诊疗提供参考。

方法 收集 2021 年 1 月—2022 年 1 月临汾市中心医院 143 株肺炎 克雷伯菌非重复临床分离株。采用基质辅助激光解吸电离飞行时间质谱进行菌种鉴定，采用全自动微生物分 析系统结合纸片扩散法检测菌株的耐药性，采用聚合酶链反应（PCR）结合基因测序技术分析 Kp 分子分群和 荚膜血清型，采用 PCR 分析肺炎克雷伯菌耐药基因和毒力基因携带情况。

结果 143 株肺炎克雷伯菌中有肺炎 克雷伯菌（KpI）135 株、变栖克雷伯菌（KpIII）4 株、类肺炎克雷伯菌（KpII）4 株。KpI主要荚膜血清型 为 K1、K2 和 K57，KpII主要为 K1，KpIII无特定血清型。KpIII和 KpII仅携带 SHV、OKP、LEN 基因，KpI携带多种耐药基因，耐药性较强。所有肺炎克雷伯菌菌株均检出毒力基因，3 群菌株 fimH、mrkD、ENT 毒力基因 携带率均>95%。KpII和 KpIII的 KFU 毒力基因携带率（100.00%）高于 KpI（73.33%），KpI、KpII、KpIII 的 YBT 毒力基因携带率分别为 54.81%、25.00%、0%。

结论 临汾市中心医院肺炎克雷伯菌临床分离株以 KpI 为主，不同分子分群肺炎克雷伯菌菌株血清型分布、毒力基因和耐药基因携带情况存在差异。

关键字：肺炎克雷伯菌，类肺炎克雷伯菌，变栖克雷伯菌，分子分群，毒力基因，耐药基因

Inter-species Spread and Evolution of BlaKPC-plasmid between Serratia Marcescens and Klebsiella Pneumoniae

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Objective In this study, we focused on a hospitalized patient with mixed infection strains, including K. pneumoniae and S. marcescens. During treatment with ceftazidime-avibactam, multiple mutations of blaKPC-2 occurred and the plasmid containing blaKPC transferred between different species. We performed a series of experiments to determine the evolution mechanism and inter-species spread of blaKPC-bearing Enterobacterales

Methods 1. Clinical strains: Five strains were isolated from the sputum samples, including S. marcescens HS1090, S. marcescens HS1219, S. marcescens HS1346, S. marcescens HS1459, K. pneumoniae HS1446. Incubation and purification of these isolates were performed on Columbia Blood Agar plates at 37℃ for 24 hours. Isolates were identified by matrix-assisted laser desorption ionization-time of flight mass spectrometry (bioMérieux, France)

2. Antimicrobial susceptibility testing and confirmation of carbapenemase production: Antimicrobial

susceptibility testing was performed using the broth microdilution method recommended by the Clinical and Laboratory Standards Institute (CLSI). Quality control and minimal inhibit concentration (MIC) results were interpreted according to the CLSI breakpoints for all agents except tigecycline and aztreonam-avibactam [20]. The tigecycline breakpoint was interpreted according to the Food and Drug Administration guidelines (susceptibility: ≤2μg/mL; intermediate: 4μg/mL; resistance: ≥8μg/mL) [21]; the aztreonam-avibactam breakpoint was interpreted according to aztreonam (susceptibility: ≤4μg/mL; intermediate: 8μg/mL; resistance: 16μg/mL). Escherichia coli ATCC 25922 was used for quality control. Confirmation of carbapenemase production (KPC, NDM, VIM, IMP, OXA) was performed using NG-Test Carba-5 and PCR-based sequencing as previously described [22].

3. Conjugation assay: The transfer of blaKPC-2 and its variants was investigated by performing conjugation assay using rifampin-resistant E. coli strain EC600 as the recipient strain and the S. marcescens HS1090 with blaKPC-2, S. marcescens HS1219 with blaKPC-71, K. pneumoniae HS1446 with blaKPC-44 as the donor strains. The conjugants were selected on Luria-Bertani (LB) agar supplemented with rifampin 50 mg/L and ampicillin 50 mg/L. Conjugation frequency was calculated as the number of transconjugants per recipient.

4. Genomic DNA extraction, whole-genome sequencing, and bioinformatic analysis: The genomic DNA of six strains was extracted by using a TIANamp bacterial DNA kit according to the manufacturer's recommendations (Tiangen Biotech Co., Ltd., Beijing, China). The genomes were sequenced using the Illumina (Illumina Inc., San Diego, CA) and the MinION platforms (Nanopore, Oxford, UK) to obtain the complete chromosome and plasmid sequences, respectively. Sequencing data were assembled using Spades (version 3.13.0) and Unicycler (0.4.9). The final genome sequence was annotated using Prokka (version 1.14.6) and scored using BUSCO (version 4.1.2). Annotation, blast, and comparison of plasmid were performed using the Proksee website (https://proksee.ca/).

5. Cloning experiment: The blaKPC-2, blaKPC-44, blaKPC-71 gene sequences containing the wild type promoter were amplified from the total DNA of S. marcescens HS1090, K. pneumoniae HS1446, S. marcescens HS1219 with pro398-BamHI-R (5'-CGACTCTAGAGGATCCAATAGATGATTTTCAGAGCCTTAC-3') and pro398-ECORI-F (5'-CCATGATTACGAATTGTGCGCGGAACCCCTATTTG-3') using the 2× Phanta Flash Master Mix (Vazyme Biotech, P520). Each PCR product was purified using the FastPure Gel DNA Extraction Mini Kit (Vazyme Biotech, DC301) and cloned into the pHSG398 vector (Takara, Beijing, China). The recombinant plasmids were transformed into chemically competent E. coli DH5α (Vazyme, Biotech, C502) and selected on LB agar containing chloramphenicol 50 μg/ml. Nucleic acid sequences and the orientation of each insert were verified by Sanger sequencing using the universal M13 primers of both orientations.

6. Kinetic parameter measurements of steady-state enzymes: Kinetic parameters of purified enzymes were measured by spectrophotometry at 23℃ and in PBS at pH 7.4. Steady-state kinetic parameters were tested by measuring the hydrolysis of β-lactam antibiotics and monitoring the cleavage of ceftazidime, imipenem, meropenem, and ertapenem at 257 nm, 299 nm, 299 nm, and 297 nm respectively. In the reaction system, wild-type KPC-2 and its variants at 200nM were mixed with substrates at different concentrations (20μM, 40μM, 60μM, 80μM, 100μM). The initial substrate cleavage rate of substrates was included in the analysis. The kinetic parameters were then calculated and analyzed using the Michaelis-Menten equation [23]. IC50 values of inhibition of wild-type KPC-2 protein and its variants protein by avibactam with nitrocefin as the substrate were determined. Enzymes were mixed with avibactam at concentrations ranging from 0 to 10 μM in PBS and incubated for 5 min, then nitrocefin was subsequently added at a concentration of 100 μM. Absorbance was recorded at 482nm after 30 min and exported to the GraphPad prism 9 software (GraphPad, La Jolla, California, USA; www.graphpad.com) to calculate IC50 values using the dose-response-inhibition, variable-slope (four parameters) equation.

Results 1. Case information

A 68-year-old man was found to have space-occupying lesions in the right lung, and was diagnosed with primary lung malignancy during the medical examination on 26 Dec 2022. He underwent thoracoscopic right upper lobe resection plus mediastinal lymph node dissection at Ningbo First Hospital on 3 January 2023. Unfortunately, he developed fever, cough, and sputum after the operation and was transferred to the intensive care unit. Although anti-infective therapy was given with cefuroxime 1.5g q12h, cefoperazone-sulbactam 2g q8h, piperacillin-tazobactam 4.5g q8h combined with meropenem 1g q8h and levofloxacin 0.5g qd in succession, he still had high fever up to 39℃ during treatment. On 31 January, carbapenem-resistant K. pneumoniae was isolated from the patient's sputum sample. The anti-infective regimen was subsequently changed to combinations of antimicrobials, including piperacillin-tazobactam 4.5g q8h plus vancomycin 1g q12h plus caspofungin 50mg qd, followed by imipenem 0.5g q8h plus tigecycline 100mg q12h. However, the symptoms of fever, cough, and sputum production didn't improve and he was admitted to our hospital on 15 March for further diagnosis and treatment (Figure 1).

The patient was admitted to the Infectious Diseases Department of our hospital and a sputum sample was

collected for bacterial culture, identification, and antimicrobial susceptibility testing. The S. marcescens HS1090 strain was then isolated. According to the results of the antimicrobial susceptibility test, ceftazidime-avibactam 2.5 g q8h was used to treat the infection, and then the symptoms of cough and sputum improved and the body temperature returned to normal. On 25 March, ten days later, the patient suddenly became dyspneic and had fever again, with carbon dioxide partial pressure up to 6.71kPa (normal) and oxygen partial pressure down to 11.01kPa (normal 12.6-13.3). We collected sputum samples from the patient and isolated S. marcescens strains HS1219 and HS1346, which were resistant to ceftazidime-avibactam. Piperacillin-tazobactam 4.5g q8h was used to treat the infection. However, K. pneumoniae HS1446 and S. marcescens HS1459 were isolated from sputum during treatment with piperacillin-tazobactam. Finally, the treatment regimen was changed to trimethoprim-sulfamethoxazole and the patient was discharged from our hospital with a stable condition (Figure 1).

2. Antimicrobial susceptibility profile and resistance genotypic profile of the clinical strains:

The results of antimicrobial susceptibility testing for five clinical strains are shown in Table 1. With the use of antimicrobial agents, bacterial susceptibility to antimicrobial agents changes, especially to ceftazidime-avibactam and carbapenems. In order to find out the mechanism behind the change in resistance profile during antimicrobial treatment, the genome of the strains was extracted and sequenced as shown in Table 2. Four S. marcescens strains showed identical resistance genotypes, including blaSRT-2, aac(6')-Ic, qnrS1, and tet(41), except for the blaKPC gene. The S. marcescens strains HS1219, HS1346 and HS1459 all carried blaKPC-71. As shown in Figure 2, blaKPC-71 had an insertion of 3 nucleotides (547_548insTCA) compared to blaKPC-2 and the mutation resulted in an amino acid insertion between Thr180 and Ser181 (Thr180_Ser181insSer). Another ceftazidime-avibactam-resistant strain K. pneumoniae HS1446 belonging to ST23 was found to carry the blaKPC-44 gene and other resistance genes including blaSHV-11, qnrS1, fosA. Compared to blaKPC-2, the blaKPC-44 gene had an insertion of 45 nucleotides (782_783insGCCGTC-TACACCCGGGCGCCTAACAAGGATGACAA-GCACAGCGAG) and the mutation resulted in the insertion of fifteen amino acids between Leu260 and Ala261 (Leu260_Ala261insAla Val Tyr Arg Ala Pro Asn Lys Asp Lys His Ser Glu) in the amino acid sequence (Figure 2).

3. Transmission and evolution of blaKPC located on plasmid between mixed strains

In this case, five strains with different blaKPC genotypes were isolated from the patient. S. marcescens HS1090 producing KPC-2, S. marcescens HS1219 producing KPC-71 and K. pneumoniae HS1446 producing KPC-44 were selected to perform the conjugation tests and whole genome sequencing to find out the location of blaKPC in the genome and its genetic text environment. The plasmids carrying the blaKPC gene can be transferred into E. coli EC600 recipient and show the antimicrobial susceptibility profiles closely related to the genotype of blaKPC-2 and its variants. Both blaKPC-44 and blaKPC-71 conjugates were resistant to ceftazidime-avibactam and restored susceptibility to imipenem and meropenem. What's more, there were still differences in phenotype between the two conjugants, with blaKPC-44 conferring resistance to aztreonam at MIC=32μg/mL, while blaKPC-71 remained susceptible to aztreonam at MIC=2μg/mL (Table 1).

The results of the whole genome sequencing showed that the blaKPC were located on a plasmid with a size of 104,146 bp (Figure 3). Analysis of the schematic alignment map showed that the sequences of pHS1090 (OR805036), pHS1219 (OR805037), and pHS1446 (0R805038) were almost identical. Meanwhile, the quinolone resistance gene qnrS1 was co-located on the plasmid with blaKPC. According to the BLAST result with the NCBI database, four plasmid sequences shared more than 99% identity with the plasmids in this case (Figure 3), predicting that the transmission of plasmids between S. marcescens and K. pneumoniae was originally derived from the S. marcescens species. What's more, all the blaKPC-bearing plasmids in this study belonged to the non-Tn4401 structural type, which was defined as blaKPC-bearing non-Tn4401 elements (NTEKPC) as previously reported[24]. In this study, blaKPC was located on the genetic structure of IS26-ΔtnpR-ISKpn27-ISKpn28-blaKPC-ΔISKpn6 (Figure 4). Apart from the obvious, there was a novel insertion element flanked by blaKPC, named ISKpn28.

To understand the evolution of blaKPC and its impact on plasmids and strains, single nucleotide polymorphism (SNP) sites were calculated between the isolated S. marcescens strains. During the entire treatment of the patient, the evolutionary trajectory of the S. marcescens strains was predicted, as shown in Figure 1. The number of SNPs among the four S. marcescens strains did not exceed 30, so it was predicted that the blaKPC-71-carrying S. marcescens strains evolved from the blaKPC-2-carrying S. marcescens strains. During the late period of treatment with trimethoprim-sulfamethoxazole, the absence of the plasmid carrying blaKPC-71 occurred in partial clones of S. marcescens HS1459 as shown in Table 1 and Table 2. Meanwhile, the transconjugant frequencies of the plasmids of the three clinical strains were calculated to be 0.42±0.23 for pHS1090, (1.39±0.14)x10-6 for pHS1219 and (0.37±0.11)x10-4 for pHS1446. The above results and analysis seemed to indicate that the evolution of blaKPC affected the conjugative efficiency and stability of the blaKPC-carrying plasmid.

4. The effects of KPC variants on antimicrobial

susceptibility profiles & enzyme kinetic

To investigate the function of KPC variants on antimicrobial susceptibility and their enzyme kinetic parameters, the blaKPC-44 and blaKPC-71 genes were cloned into the pHSG398 vector and introduced into E. coli DH5α strain. When expressed in the E. coli host, the blaKPC-44 and blaKPC-71 genes were found to play a major role in resistance to ceftazidime-avibactam. As shown in Table 1, compared to blaKPC-2, blaKPC-44, and blaKPC-71 mediated resistance to ceftazidime (MIC≥32μg/mL) and ceftazidime-avibactam (MIC=32μg/mL and MIC=16μg/mL, respectively), meaning that avibactam couldn't inhibit the activity of blaKPC variants. Meanwhile, the side effects of blaKPC-44 and blaKPC-71 were reflected in the restoration of susceptibility to carbapenems, which mediated susceptibility to imipenem and meropenem. Kinetic data using the enzyme showed that compared to KPC-2, the hydrolytic activity of the KPC variants was lower for carbapenems, including imipenem, meropenem, and ertapenem. The reduced catalytic efficiency for carbapenems was mainly due to the decreased affinity and turnover number, which corresponded to the recovery of carbapenem antimicrobial activity. In addition, KPC-71 and KPC-44 were strongly inhibited by avibactam, with a higher IC50 (IC50=0.13 and 0.27 for KPC-71 and KPC-44, respectively) (10~20-fold) than wild-type KPC-2 (IC50=0.015). It was therefore predicted that the KPC variants are responsible for resistance to ceftazidime-avibactam.

Conclusion In this study, we have described the entire diagnostic and treatment process of the patient carrying carbapenem-resistant S. marcescens and elucidated the mechanism of resistance to carbapenems and ceftazidime-avibactam associated with blaKPC-2 and its variants. We have also focused on understanding the consequences of blaKPC evolution. In the future, it is crucial to pay more attention to the evolution and horizontal transmission of blaKPC

关键字：Serratia marcescens, Klebsiella pneumoniae, KPC-44, KPC-71, Evolution

Carbapenem-resistant Organisms Screening Based on Immediate Rectal Swabs Xpert Carba-R Reduces Infection Mortality in HSCT Patients：a Historically Controlled Prospective Trial

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Objective The emergence of carbapenem-resistant organisms (CRO) has posed a huge challenge to clinical infection control and the patients undergoing allogeneic stem cell transplants (HSCT) infected by CRO are at the highest risk of mortality. Proactive screening of HSCT patients with CRO colonization not only provides recommendations for early and accurate anti-infective therapy, reduces the probability of secondary infections and improves patient prognosis, but also contributes to nosocomial infection prevention and control

Methods This historically controlled prospective study was registered on chictr.org.cn (ChiCTR2100041976).The study group design is shown in Figure1A. From August 2021 to August 2022, 184 consecutive recipients were observed in the study group. Among them, real-time rectal swabs were collected in the admission and weekly for the patients who remained hospitalized. 2 rectal swabs per patient were simultaneously collected for CRO traditional culture (RS-culture) and Xpert Carba-R assay (immediate RS-Carba-R). Once positive RS-culture and/or immediate RS-Carba-R was found, the purified colony was stored in a -80°C freezer for Carba-R testing later (purified-colonies Carba-R) to confirm the presence of carbapenemase genes. For HSCT patients with RS-culture (+) and/or immediate RS-Carba-R (+) undergo guideline-directed and stringent infection-control measures, including consecutively screening for colonization, isolation of infected and colonized patients, a single room and use of gloves and gowns by staff on room entry, and increased emphasis on appropriate hand hygiene12,20. Prophylactic antibiotics were not used for all patients. Empirical antifungal therapy prophylaxis is administrated in HSCT patients in particular to the allogeneic recipients according to current guideline recommendations24. On the first episode of fever neutropenia (FN) after HSCT, blood cultures were performed, and then antibiotics treatments were initiated according to the result of RS-culture and immediate RS-Carba-R. For FN patients with RS-culture (-) and immediate RS-Carba-R (-) which were defined as CRO non-colonized group, first-line empirical therapy contained sulbactam/cefopcrazone, piperacillin/tazobactam, cefepime, ceftazidime and carbapenem including meropenem and imipenem according to current guideline recommendations24,25. If ineffective in 72h, antibiotic therapy was changed according to current guidelines24. For FN patients with RS-culture (+) and/or immediate RS-Carba-R (+) which were defined as CRO colonized group, CRO-targeted therapy was adopted directly based on carbapenemase genes diagnosed by Carba-R, including tigecycline, polymyxins, and/or a combination of ceftazidime-avibactam with aztreonam26.Figure1B shows the flow chart

of historic group. we collected the clinical characteristics and outcomes of the historic matched control group(n=197) which was diagnosed as CRO gut colonization only by RS-culture during the same period of previous year and the antibiotics treatments were consistent with those described above, which was regulated according to the status of colonization

Results During the study period, the point prevalence of newly detected CRO carriage in HSCT patients decreased from 22.3% in the survey commenced in August 2021 to 5.8% in that begun in August 2022. the univariate and multivariate analysis indicated that the Xpert Carba-R screening group received a shorter the total duration of hospitalization than the historic group (OR 0.94, 95%CI 0.88-0.99, p=0.038) and CRO-related mortality was signifcantly lower in the Xpert Carba-R screening group than that in the historic group (OR 0.12, 95%CI 0.01-0.75, p=0.021)

Conclusion Our study showed a positive effect of screening based on immediate rectal swabs Xpert Carba-R for carbapenem-resistant organisms, with reductions in infection mortality in HSCT patients. Xpert Carba-R screening can guide CRO-targeted therapy of subsequent infection which can effectively overcome the drug resistance and break the chains of transmission

关键字：Carbapenem-resistant organisms; HSCT; Colonization; Infection; Xpert Carba-R assay

四川地区29家医院临床分离真菌的菌种分布及耐药性监测

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目的 了解 2022 年四川地区临床分离真菌的菌株分布以及其对常用抗真菌药物的耐药性，促进四川地区抗真菌药物的合理选择。方法 收集 2022 年 1 月 1 日～2022 年 12 月 31 日全国真菌病监测网四川省 29 家成员单位临床微生物标本中分离出的非重复真菌菌株，参照美国临床和实验室标准协会（CLSI）推荐标准，运用 WHONET 5.6 及 Microsoft Excle 进行数据统计与分析。

方法 收集 2022 年 1 月 1 日至 2022 年 12 月 31 日四川省 29 家医院临床分离的真菌菌株 19633 株，剔除同一患者的重复菌株后，共获得 16969 株真菌菌株（其中住院患者菌株 15737 株，门急诊患者菌株 1232 株），真菌菌株的筛选严格按照《全国临床检验操作教程》（第四版）进行操作，将筛选的真菌菌株通过全自动 VITEK 系统、质谱系统等产品进行真菌种类的鉴定,使用 WHONET5.6 软件及 Microsoft Excle 进行分析。

结果 2022 年四川省 29 家成员单位的样本真菌菌株共计 16969 株，其中念珠菌属占 86.95%（14755/16969）；隐球菌属占 0.47%（80/16969）；丝状真菌占 8.07%（1371/16969）；其他酵母占 4.49%（763/16969）。在念珠菌属中，分离最多的三种菌分别为白念珠菌（63.36%，9350/14755）、光滑念珠菌（15.09%，2222/14755）及热带念珠菌（6.44%，951/14755）；在隐球菌属中，新生隐球菌占 97.50%（78/80）；在丝状真菌中，分离最多的三种菌分别为烟曲霉复合群（56.16%，770/1371）、黄曲霉复合群（15.82%，217/1371）、青霉菌属（10.57%，145/1371）。所有念珠菌属对两性霉素 B 的非野生型菌株占比较低，对棘白菌素类药物的耐药性或非野生型占比均较低，光滑念珠菌和热带念珠菌对唑类药物的耐药性相对较高。新生隐球菌对两性霉素 B 的非野生型占比为 10.29%，总体略高于对唑类药物的非野生型占比。除黄曲霉复合群对卡泊芬净非野生型占比较高（50%）外，丝状真菌总体对两性霉素 B 和唑类抗生素以及卡泊芬净的非野生型占比较低。

结论 四川省 2022 年临床分离的真菌以念珠菌属为主，光滑念珠菌和热带念珠菌对唑类抗真菌药物的耐药率较高，其他种类的念珠菌属对临床常用的抗真菌药物敏感度或野生型占比较高。

关键字：四川，真菌，耐药性

耐多黏菌素和碳青霉烯类肺炎克雷伯菌的危险因素分析

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目的 探究耐多黏菌素和碳青霉烯类肺炎克雷伯菌（polymyxin resistant and carbapenemase-resistant Klebsiella pneumoniae， PR-CRKP）的危险因素。

方法 收集 2020 年 7 月至 2023 年 10 月在苏州大学附属第三医院住院期间检出 CRKP 的患者资料，根据对多黏菌素 B 的药敏试验结果分为 CRKP 组和 PR-CRKP 组，回顾性分析患者的临床资料，采用多因素 Logistic 回归分析 PR-CRKP 的危险因素。采用 SPSS 26. 0 软件对数据进行统计分析。

结果 共纳入 CRKP 感染患者 170 例，CRKP 组 123 例，PR-CRKP 组 47 例。单因素分析显示，与 CRKP 组相比，PR-CRKP 组的年龄更高（$Z=-2.186$， $P=0.029$），入院前 6 个月半合成青霉素类、碳青霉烯类、多黏菌素类和喹诺酮类药物的暴露史比例更高（$\chi2=3.930$、5.414、11.939、8.478，P 值均 <0.05），入院时诊断为感染的比例和血尿素氮水平更高（$\chi2=7.268$，$Z=-2.406$， $P=0.007$ 和 0.016），血红蛋白水平更低（$t=2.641$， $P=0.009$），

住院时间和气管插管、导尿管、深静脉置管时间更长（Z =−4. 243、−4. 660、−5. 341、−4. 583，P 值均<0. 001），碳青霉烯类药物和多黏菌素 B 使用时间更长（Z =−4. 757 和−7. 554，P 值均<0. 001），合并耐喹诺酮类肠杆菌（quinolone-resistant Escherichia coli，QREC）和碳青霉烯类耐药革兰阴性菌（carbapenem-resistant organism，CRO）感染、血流感染和收治重症监护病房的比例均更高（$\chi 2$ = 33. 737、42. 041、5. 426、12. 991，P < 0. 05）。多因素分析显示，多黏菌素 B 使用时间（OR = 1. 179，95%CI 1. 059 ~ 1. 312，P = 0. 003）、合并 QREC 感染（OR = 5. 357，95%CI 2. 100 ~ 13. 669，P < 0. 001）和合并 CRO 感染（OR = 3. 302，95%CI 1. 146 ~ 9. 514，P = 0. 027）是 PR-CRKP 的独立危险因素。

结论 长时间使用多黏菌素 B 是 PR-CRKP 的独立危险因素，混合 QREC 和 CRO 感染可增加 PR-CRKP 的风险。

关键字：肺炎克雷伯菌，碳青霉烯类耐药，多黏菌素耐药，喹诺酮耐药

高毒力和碳青霉烯耐药肺炎克雷伯菌血流感染临床及分子流行病学特征

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目的 探讨高毒力肺炎克雷伯菌(hvKp)和碳青霉烯耐药肺炎克雷伯菌(CRKP)血流感染临床及分子流行病学特征。

方法 收集 2020 年 1 月-2022 年 6 月广东省人民医院经临床检验血培养确诊的由肺炎克雷伯菌所致血流感染患者的病历资料及相关菌株，共 32 株纳入研究，包括 hvKp 16 株、CR-hvKp 1 株，共 17 株定义为 hvKp; CRKP 15 株。采用全基因组测序方法，分析菌株耐药基因、毒力基因分布特征及荚膜血清型。运用多位点序列分型(MLST)技术分析菌株序列型(ST)。

结果 血流感染患者均伴有多种基础疾病，CRKP 感染患者侵入性操作较多、病死率较高(P<0.05),患者主要分布于重症监护室(ICU)、感染科、儿科等科室。测序结果分析显示：CRKP 主要携带 blaKPC-1、blaNDM-1 耐药基因，毒力基因以 entA、entB、entE、fepA、fepC、fepG、ompA、xcpR、yagV/ecpE、ykgK/ecpR 等为主，荚膜血清型以 K14、K64 为主，MLST 分型结果以 ST11 为主。而 hvKp 主要携带的毒力基因以 entA、entB、entE、fepB、fimA、irp1、mgtB、ompA、yagV/ecpE、ybtA 等为主，荚膜血清型以 K1、K2 为主，MLST 分型以 ST23、ST25 为主。其中 1 株 CR-hvKp 同样携带多种毒力基因，为 ST751 型。

结论 血流感染患者分离的 hvKp、CRKP 菌株携带多种毒力基因和耐药基因，给临床抗感染治疗和预后带来挑战，且 CR-hvKp 的出现极大威胁患者健康。实验室应加强对此类病原菌监测，检出后应及时报告临床，并采取积极措施，减少其在医院播散。

关键字：高毒力肺炎克雷伯菌；碳青霉烯耐药肺炎克雷伯菌；血流感染；临床特征；分子流行病学

2019-2021 年安徽省血流感染病原菌分布及其耐药性分析

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目的 2019-2021 年安徽省血流感染病原菌分布及其耐药性分析

方法 采用 WHONET 5.6 软件对 2019-2021 年血流感染病原菌的构成及其耐药性进行统计分析

结果 10 所三级医院 3 年血流感染标本共分离病原菌 3872 株，其中革兰阴性菌 2823 株（72.9%），革兰阳性菌 1049 株（27.1%），分离的菌株构成和比例基本稳定。排前 3 位的细菌依次为大肠埃希菌（1434 株，37.0%）、肺炎克雷伯菌（735 株，19.0%）、金黄色葡萄球菌（392 株，10.1%）。其中耐甲氧西林金黄色葡萄球菌（MRSA）检出率为 28.6%，MRSA 对喹诺酮类药物、四环素的耐药率呈逐年递增趋势，未发现对万古霉素、利奈唑胺、替考拉宁耐药；屎肠球菌对大部分抗菌药物耐药率高于粪肠球菌；大肠埃希菌对碳青霉烯类药物的耐药率低于 4%；肺炎克雷伯菌对碳青霉烯类药物耐药率呈先升后降趋势，2020 年耐药率达 20%以上；铜绿假单胞菌对常用抗菌药物的耐药率均偏低，对氨基糖苷类抗生素的耐药率甚至低于 5%，对碳青霉烯类药物耐药率呈明显下降趋势；鲍曼不动杆菌对常用抗菌药物的耐药率较高，多数药物可达 60%以上。

结论 2019-2021 年安徽省血流感染病原菌以革兰阴性菌为主，大肠埃希菌和肺炎克雷伯菌占绝对优势，鲍曼不动杆菌耐药情况较严重，各医疗机构应加强血流感染细菌耐药性监测，指导临床合理使用抗菌药物。

关键字：血流感染，病原菌，耐药性，安徽省

Genomic Revisitation and Reclassification of The Genus Providencia

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Objective Members of Providencia, although typically opportunistic, can cause severe infections in immunocompromised hosts. In this study, we aim to utilize advanced genomic technologies to accurately reclassify the species within the Providencia genus, addressing existing classification confusion and providing new insights from a genomic perspective. By conducting an in-depth study of the species within this genus, we aim to reveal their genetic diversity and antimicrobial resistance mechanisms, guiding future monitoring and treatment strategies

Methods We constructed a high-quality database containing 545 genomes using public databases and previously collected strains. The species within the Providencia genus were reclassified by calculating Average Nucleotide Identity (ANI) and digital DNA-DNA hybridization (dDDH) values and validated using phylogenetic trees. Pan-genomic analysis was employed to identify the core genome and analyze its functions. Antimicrobial resistance genes and mobile genetic elements were identified by comparing with the NCBI AMRFinder Plus and ISfinder databases. The distribution and clustering of plasmids were analyzed using MOB-suite, further understanding the transmission mechanisms of resistance genes

Results This study reclassified 545 genomes into 20 species, including one newly discovered species named Providencia zhijiangensis and seven unnamed clades (Taxon 1-7), further subdivided into 23 lineages. We found that Providencia stuartii and Providencia thailandensis actually belong to the same species. The pan-genome analysis identified 1,550 core genes, with the largest proportion being coenzyme-related, highlighting the significant metabolic activities within the genus. The analysis of antimicrobial resistance revealed that 82.61% of the lineages carry antibiotic resistance genes, most of which are located on plasmids, emphasizing the crucial role of plasmids in the evolution of resistance. Notably, three species or lineages (P. stuartii, Taxon 3, and Providencia hangzhouensis L12) demonstrated diversity in carbapenem resistance genes, indicating their potential impact on clinical treatments

Conclusion This study successfully resolved the classification confusion within the Providencia genus and expanded our understanding of its genomic characteristics. Through the study of the core genome, we revealed the metabolic traits of the genus and highlighted the importance of monitoring and researching the antimicrobial resistance of Providencia. This work lays the foundation for developing effective monitoring and management strategies against the Providencia genus, especially regarding its resistance features

关键字：novel species, Providencia, pangenome, plasmids, antibiotic resistance

The Draft Genome Sequence of BlaIMP-4-carrying Enterobacter Soli Isolated From Human Blood

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Objective The primary aim of this study was to elucidate the genomic characteristics and antibiotic resistance profile of an Enterobacter soli strain (designated as strain 140044), which was isolated from the blood of a patient suffering from acute pancreatitis and subsequent bloodstream infection. This investigation was motivated by the growing concern over the dissemination of carbapenemase-producing Enterobacteriaceae in clinical settings, which poses a significant challenge to current therapeutic strategies due to their extensive drug resistance capabilities. Specifically, the study focused on characterizing the blaIMP-4 gene within this isolate, a known carbapenemase gene that significantly contributes to carbapenem resistance, and determining the comprehensive antibiotic resistance gene profile of the strain

Methods The Enterobacter soli strain 140044 was isolated from a blood culture of a patient diagnosed with acute pancreatitis. Identification of the strain was initially performed using standard microbiological techniques and further confirmed through molecular methods. Whole-genome sequencing (WGS) of the Enterobacter soli strain was then carried out to obtain a detailed understanding of its genetic makeup. The sequencing data were assembled and annotated using bioinformatic tools. The genome was screened for the presence of antibiotic resistance genes. Additional analyses were conducted to identify resistance determinants and virulence factors that could contribute to the pathogenicity and drug resistance of the isolate

Results The genome of Enterobacter soli strain 140044 was found to be approximately 5.37 megabases (Mb) in size, encoding a wide array of genes associated with antibiotic resistance, virulence, and metabolism. The sequencing efforts revealed a high-quality, circular genome that provides insights into the genetic basis of its pathogenicity and resistance mechanisms. The strain demonstrated a broad spectrum of resistance against several classes of antibiotics, including aminoglycosides, rifamycin, penicillins, cephalosporins, quinolones, and sulfonamides. Central to its carbapenem resistance phenotype was the presence of the blaIMP-4 car-

bapenemase gene. This gene is known for its role in hydrolyzing carbapenems, thereby rendering them ineffective. Besides blaIMP-4, the genome analysis unveiled multiple other resistance genes, which collectively contribute to the multidrug-resistant nature of this isolate

Conclusion The genomic analysis of the Enterobacter soli strain 140044 isolated from human blood reveals a complex antibiotic resistance profile underscored by the presence of the blaIMP-4 carbapenemase gene. The comprehensive resistance gene repertoire poses a significant concern for treatment options, emphasizing the need for vigilant surveillance and innovative approaches to manage infections caused by such multidrug-resistant organisms. This study highlights the importance of whole-genome sequencing in understanding the genetic underpinnings of antibiotic resistance in clinical isolates. Furthermore, it underscores the evolving challenge of carbapenem-resistant Enterobacteriaceae in healthcare settings, necessitating a proactive approach to antimicrobial stewardship and infection control measures to mitigate the spread of these formidable pathogens

关键字：IMP-4,Enterobacter,carbapenemase,blood

2015－2021 年中国 CHINET 血液标本临床分离菌的分布及耐药性

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目的 了解 2015-2021 年中国 CHINET 血液样本临床分离菌的分布和耐药性。

方法 对 2015-2021 年中国 CHINET 5[1] 2 家医疗机构血液样本临床分离菌进行细菌耐药性分析。

结果 临床分离 153591 株血培养阳性的细菌中革兰阳性菌 48.8%，革兰阴性菌为 51.1%。前五位的分离菌依次是凝固酶阴性葡萄球菌（28.2%）、大肠埃希菌（20.7%）、克雷伯菌属（13.7%）、肠球菌属（7.2%）、金黄色葡萄球菌（6.6%）。血液样本分离菌主要分离自内科（21.9±2.8）%、ICU（17.9±2.3）%、外科（14.1±3.2）%；男性患者分离菌的分布均高于女性患者；成人患者分离菌的分布高于儿童患者。肠杆菌目细菌对抗菌药的耐药率不尽相同。肺炎克雷伯菌对亚胺培南和美罗培南耐药率的变迁显示分别从 2015 年的 21.4%和 19.9%上升至 2021 年的 25.7%和 26.6%，但碳青霉烯类对其余肠杆菌目细菌仍然保持良好的抗菌活性。不动杆菌属对亚胺培南和美罗培南的耐药率分别为 68.0%和 67.7%；铜绿假单胞菌对碳青霉烯类的耐药率分别为 21.7%和 18.4%。成人和儿童肺炎链球菌的 PRSP 的检出率分别为 1.5%、0.8%。屎肠球菌和粪肠球菌对万古霉素、替考拉宁和利奈唑胺的耐药率均低于 3.0%。耐甲氧西林金黄色葡萄球菌（MRSA）和表皮葡萄球菌（MRSE）的检出率分别为 32.1%和 81.7%。

结论 2015-2021 年 CHINET 血液样本分离菌以凝固酶阴性葡萄球菌、大肠埃希菌和肺炎克雷伯菌为主，不同年龄和性别的患者主要分离菌分布差异有显著性意义。血液样本主要临床分离菌的耐药率在锯齿形变化中有一定缓慢下降趋势，但伴随着血液样本新的多重耐药菌的不断检出，提示我们应继续对血液样本分离菌进行耐药性监测，为临床合理应用抗菌药提供准确地耐药监测数据，遏制细菌耐药。

关键字：血液样本；病原菌分布；耐药性

Coexistence of BlaKPC-2 and BlaNDM-1 on An IncR Plasmid Carried by Clinical Citrobacter Freundii with Urinary Tract Infection in Children

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The rise of carbapenem-resistant Enterobacteriaceae (CRE) coharboring KPC-2 and NDM-1 (KPC-2-NDM-1-CRE) poses a significant public health threat. Among them, KPC-2-NDM-1-Citrobacter freundii (KPC-2-NDM-1-CRCF) remains underreported in clinical settings. In this study, we report the largest cohort to date of 8 KPC-2-NDM-1-CRCFs isolates from children with urinary tract infections. Species identification of Citrobacter freundii was performed by MALDI-TOF MS and 16s rRNA gene sequencing. Comprehensive characterization, including antimicrobial susceptibility testing, plasmid conjugation, whole-genome sequencing (WGS), and comparative genomics, was conducted for the KPC-2- NDM-1-CRCF clinical isolates. Antimicrobial susceptibility testing indicated all isolates were resistant to meropenem (MICs of >8μg/mL) and imipenem (MICs of >=8μg/mL). Genotyping and comparative genomics analysis identified the 8 KPC-2-NDM-1-CRCFs as ST523, exhibiting a close relationship with 45 single nucleotide polymorphisms (SNPs). Whole-genome sequencing and plasmid analysis confirmed the presence of blaKPC-2 and blaNDM-1 on a 46,050 bp IncR plasmid, transferable via mediation by other binding transfer elements. A conserved structural sequence (ΔISAba125-blaNDM-1-ble-MBL-trpF-dsbD-ISCR1) was detected upstream and downstream of the blaNDM-1 gene. Our research detected that ST523 KPC-2-NDM-1-CRCFs were disseminated in a children's hospital. Further investigations will be necessary to control and prevent the spread of KPC-2-NDM-1-CRCFs.

关键字：Citrobacter freundii, KPC-2-NDM-1-CRCFs, dissemination, comparative genomic analysis

Infection with Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae：clinical, Virulence and Molecular Epidemiological Characteristics

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Objective Carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKP) is gradually becoming the dominant nosocomial pathogens in the healthcare setting

Methods A retrospective study was conducted on patients with CR-KP from July 2021 to May 2022 in a teaching hospital. We identified bacterial isolates, collected the clinical data, and performed antimicrobial susceptibility testing, hypermucoviscosity string test, antimicrobial and virulence-associated genotype, as well as multi-locus sequence typing. CR-hvKP was defined as the presence of some combination of rmpA and/or rmpA2 with iucA, iroB, or peg-344. SPSS was used for data analysis. Univariate logistic regression analyses were used for risk factor and all statistically significant variables were included in the multivariate model. Statistical significance was taken to be $P < 0.05$

Results A total of 69 non-duplicated CR-KP isolates were collected, 27 of which were CR-hvKP. Out of the 69 CR-KP strains under investigation, they were distributed across 14 distinct sequence types (STs), wherein ST11 exhibited the highest prevalence, constituting 65.2% (45/69) of the overall isolates. The principal carbapenemase genes identified encompassed blakpc-2, blaNDM-1, and blaOXA-48, with blakpc-2 prevailing as the predominant type, accounting for 73.9% (51/69). A total of 69 CR-KP strains showed high resistance to common clinical antibiotics, with the exception of ceftazidime/avibactam. The ST11 ($P = 0.040$), ST65 ($P = 0.030$) and blakpc-2 ST11 clones ($P = 0.010$) were found to be highly related to hvKp. Regarding the host, tracheal intubation ($P = 0.008$), intracranial infection ($P = 0.020$) and neutrophil count ($P = 0.049$) were significantly higher in the patients with CR-hvKP. Multivariate analysis showed tracheal intubation to be an independent risk factor for CR-hvKP infection ($P = 0.030$, $OR = 4.131$). According to the clinical data we collected, tracheal intubation was performed mainly in the elderly with severe underlying diseases, which implied that CR-hvKP has become prevalent among elderly patients with comorbidities

Conclusion The prevalence of CR-hvKP may be higher than expected in the healthcare setting. CR-hvKP is gradually becoming the dominant nosocomial pathogen, and its prevalence and treatment will be a major challenge. It is essential to enhance clinical awareness and management of CR-hvKP infection

关键字：CR-hvKP，clinical，virulence，molecular epidemiological characteristics

Chromosomal Integration and Plasmid Fusion Occurring in ST20 Carbapenem-resistant Klebsiella Pneumoniae Isolates Coharboring BlaNDM-1 and BlaIMP-4 Induce Resistance Transmission and Fitness Variation

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Objective To investigate the epidemiology of ST20 carbapenem-resistant Klebsiella pneumoniae (CRKP) in China, and further explore the genomic characteristics of blaIMP-4 and blaNDM-1 co-harboring isolates and plasmids contribution to resistance and fitness

Methods We collected seven ST20 CRKP isolates nationwide, and the antimicrobial susceptibility testing (AST) was performed. Antimicrobial resistance genes, virulence genes, and plasmid replicon were identified using whole-genome sequencing-based analysis, and the clonality was performed by core-genome multilocus sequence typing. The plasmid transmission ability of blaIMP-4 and blaNDM-1 co-harboring isolates was carried out by conjugation experiment, and these isolates were further picked for long-read sequencing. The gene was located by Southern blotting, the formation of blaIMP-4 different locations was performed by genomic comparison, and the transposon unit was detected by inverse-PCR. The gene stability was performed by experimental passage, and the contributions to resistance and fitness of different plasmids were revealed by AST and growth curve, using plasmid curing isolates

Results We found four dual-harboring MBLs isolates, and the plasmid location experiment showed that blaIMP-4 was located in separated plasmid, self-conjugative fusion plasmid, and bacteria chromosome, respectively. Then, we found that the blaIMP-4 on fusion plasmid and bacteria chromosome was formed by

IS26 and ltrA, respectively, and circular transposon unit was relative to the cointegration. The blaNDM-1-harboring plasmid contributed to increase the resistance toward β-lactam and shorten the lag time in these isolates

Conclusion ST20 CRKP is a high-risk clone. With the use of ceftazidime/avibactam, the MBLs positive isolates, especially dual-MBLs isolates, should be given more additional attentions

关键字：carbapenem-resistant Klebsiella pneumoniae, ST20, NDM, chromosomal integrated IMP, plasmid recombination

孕产妇生殖道无乳链球菌的血清型分布及耐药基因分析

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目的 研究孕产妇生殖道分离的无乳链球菌（Streptococcus agalactiae，GBS）血清型分布及耐药基因，为临床防治 GBS 感染、合理使用抗菌药物提供参考依据。

方法 选择 2021 年 1 月-2022 年 6 月住院的妊娠晚期孕妇生殖道分泌物进行分离培养、纯化，并进行病原菌鉴定和药敏试验，使用 DNA 提取试剂盒提取 GBS 基因组 DNA，采用多重 PCR 扩增及基因测序的方法对 GBS 进行基因分型及耐药基因检测。

结果 共分离出 62 株 GBS，GBS 的血清型分别为III型（30 株，48.4%）、Ia 型（16 株，25.8%）、Ib 型（8 株，12.9%）、V 型（6 株，9.7%）、VI 型（2 株，3.2%）。GBS 药敏试验结果显示，GBS 对四环素、红霉素、克林霉素有着较高的耐药性，耐药率分别为 77.4%、71.0%、67.7%，对氨苄西林、青霉素 G、喹奴普丁达福普丁、利奈唑胺、万古霉素等均无耐药。四环素耐药基因 tetM、tetO、tetL 携带率分别为 75.0%（36/48）、33.3%（16/48）、8.3%（4/48）；红霉素耐药基因 ermB、mefA/E、ermA、ermTR 携带率为分别为 72.7%（32/44）、22.7%（10/44）、18.2%（8/44）、13.6%（6/44）；克林霉素耐药基因 linB 携带率为 42.9%（18/42）。GBS 红霉素和克林霉素耐药表型主要以内在型（cMLSB）表型为主，占 75.0%（36/48），主要由 ermB（44.4%，16/36）、ermB+linB（27.8%，10/36）基因介导。

结论 孕产妇生殖道 GBS 血清型以 III 型最为常见，GBS 对四环素、红霉素、克林霉素的耐药性较高，四环素耐药以 tetM、tetO 基因介导为主，红霉素耐药以 ermB 基因介导的 cMLSB 型为主，克林霉素耐药以 linB 基因介导为主。

关键字：孕产妇；无乳链球菌；血清型；耐药性；耐药基因

Plasmid-mediated Azithromycin Resistance in Nontyphoidal Salmonella Recovered From Human Infections.

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Objective Mechanisms of nontyphoidal Salmonella (NTS) resistance to azithromycin (AZM) have rarely been reported. To investigate the epidemiology and genetic features of AZM-resistance NTS

Methods A total of 457 NTS isolates were collected from a tertiary hospital in Guangzhou. We performed antimicrobial susceptibility tests, conjugation experiments, efflux pump expression tests, Whole-genome sequencing, and bioinformatics analysis to conduct the study

Results The results revealed that 10 NTS strains (2.8%) were resistant to AZM with MICs ranging from 128 to 512 mg/L and exhibited multidrug resistance. The phylogenetic tree revealed that 5 S. London strains discovered at different times and departments were closely related (3-74 SNPs) and 2 S. Typhimurium strains were clones (<3 SNPs) at three-month intervals. The AZM resistance was conferred by mph(A) gene found on different plasmids, including IncFIB, IncHI2, InFII, IncC, and IncI plasmids. Among them, IncFIB, InFII, and IncHI2 plasmids carried different IS26-class 1 integron (intI1) arrangement patterns that mediated multidrug resistance transmission. Conjugative IncC plasmid encoded resistance to ciprofloxacin, ceftriaxone, and AZM. Furthermore, phylogenetic analysis revealed that mph(A)-positive plasmids closely related to 10 plasmids in this study were mainly discovered from NTS, Escherichia coli, Klebsiella pneumonia, and Enterobacter hormaechei. The genetic environment of mph(A) in 10 NTS strains was cluster IS26-mph(A)-mrx(A)-mphR(A)-IS6100/IS26 that co-arranged with intI1 harbor multidrug resistance gene cassettes on diverse plasmids

Conclusion These findings highlight the dissemination of plasmids carrying mph(A) and various intI1 multidrug resistance gene cassettes would seriously restrict the availability of essential antimicrobial agents for treating NTS infections

关键字：Nontyphoidal Salmonella, azithromycin, multidrug resistance, mph(A)-positive plasmid, class 1 integron

Study on The Molecular Characteristics and

Pathogenic Mechanisms of A KPC-3 Producing ST23-K1 Type Hypervirulent Carbapenem-resistant Klebsiella Pneumoniae

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Objective To screen hypervirulent carbapenem-resistant Klebsiella pneumoniae (CR-hvKP) in the Ningbo region, and to study its molecular characteristics and pathogenic mechanism, so as to give evidence-based details for the prevention and elimination of nosocomial infection and clinical diagnosis and treatment in the local district

Methods A total of 96 strains of carbapenem-resistant Klebsiella pneumoniae were collected from the Ningbo area from January 2021 to December 2022, and major virulence genes rmpA, aerobactin and carbapenem-resistant genes were profiled by PCR. The identified CR-hvKP was screened by whole genome sequencing and bioinformatic methods to characterize underlying molecular characteristics. The minimum inhibitory concentrations (MIC) of common clinical antibiotics were determined by VITEK-2 Compact automatic microbiological analyzer, and the MIC of polymyxin, tigecycline and ceftazidime/avibactam were determined by microbroth dilution method. The transferability of resistance plasmids was evaluated through plasmid conjugation experiments. Finally, the pathogenic mechanisms were explored using mouse virulence assays

Results Among the 96 strains, one strain of CR-hvKP was isolated, with an isolation rate of 1.04%. Results from PCR assays revealed the presence of the virulence genes rmpA and aerobactin. Whole-genome sequencing revealed the strain to be of the ST23 serotype with a K1 capsule. This strain contains one chromosome and three plasmids. Besides carrying the extended-spectrum beta-lactamase gene blaSHV-11 on its chromosome, it also harbours the MFS efflux pump genes emrA, emrB, emrD, and the RND efflux pump genes oqxA and oqxB. Plasmid 1 is a pLVPK-like virulence plasmid carrying virulence genes rmpA2, iroB, icuA, and terB, among others. Plasmid 2 contains transposable element sequences such as IS15 and IS26. Plasmid 3, a resistance plasmid, carries the blaKPC-3 carbapenem resistance gene. Mouse virulence assays demonstrated that CR-hvKP has a high mortality rate, and its pathogenic mechanism is associated with the activation of the NF-κB signalling pathway

Conclusion The Ningbo region has confirmed the emergence of hypervirulent CR-hvKP, likely resulting from the acquisition of a pLVPK-like virulence plasmid and a blaKPC-3 resistance plasmid by the ST23-K1 type Klebsiella pneumoniae. Consequently, there is a pressing need for more judicious use of antimicrobial drugs to mitigate the occurrence of resistance. Additionally, it is crucial to strengthen infection prevention and control measures to minimize the dual transmission of virulence and resistance plasmids

关键字： Hypervirulent Carbapenem-resistant Klebsiella Pneumoniae; Virulence genes; Resistance genes; Whole-genome Sequencing; pLVPK-like Virulence Plasmid; blaKPC-3 Resistance Plasmid; NF-κB Signaling Pathway

Deletion of The HFQ Gene Exacerbates Systemic Inflammatory Response in Mice Induced by Outer Membrane Vesicles of Klebsiella Pneumoniae

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Objective This study aimed to investigate the impact of HFQ gene deletion on the transcriptome of Klebsiella pneumoniae (NTUH-K2044 strain), the characteristics of its outer membrane vesicles (OMVs), and the inflammatory response they induce in a mouse model

Methods Through RNA-seq technology, we analyzed the differences in the transcriptome between the wild-type WT and the Δhfq knockout strain during the logarithmic growth phase and examined the KEGG pathways of the differentially expressed genes. Additionally, the protein concentration of OMVs was determined using the Bradford method, and the protein composition of OMVs was compared using SDS-PAGE and silver staining. Moreover, the effects of HFQ gene deletion on the morphology and size of OMVs were studied using transmission electron microscopy (TEM) and nanoscale particle analysis (NTA). OMVs were introduced into the mouse lung through tracheal instillation to observe their impact on the mouse's lungs, spleen, and liver

Results Transcriptome analysis revealed 1953 differentially expressed genes, with 1450 downregulated and 503 upregulated in the Δhfq knockout strain. KEGG pathway analysis indicated that metabolic pathways were most affected. Notably, two-component system (TCS) related genes were regulated by HFQ, influencing the bacterium's response to environmental changes. HFQ gene deletion reduced the protein concentration of OMVs, altered their protein profile, and significantly changed the morphology and size of OMVs, increasing particle concentration. In the mouse

model, HFQ knockout enhanced the systemic inflammatory response induced by OMVs, particularly causing more severe damage and inflammatory reactions in the lungs, spleen, and liver

Conclusion The HFQ gene plays a crucial role in the gene expression regulation, characteristics of OMVs, and the inflammatory response they induce in Klebsiella pneumoniae. Deletion of the HFQ gene not only affects the bacterium's transcriptome expression and metabolic pathways but also significantly alters the protein composition, morphology, and size of OMVs, thereby exacerbating the inflammatory response in the mouse model. This study provides new insights into the pathogenicity of Klebsiella pneumoniae

关键字： Klebsiella pneumoniae1;HFQ gene knockout2;.RNA-seq analysis3; Outer Membrane Vesicles4;Inflammatory Response5.

Emergence of Ceftazidime/avibactam Resistance in NDM-5-producing Klebsiella Pneumoniae in A Tertiary Hospital in China

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Objective This study aims to explore the molecular biology characteristics of a Klebsiella pneumoniae strain exhibiting resistance to ceftazidime/avibactam

Methods The Klebsiella pneumoniae strain, designated as KP217360, isolated from a urine sample at the Li Huili Hospital of Ningbo Medical Center, was subjected to minimum inhibitory concentration (MIC) determination for various antibiotics using the VITEK-2 Compact fully automated microbiology analyzer. MICs for polymyxin, tigecycline, and ceftazidime/avibactam were established using a broth microdilution method. Bacterial genome de novo sequencing and analysis were conducted to identify resistance genes and virulence factors. Experiments on conjugation were conducted to evaluate the transmissibility of the resistance plasmids. Finally, the virulence of the strain was determined using a Galleria mellonella infection model

Results Klebsiella pneumoniae KP217360 exhibited resistance to most antibiotics, including imipenem, ertapenem, and ceftazidime/avibactam. It belonged to the KL16 capsular type and carried multiple resistance genes, including blaCTX-M-65, blaSHV-103, blaTEM-1, and several iron acquisition-related virulence genes such as iutA, entABCDEF, and iroN. The strain harbored three plasmids, with one being of the IncX3 type carrying the blaNDM-5 resistance gene, while the functions of the other two remained unclear. Therefore, KP217360 was identified as a carbapenem-resistant high-virulence Klebsiella pneumoniae; in the toxicity test on Galleria mellonella, it was found that the survival rate of the KP217360 group was only 40% after 72 hours, significantly lower than the 70% survival rate of the control group

Conclusion This study identified a highly virulent carbapenem-resistant Klebsiella pneumoniae strain of the ST685 type with blaNDM-5 in Ningbo, Zhejiang, China. This highlights the need for enhanced surveillance of antibiotic resistance and infection control measures to reduce the transmission of IncX3-type blaNDM-5 resistance plasmids in the local area

关键字： hypervirulent Klebsiella pneumoniae, whole genome sequencing, blaNDM-5

Seasonal Meropenem Resistance in Acinetobacter Baumannii and Influence of Temperature-Driven Adaptation

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Objective Recognition of seasonal trends in bacterial infection and drug resistance rates may enhance diagnosis, direct therapeutic strategies, and inform preventive measures. Limited data exist on the seasonal variability of Acinetobacter baumannii. We investigated the seasonality of A. baumannii, the correlation between temperature and meropenem resistance, and the impact of temperature on this bacterium

Methods Antimicrobial resistance data from 45 Hebei Province hospitals, collected between January 2020 and December 2022, were analyzed using software WHONET 5.6 and SPSS 24.0. The study investigated the seasonality of A. baumannii meropenem resistance rates and their correlation with temperature. Acclimatization of A. baumannii to different temperatures was assessed by growth rate, survival rate, and competition index. Additionally, preliminary investigation of the effect of temperature on the expression of drug resistance genes by qRT-PCR

Results Meropenem resistance rates increased with lower temperatures, peaking in winter/colder months. The difference in the rate of resistance between quarters of the same year reached 13.4%−28.0%. Nonresistant strain detection exhibited temperature-dependent seasonality, rising in summer/warmer months and declining in winter/colder months. In contrast, resistant strains showed no seasonality. Variations in meropenem-resistant and nonresistant bacterial resilience to temperature changes were observed. Nonresistant strains displayed growth advantages at temperatures ≥25°C, whereas, in vitro competition experimental results show that exposure to low temperatures reversed the fitness cost imposed on A. baumannii by the drug-resistant plasmid poxa23. At 4°C, the strain AB7434-

poxa23, which obtained the drug-resistant plasmid, showed a clear competitive advantage compared to the sensitive strain AB7434. Furthermore, a 4°C low-temperature treatment increased the survival of A. baumannii ATCC19606 under meropenem stress. Low temperature and meropenem exposure upregulated the expression of drug resistance-related genes adeJ and oxa-51

Conclusion Meropenem resistance rates in A. baumannii display seasonality and are negatively correlated with local temperature, with rates peaking in winter, possibly linked to the differential adaptation of resistant and nonresistant isolates to temperature fluctuations. Furthermore, due to significant resistance rate variations between quarters, compiling monthly or quarterly reports might enhance comprehension of antibiotic resistance trends. Consequently, this could assist in formulating strategies to control and prevent resistance within healthcare facilities

关键字：Acinetobacter baumannii, antibiotic resistance, seasonality, meropenem, temperature

Elucidating Mechanisms of Cefiderocol Resistance in Hypervirulent Klebsiella Pneumoniae: Insights Into CirA Deficiency and Co-Production of KPC-2 and SHV-12

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Objective Cefiderocol is a novel cephalosporin antibiotic showing a potent and broad-spectrum activity against Gram-negative multidrug-resistant (MDR) pathogens. We identified a hypervirulent carbapenem-resistant Klebsiella pneumoniae strain that displayed resistance to cefiderocol, leading to metastatic infections, including ocular, bloodstream, urinary and central nervous system involvement

Methods In this study, YDDB, YDDU and YDDCSF were the primary study strains isolated from the same patients. We used the TruePrep DNA Library Prep kit v2 (Vazyme Biotech, Nanjing, China) to prepare DNA from YDDB, YDDU and YDDCSF for next-generation sequencing on the Illumina HiSeq X 10 platform (Illumina, San Diego, CA) with 100-bp paired-end reads and using HiSeq SBS kit v4 (Illumina, San Diego, CA). MLST, serotype, antimicrobial resistance and virulence genes were identified using Kleborate [20]. Plasmid type was identified by PlasmidFinder-2.0. Circular plasmid maps were depicted by CGView Server (https://proksee.ca/). Synteny plots of plasmid alignment were generated by R v.3.6.2 after pairwise BLASTN comparisons. Cloning and sequencing were performed to clafify the contribution of SHV-12 and KPC-2 to cefiderocol resistance. Antimicrobial susceptibility in this study was determined by broth microdilution method recommended by CLSI

Results This strain, belonging to sequence type (ST) 11 and K locus (KL) 5, carried a pLVPK-like virulence plasmid and produced KPC-2 and SHV-12 enzymes. Additionally, an amino acid mutation was observed in catecholate siderophore receptor CirA, resulting in truncation of the CirA protein. Ultimately, we determined that the deficiency in CirA, along with the production of KPC-2 and SHV-12, collectively contributed to the resistance to cefiderocol

Conclusion The convergence of hypervirulence and carbapenem resistance presents significant challenges in treatment. Our study represents the first documentation of the coexistence of hv-CRKP and cefiderocol resistance. While cefiderocol has yet to receive approval in China, it is imperative to elevate awareness and undertake concerted efforts to manage this emerging situation

关键字：Klebsiella pneumoniae, CirA, hvKP, cefiderocol, KPC-2, SHV-12

Multidrug Resistance and Virulence Plasmids Recombination During Conjugation Drives The Prevalence of of ST11 KPC-producing Hypervirulent Klebsiella Pneumoniae in China

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Objective Sequence type (ST)11 carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKP) can cause life-threatening infections and is thus of concern for global dissemination. Despite its importance, the evolutionary history and mechanism for the formation of ST11 CR-hvKP are unclear. In this study, we performed conjugation experiments to explore the formation process and mechanism of ST11 CR-hvKP

Methods Conjugation experiment was conducted between an hypervirulent Klebsiella pneumoniae (hvKP) strain AP8555 and a ST11 carbapenem-resistant Klebsiella pneumoniae (CRKP) strain. Transconjugants obtained from conjugation assays were confirmed by XbaI and S1 nuclease pulsed-field gel electrophoresis (PFGE), PCR detection and whole-genome sequencing (WGS).We characterized these strains for their virulence phenotype, plasmid stability and adaptability using Galleria mellonella, pairwise competition assay and growth curve measurements

Results Conjugation experiment generated two ST11 CR-hvKP strains. Research had confirmed that the

virulence plasmid pAP855 was horizontally transferred to the CRKP strain to form the conjugant S270-1, which was then recombined to form the conjugant S270v. The process was accompanied by the acquisition of high virulence, high plasmid stability and stronger adaptability. Interestingly, the conjugant S270v had highly homology to clinically prevalent ST11 CR-hvKP strains

Conclusion This is the first demonstration that plasmids recombination in vitro led to the formation of ST11 CR-hvKP strains. The clinical setting is a multifactorial and multi-selection pressures environment that may stimulates the evolution of conjugant strain in transition period to local strain in stable period, and surveillance is urgently needed for infection control

关键字：Klebsiella pneumoniae, CR-hvKP, conjugation, fitness costs

Virulence Plasmid with IroBCDN Deletion Promoted Cross-regional Transmission of ST11-KL64 Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae in Jiangxi, China

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Objective Carbapenem-resistant and hypervirulent Klebsiella pneumoniae (CR-hvKP) caused infections of high mortality and brought a serious impact on public health. This study evaluated the transmissibility of CR-hvKP among different regions to provide corresponding advice for cross-regional prevention

Methods Clinical K. pneumoniae strains were collected from Jiujiang region and Nanchang region in Jiangxi province from November 2021 to June 2022. We characterized these strains for their genetic relatedness, virulence phenotype, and dissimilarities in virulence plasmid structures using PFGE, Galleria mellonella, Whole-genome sequencing. Conjugation assay was performed to evaluate the transmissibility of virulence plasmids

Results Among 609 strains, 45 (7.4%) CR-hvKP were identified, while the strains isolated from Nanchang and Jiujiang accounted for 10.05% (36/358) and 3.59% (9/251). We observed that ST11-KL64 CR-hvKP had an overwhelming epidemic dominance in these two regions. Significant genetic diversity was identified among all ST11-KL64 CR-hvKP cross-regional transmission between Nanchang and Jiujiang serving as major drivers of clonal clusters. Virulence genes profile revealed that ST11-KL64 CR-hvKP might harbour incomplete pLVPK-like plasmids and primarily evolved from CRKP by acquiring the hypervirulence plasmid. We found the predominance of truncated-IncFIB/IncHI1B type virulence plasmids with a 25kb fragment deletion that encoded iroBCDN clusters. Virulence plasmids harbored in CR-hvKP isolates with iroBCDN deletion fragment exhibited a higher conjugation success rate and efficiency

Conclusion ST11-KL64 is the most cross-regional prevalent type CR-hvKPs in Jiangxi province, which mainly evolved from CRKPs by acquiring a truncated-IncHI1B/IncFIB virulence plasmid with the deletion of iroBCDN. Stricter surveillance and control measures are urgently needed to prevent the epidemic transmission of ST11-KL64 CR-hvKP

关 键 字 ： Carbapenem-resistant hypervirulent Klebsiella pneumoniae, Virulence plasmid, Whole genome sequencing, MLST, Capsular serotypes.

Cryo-electron Microscopy Structure and Complementary Drug Efflux of Acinetobacter Baumannii Multidrug Efflux Pump AdeG

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Objective Multidrug-resistant A. baumannii has emerged as one of the most antibiotic-resistant bacterial pathogens associated with nosocomial infection in intensive care units, which is highly dependent on the multidrug efflux pump system. Acinetobacter drug efflux G (AdeG), a member of the resistance-nodulation-cell division (RND) family, reported to be involved in drug resistance to chloramphenicol, trimethoprim, ciprofloxacin and clindamycin. Considering the low sequence identity but similar function between AdeG and AdeJ or AdeB and the intimate connection between multiple RND efflux pumps, we solved the AdeG structure with systematical functional study

Methods We expressed and purified the full-length adeG, and solved the cryo EM structure of AdeG efflux pump with systematic structural alignment and docking analyses. We further validated the physiological role the efflux pump with construction of chromosomal AdeB/AdeG/AdeJ deletion using RECAB system

Results We report the cryo-EM structure of the AdeG efflux pump from A. baumannii ATCC 19606. The full-length AdeG protein consists of 1039 amino acids, all of which were included in our final model. Our resulting structural model of AdeG reveals a typical-homotrimeric hydrophobe-amphiphile efflux (HAE)-RND efflux pump, consisting of a transmembrane domain, a periplasmic domain, and a small cytoplasm domain. We carried out systematic structural alignment and docking analyses between AdeG, AdeB and AdeJ. We further carried out antibiotic resistance profiling between knockouts of the AdeABC, AdeFGH and AdeIJK efflux pumps. This suggests that three resistance-nodulation-

cell division (RND) transporters confer resistance to antibiotics with complementary activities: with deletion of one of the RND transporters, the others are overexpressed, allowing Acinetobacter baumannii to maintain multidrug resistance.

Conclusion We systematically compare the assembly and potential substrate binding specificity of AdeG, AdeB and AdeJ multidrug efflux pumps and demonstrate the potentially complementary drug efflux mechanism between the AdeABC, AdeFGH and AdeIJK

关键字：Acinetobacter baumannii, Efflux Pump, Multidrug Resistance, AdeG, Cryo-Electron Microscopy

Cefiderocol Resistance Profile and Molecular Mechanisms of Carbapenem-resistant Klebsiella Pneumoniae before Its Use in Jiangxi, China

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Objective As one of the most pressing public health threats in China, Carbapenem-resistant Klebsiella pneumoniae (CRKP) requires effective drugs such as cefiderocol (FDC) as a 'last resort'. In this study, we reported the FDC resistance profile in non-cefiderocol treated Jiangxi, China and explored the resistance mechanisms of non-susceptible isolates

Methods We retrospectively selected 477 non-duplicate CRKP clinical isolates and characterized these isolates for their FDC susceptibility, virulence genes and MLST by broth microdilution method, PCR and sequencing. Whole genome sequencing was performed on four non-susceptible isolates to investigate their resistance mechanism

QPCR was employed to further investigate the expression of blaKPC-2.

Results FDC had a high antibacterial activity against CRKP isolates in Jiangxi (99.6%) and MIC50/90 value was 1/2 mg/L. The MICs of ST11 CRKP were significantly higher than those of non-ST11 CRKP. Furthermore, the MICs value of CR-hvKp were significantly higher than those of CR-cKp. Among the 477 CRKP isolates analyzed, three non-susceptible isolates of ST11 and one intermediate isolate of ST15 were identified. The non-susceptible isolates all contained only serine-β-lactamases (SBLs), and all showed a significant increase in FDC activity against the isolates after addition of the serine enzyme inhibitor avibactam (8- to 16-fold decrease in MIC). The ST15 isolate harbored two copies of KPC-2, and its expression of KPC-2 was higher compared to the other three isolates. Both resistant isolates contained mutations of the cirA gene, leading to truncation and defect in the CirA protein

Conclusion Cefiderocol is a highly effective antimicrobial drug, but its activity against ST11 CR-hvKp may be compromised. FDC resistance is attributed to various factors, including the expression and multiple copies of SBLs and CirA defect, while high-level resistance against FDC is often associated with mutations of the cirA gene

关键字：Carbapenem-resistant Klebsiella pneumoniae; Cefiderocol resistance; ST11; Serine-β-lactamases; CirA

Within-host Sequence Type Selection From ST15 To ST11 of Carbapenem-resistant Klebsiella Pneumoniae with Low Fitness Cost During Multiple Antibiotic Therapy

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Objective Carbapenem resistant Klebsiella pneumoniae (CRKP) has posed great threat to public health and clinical practice. Here we reported a CRKP-associated fatal infection and reveal the sequence type within-host selection under antibiotic pressure

Methods Five CRKP strains were isolated from a gallbladder cancer patient in continual antimicrobial treatment during 3 months. After three months of treatment, the dominant sequence type of CRKP shifted from ST15 to ST11 strains. We characterized these strains for their virulence phenotype, genetic relatedness and fitness using Galleria mellonella, whole genome sequencing and growth curve measurements

Results WGS analysis found all ST11 CRKP were wzi64-KL64 clones while the ST15 CRKP was wzi19-KL19. Among these ST11 CRKP strains, all were resistant to amikacin, colistin and ceftazidime/avibactam. Furthermore, ST15 CRKP strain was positive for the KfuB virulence gene and more resistant to serum killing compared to the ST11 CRKP strains. As determined in the Galleria mellonella model, the virulence of the ST15 strain was higher than that of ST11 strains. Compared to ST15, the ST11 CRKP strain has lower fitness cost at higher concentration of meropenem

Conclusion Overall, our study depicted a patient sequence type selection shift from ST15 to ST11 with lower fitness cost of CRKP under carbapenem selection pressure. The changes show how a patient's treatment history might shape the sequence type selection of CRKP and effective measures should be taken to prevent its transmission in clinical practice

关键字：Carbapenem-resistant Klebsiella pneumoniae; virulence; fitness; sequence type selection

Epidemiology and Azole Resistance of Clinical Isolates of Aspergillus Fumigatus From A Large Tertiary Hospital in Ningxia, China

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Purpose The objective of this study was to determine the clinical distribution, in vitro antifungal susceptibility and underlying resistance mechanisms of Aspergillus fumigatus (A. fumigatus) isolates from the General Hospital of Ningxia Medical University between November 2021 and May 2023

Methods Antifungal susceptibility testing was performed using the Sensititre YeastOne YO10, and isolates with high minimal inhibitory concentrations (MICs) were further confirmed using the standard broth microdilution assays established by the Clinical and Laboratory Standards Institute (CLSI) M38-third edition. Whole-Genome Resequencing and RT-qPCR in azole-resistant A. fumigatus strains were performed to investigate the underlying resistance mechanisms

Results Overall, a total of 276 A. fumigatus isolates were identified from various clinical departments, showing an increasing trend in the number of isolates over the past 3 years. Two azole-resistant A. fumigatus strains (0.72%) were observed, one of which showed overexpression of cyp51A, cyp51B, cdr1B, MDR1/2, artR, srbA, erg24A, and erg4B, but no cyp51A mutation. However, the other strain harbored two alterations in the cyp51A sequences (L98H/S297T). Therefore, we first described two azole-resistant clinical A. fumigatus strains in Ningxia, China, and reported one azole-resistant strain that has the L98H/S297T mutations in the cyp51A gene without any tandem repeat (TR) sequences in the promoter region

Conclusions This study emphasizes the importance of enhancing attention and surveillance of azole-resistant A. fumigatus, particularly those with non-TR point mutations of cyp51A or non-cyp51A mutations, in order to gain a better understanding of their prevalence and spread in the region

关键字：Keywords: Aspergillus fumigatus; azole resistance; cyp51A mutation; tandem repeat sequences

Genome-wide SRNA and MRNA Transcriptomic Profiling Insights Into Carbapenem-resistant Acinetobacter Baumannii

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Objective Acinetobacter baumannii (AB) is rising as a human pathogen of critical priority worldwide as it is the leading cause of chronic opportunistic infections in healthcare settings and carbapenem-resistant AB is listed as “super bacterium” or “priority pathogen for drug resistance” by the World Health Organization. In order to disclosing the precise mechanisms of how the sRNAs are implicated in bacterial resistance to antimicrobial drugs, this study will preliminarily screen sRNAs related to carbapenem resistance genes in A. baumannii and speculate on possible target genes and drug resistance mechanisms

Methods Clinical isolates of A. baumannii were collected and tested for antimicrobial susceptibility. Among them, carbapenem-resistant and carbapenem-sensitive A. baumannii were subjected to prokaryotic transcriptome sequencing. The change of sRNA and mRNA expression was analyzed by bioinformatics and validated by quantitative reverse transcription-PCR

Results We have currently collected 687 clinical isolates of A. baumannii from January 2022 to March 2023. The drug sensitivity results showed that 336 strains of carbapenem resistant A. baumannii were also resistant to piperacillin/tazobactam, ciprofloxacin, ceftazidime, and cefepime. 351 strains of carbapenem sensitive A. baumannii were partially sensitive to levofloxacin, tobramycin, cefoperazone/sulbactam, or amikacin, while 687 strains of A. baumannii were all sensitive to polymyxin. 506 differentially expressed genes were discovered through the transcriptomic profile analysis between carbapenem-resistant isolates and carbapenem-sensitive isolates. We aligned these 506 differentially expressed gene sequences to the CARD resistance database (The comprehensive antimicrobial resistance database, https://card.mcmaster.ca/). A total of 54 differentially expressed genes were successfully compared to the drug resistance database. There were 92 new transcripts discovered, including 40 sRNA candidates and 52 new potential coding transcripts. The lengths of the 40 sRNA candidates range from 56 to 330 nucleotides. 19 differentially expressed sRNA candidates were identified in bacterial resistance to carbapenem (adjusted P-values (P-adj) < 0.05; $|\log2(\text{fold change})| \geq 1$). Both IntaRNA and targetRNA3 databases have predicted potential binding sites for sRNA21 and AdeK, sRNA27 and PgaC, sRNA29 and AdeB, sRNA36 and KatG. The target genes were predicted using IntaRNA, which calculates the combined energy score of the interaction as the sum of the free energy of hybridization and the free energy required to make the interaction sites accessible. We used 20 clinical carbapenem resistant and 20 sensitive strains each to perform RNA extraction and qRT-PCR to detect the relative expression levels of sRNA21, sRNA27, sRNA29, sRNA36, AdeK, PgaC, AdeB, and KatG. There were showed a negative correlation between sRNA21 and AdeK (r = -0.581, P = 0.007), sRNA27 and PgaC (r = -

0.612, P = 0.004), sRNA29 and AdeB (r = -0.516, P = 0.020). There was no correlation between the relative expression levels of sRNA36 and KatG (r = -0.365, P = 0.113)

Conclusion This study preliminarily screened differentially expressed mRNA and sRNA in carbapenem-resistant A. baumannii, and explored possible targeting relationships, which will help further reveal the resistance mechanism and provide a theoretical basis for the development of drugs targeting sRNA for the prevention and treatment of carbapenem-resistant A. baumannii infection

关键字：Acinetobacter baumannii, carbapenem resistance, transcriptomic profiling, small RNA (sRNA), target gene

PenA Profile of Neisseria Gonorrhoeae in Guangdong, China: Novel PenA Alleles Are Related To Decreased Susceptibility To Ceftriaxone Or Cefixime

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Objective Resistance to extended-spectrum cephalosporins (ESC) has become a public health concern with the spread of Neisseria gonorrhoeae and increasing antimicrobial resistance. Mutation of penA, encoding penicillin-binding protein 2, constitutes a considerable mechanism of ESC resistance. In this study, we sought to assess penA alleles and mutations associated with decreased susceptibility (DS) to ESC in Neisseria gonorrhoeae

Methods In 2021, 347 gonococci were collected in Guangdong, China. MIC of ceftriaxone and cefixime, whole-genome sequencing, and phylogenetic analysis were performed. MLST and conventional resistance determinants such as penA, mtrR, PonA, and PorB were analyzed. penA was genotyped and sequence-aligned using PubMLST

Results Genome-wide phylogenetic analysis reveals that ESC-DS prevalence was highest in Clade 11.1 (100.0%), Clade 2 (66.7%), and Clade 0 (55.7%), and the leading cause was strains with penA-60.001 or new penA alleles in clades. The penA phylogenetic tree is divided into two branches: non-mosaic penA and mosaic penA. The latter contained penA-60.001, penA-10, and penA-34. penA profile analysis indicated A311V and T483S are closely related to ESC-DS in mosaic penA. The new alleles NEIS1753_2840 and NEIS1753_2837 are close to penA-60.001, with 100% DS to ceftriaxone and cefixime. NEIS1753_2660, derivative from penA-10 (A486V), has increased ceftriaxone DS. NEIS1753_2846, derivative from penA-34.007 (G546S), displayed cefixime DS

Conclusion Our study discloses critical penA alleles related to elevated MICs and trends of gonococcus-evolved mutated penA associated with ESC-DS in Guangdong

关键字：Neisseria gonorrhoeae; decreased susceptibility; extended-spectrum cephalosporins (ESC); penA; phylogenetic analysis; whole-genome sequencing

Colistin Heteroresistance in Enterobacter Due To Base Heterozygosity at Certain PhoP and PhoQ Locations

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Objective The objective of this study was to investigate colistin heterogeneous resistance (CHR) in Enterobacter clinical strains causing bloodstream infections, elucidate the mechanism underlying CHR, and explore its clinical significance

Methods We conducted in vitro time-killing experiments and in vivo murine intra-abdominal infection models to evaluate the impact of CHR on colistin treatment failure. Whole-genome sequencing and ultra-deep amplicon sequencing were performed to identify genetic alterations associated with colistin resistance and to analyze the heterogeneity of resistance within Enterobacter strains

Results We found that 30% of Enterobacter clinical strains exhibited CHR, which was associated with failure of colistin treatment both in vitro and in vivo. Novel base alterations in the two-component system gene phoP or phoQ were identified as the mechanism for colistin resistance. Additionally, we detected the presence of colistin-resistance-mediated base alterations in minor subpopulations of the same strain, resulting in heterogeneity of colistin resistance. Base heterozygosity pre-existed before exposure to colistin, indicating a survival strategy. Multiple colistin-resistant subpopulations were found to coexist within the same strain, enhancing flexibility in response to antimicrobial selection pressure

Conclusion Our study reveals the genetic heterogeneity in CHR Enterobacter strains and provides genetical explanations for the unstable and transient heterogeneous resistance. These findings underscore the clinical significance of CHR and offer important insights into the mechanisms underlying antimicrobial resistance heterogeneity

关键字：Enterobacter, colistin heterogeneous resistance, antimicrobial resistance, genetic heterogeneity

ST218 Klebsiella Pneumoniae Became A High-risk Clone for Multidrug Resistance and Hypervirulence

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Objective The occurrence of multidrug-resistant and hypervirulent Klebsiella pneumoniae (MDR-hvKp) worldwide poses a great challenge for public health. Few studies have focused on ST218 MDR-hvKp

Methods Retrospective genomic surveillance was conducted at the Peking University Third Hospital from 2017 and clinical information was obtained. To understand genomic and microbiological characteristics, antimicrobial susceptibility testing, plasmid conjugation and stability, biofilm formation, serum killing, growth curves and whole genome sequencing were performed. We also assessed the clinical and microbiological characteristics of ST218 compared with ST23

Results A total of eleven ST218 Kp isolates were included. The most common infection type was lower respiratory tract infection (72.7%, 8/11) in our hospital, whereas ST23 hvKp (72.7%, 8/11) was closely associated with bloodstream infection. Notably, nosocomial infections caused by ST218 (54.5%, 6/11) was slightly higher than ST23 (36.4%, 4/11). All of the ST218 and ST23 strains presented with the virulence genes combination of iucA + iroB + peg344 + rmpA + rmpA2. Interestingly, the virulence score of ST218 was lower than ST23, whereas one ST218 strain (pPEKP3107) exhibited resistance to carbapenems, cephalosporins, β-lactamase/inhibitors and quinolones and harbored an ~ 59-kb IncN type MDR plasmid carrying resistance genes including blaNDM-1, dfrA14 and qnrS1. Importantly, blaNDM-1 and qnrS1 were flanked with IS26 located within the plasmid that could successfully transfer into E. coli J53. Additionally, PEKP2044 harbored an ~ 41-kb resistance plasmid located within tetA indicating resistance to doxycycline

Conclusion The emergence of blaNDM-1 revealed that there is great potential for ST218 Kp to become a high-risk clone for MDR-hvKp, indicating the urgent need for enhanced genomic surveillance

关键字：Hypervirulent Klebsiella pneumoniae, Multidrug resistant, ST218, blaNDM-1

Antimicrobial Resistance in Severe Pneumonia: Surveillance, Mechanisms, and Impact on Clinical Outcomes

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Objective The global rise in antimicrobial resistance (AMR) among bacterial and fungal pathogens complicates the treatment of severe pneumonia, leading to increased morbidity and mortality. This study aims to evaluate the current state of AMR in severe pneumonia cases, focusing on prevalent pathogens and underlying resistance mechanisms

Methods A retrospective study was conducted, analyzing clinical isolates from 1,510 patients diagnosed with severe pneumonia collected by the National Respiratory Medicine Center in the southern region from January 2018 to December 2021. The study assessed AMR patterns using phenotypic and genotypic methods, including disk diffusion, E-test, and whole-genome sequencing. The data were correlated with clinical outcomes to identify resistance trends and potential therapeutic implications

Results Resistance to third-generation cephalosporins was identified in 78% of Klebsiella pneumoniae isolates, with 60% exhibiting extended-spectrum beta-lactamase (ESBL) production. Among Pseudomonas aeruginosa isolates, 45% were resistant to carbapenems. Candida species showed an alarming 30% rate of resistance to fluconazole. The mecA gene, responsible for methicillin resistance, was present in 85% of Staphylococcus aureus samples. Multidrug-resistant (MDR) pathogens were associated with a 35% increase in hospital stay length and a 50% increase in mortality compared to non-MDR pathogens. Genomic analysis revealed novel resistance genes and mutations contributing to AMR

Conclusion The study highlights a concerning trend of rising AMR among pathogens causing severe pneumonia, with significant clinical implications. The identification of novel resistance mechanisms underscores the need for ongoing surveillance, the development of new antimicrobial agents, and the judicious use of existing antibiotics. Addressing the AMR challenge requires a multifaceted approach, integrating advanced diagnostic techniques, personalized medicine, and comprehensive infection control practices

关键字：severe Pneumonia, antimicrobial resistance, bacterial pathogens, fungal pathogens, resistance mechanisms, clinical outcomes

Molecular Characterization of Extensively

Drug-resistant Hypervirulent Pseudomonas Aeruginosa Isolates in China

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Objective Recently, extensively drug-resistant Pseudomonas aeruginosa (XDR-PA) isolates have been increasingly detected and posed great challenges to clinical anti-infection treatments. However, little is known about extensively resistant hypervirulent P. aeruginosa (XDR-hvPA). In this study, we investigate its epidemiological characteristics and provide important basis for preventing its dissemination

Methods Clinical XDR-PA isolates were collected from January 2018 to January 2023 and identified using matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry; antibiotic susceptibility testing was performed by broth microdilution method, and minimum inhibitory concentrations (MICs) were evaluated. Virulence was evaluated using the Galleria mellonella infection model; molecular characteristics, including resistance genes, virulence genes, and homology, were determined using whole-genome sequencing

Results A total of 77 XDR-PA strains were collected; 47/77 strains were XDR-hvPA. Patients aged >60 years showed a significantly higher detection rate of XDR-hvPA than of XDR-non-hvPA. Among the 47 XDR-hvPA strains, 24 strains carried a carbapenemase gene, including blaGES-1 (10/47), blaVIM-2 (6/47), blaGES-14 (4/47), blaIMP-45 (2/47), blaKPC-2 (1/47), and blaNDM-14 (1/47). ExoU, exoT, exoY, and exoS, important virulence factors of PA, were found in 31/47, 47/47, 46/47, and 29/47 strains, respectively. Notably, two XDR-hvPA simultaneously co-carried exoU and exoS. Six serotypes (O1, O4–O7, and O11) were detected; O11 (19/47), O7 (13/47), and O4 (9/47) were the most prevalent. In 2018–2020, O4 and O7 were the most prevalent serotypes; 2021 onward, O11 (16/26) was the most prevalent serotype. Fourteen types of ST were detected, mainly ST235 (14/47), ST1158 (13/47), and ST1800 (7/47). Five global epidemic ST235 XDR-hvPA carried blaGES and showed the MIC value of ceftazidime/avibactam reached the susceptibility breakpoint (8/4 mg/L)

Conclusion The clinical detection rate of XDR-hvPA is unexpectedly high, particularly in patients aged >60 years, who are seemingly more susceptible to contracting this infection. Clonal transmission of XDR-hvPA carrying blaGES, which belongs to the global epidemic ST235, was noted. Therefore, the monitoring of XDR-hvPA should be strengthened, particularly for elderly hospitalized patients, to prevent its spread

关键字：Pseudomonas aeruginosa; extensive drug resistance; clinical features; virulence; drug resistance mechanism; molecular epidemiology

Dissemination of Ceftriaxone-Resistant Salmonella Enteritidis Harboring Plasmid Encoding BlaCTX-M Gene Mediated by IS26 and ISEcp1 in China

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Objective To investigate the resistance mechanism and transmission characteristics of ceftriaxone-resistant Salmonella enteritidis (CTX-RSE)

Methods There were 235 S. Enteritidis strains isolated from patients in different clinic departments in Hangzhou First People's Hospital from 2010 to 2020. Antimicrobial susceptibility testing revealed that 8.51% strains were resistant to ceftriaxone. Subsequently, we elucidated the ceftriaxone resistance mechanism in the CTX-RSE isolates through whole-genome sequencing. The sequencing results revealed that all 20 isolates harbored antibiotic resistance gene blaCTX-M-55 or blaCTX-M-14. Plus, nine CTX-RSE isolates were annotated by Prokka, and then by using Easyfig v2.2.5 (http://easyfig.sourceforge.net/), proksee (https://proksee.ca/) and BRIG v0.95 (https://sourceforge.net/projects/brig/)to align different plasmids which contain same type ESBL gene. In addition to, we also use BLAST of the NCBI to seek similar plasmids which contain blaCTX-M-55 or blaCTX-M-14. 20 ceftriaxone-resistant isolates were used for phylogenetic relationship analysis based on their single-nucleotide polymorphisms (SNPs). The different types of plasmids carrying CTX-M were conjugated to observe the transmissibility

Results The majority of the strains were from infectious disease department (79/235). Additionally, the antimicrobial resistance rates against to agents for other antibiotics were as follows: ciprofloxacin 4.26% (10/235), azithromycin 19.15% (45/235), ampicillin 79.15% (186/235), cefoxitin 1.28% (3/235), imipenem 0, compound sulfamethoxazole 6.81% (16/235), chloramphenicol 5.11% (12/235), and tetracycline 28.51% (67/235). MLST results revealed that all 20 CTX-RSE isolates belong to ST11, with the MLST profile (aroC 5, dnaN 2, hemD 3, hisD 7, purE 6, sucA 6, thrA 11). Additionally, of the 20 isolates, 18 strains carried blaCTX-M-55, and two strains carried blaCTX-M-14. These isolates exhibited varying numbers of plasmids, and all CTX-M-type enzymes were located on plasmids. The blaCTX-M-55 is located on the plasmids with several replicons in CTX-RSE. Among these replicons, IncX1, IncFII(pHN7A8), IncN, IncFIB(S) and IncFII(S) were associated with the plasmid harboring blaCTX-M-55. Furthermore, various other ARGs were predominantly located on plasmids (fosA3; aph(3')- IIa; blaTEM; aph(6)-Id; aph(3")-Ib; sul2; oqxB; oqxA2; aph(6)-Id;

tet(A); floR) rather than on the chromosome. Among 18 CTX-RSE isolates harboring blaCTX-M-55 gene, 17 isolates shared a common genetic structure surrounding blaCTX-M-55: IS26-blaTEM-hypothesis protein-blaCTX-M-55-IS26. Notably, While S114 presented a unique genetic structure: ISEcp1-blaCTX-M-55-hypothesis protein. The transmission of the blaCTX-M-bearing IncI1-type plasmid across different genera of bacteria and between the environment, animals, and humans. S114-p1, carrying blaCTX-M-55 gene, exhibited a similar structure to S808-p1 carrying blaCTX-M-14 gene. Furthermore, S808-p1 shared a similar structure with plasmids that contain ISEcp1-blaCMY-2. Plasmids fusion phenomenon had been observed in S204, S131, S273, S379 and S664 with S161 serving as the reference sequence. In particular, this fusion plasmid, S161-p1, hadn't been reported in NCBI, and the most similar plasmid was p12367A from Salmonella enterica subsp. (CP041177, coverage 68%, identity 99.99%). A fusion or a cleavage event involving dissemination of evidence of two plasmids with fusing different incompatibility types, IncX1, IncFII(pHN7A8), IncFII(S) and IncFIB. And this process was mediated by IS26 with 8bp target site duplications (TSD, TTTTTTCG) .In addition, we observed intramolecular replicative transposition that led to the reversal of the segment between the original IS26 and the targeted site. Evidence supporting this phenomenon was derived from the presence of 8-bp sequences that were reverse complements of each other, found adjacent to the opposite ends of two IS26 copies. It is of interest that S808-p1 even could be conjugated to A. baumannii ATCC17978, which crosses the order Enterobacteriales and has the potential to spread to Moraxella. Susceptibility testing of conjugants showed that the resistance of the recipient bacteria to ceftriaxone increased significantly after the plasmids containing blaCTX-M resistance gene were conjugated

Conclusion The spread of blaCTX-M-55 is associated with IS26 and ISEcp1, while the spread of blaCTX-M-14 is associated with ISEcp1. Additionally, the replicons IncI1(Alpha), IncFII(S), IncFII(pHN7A8), IncFIB(S) and IncX1 are relevant to the dissemination of CTX-M-type genes, plus, the plasmid with IncI1(Alpha) replicon from S. Enteritidis can even be conjugated into Acinetobacter baumannii ATCC17978. We also identified a fusion or a cleavage event involving dissemination of evidence of two plasmids with fusing different incompatibility types, IncX1, IncFII(pHN7A8), IncFII(S) and IncFIB. However, the fusion plasmid was not easily transmitted

关键字：ceftriaxone-resistant Salmonella Enteritidis，blaCTX-M， IS26，ISEcp1，plasmid fusion，type IV secretion system

Outbreak of NDM-5 Producing Klebsiella Pneumoniae ST307: An Emerging High-risk Antimicrobial Resistance Clone in Shanghai, China

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The high-risk clone K. pneumoniae ST307, associated with various carbapenem resistance genes, exhibits a global distribution and prevalence. However, in China, it has remained sporadic and rarely been detected. In this study, we reported an outbreak caused by nine ST307 CRKP isolates harboring blaNDM-5 in Shanghai, China in 2022. We employed antimicrobial susceptibility testing, conjugation assay, WGS and comparative genomics, phylogenetic analysis, fitness and virulence comparison to further characterize the isolates causing the outbreak. Besides blaNDM-5, these nine isolates co-carried blaCTX-M-15 and blaDHA-1, exhibiting nearly identical resistance profiles with high-level resistance to carbapenems and ceftazidime/avibactam, while showing susceptibility to colistin and tigecycline. blaNDM-5 was located on an IncX3 plasmid of 45403bp with high frequency of conjugative ability. Phylogenetic and SNP analysis indicated the nature of clonal transmission with a maximum of five SNPs between these nine isolates, and they were closely related to strains obtained from the USA. ST307 isolates in our study showed a relatively lower virulence but higher growth rates and certain adaptability compared with ST11 isolates. Clinical investigation revealed that shared nursing staff in a mixed EICU ward and doctors' movement between wards might be responsible for the outbreak. The non-existence before and sudden emergence of ST307 suggested that the currently circulating ST307 clone was a newly introduced superbug in our hospital. In conclusion, we revealed that blaNDM-5-producing ST307 CRKP isolates, a globally significant high-risk clone, are spreading in China, posing a substantial threat to public health.

关键字：Carbapenem resistance; Klebsiella pneumoniae; Outbreak; ST307 high-risk clone

Multifunctional CRISPR–Cas9–Based Nanobomb Against Carbapenem-Resistant Acinetobacter Baumannii Infection Through Cascade Reaction and Amplification Synergistic Effect

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Objective Carbapenems have been considered

as the preferred antibiotics against Acinetobacter baumannii thus far. However, the prevalence of carbapenem-resistant Acinetobacter baumannii (CRAB) has gradually escalated worldwide, and it frequently caused respiratory and bloodstream infections. Its resistance may lead to high mortality, and therefore there is an urgent need to develop antibacterial drugs

Methods Making various characterization experiments of nanoparticles to verify the successful construct, such as transmission and scanning electron microscopy, dynamic light scattering, fourier transform infrared spectrometry. In order to assess the antibacterial effect for sgRNA-I/L@ZS nanosystem, we used the time-growth monitoring method, dilution method, disk diffusion method,live/dead backlight bacteria assay and scanning electron microscopy. To verify the function of bactericidal effect and resistance reversal for sgRNA-I/L@ZS nanocomposite by the checkboard test and the DNA sequence. The NO generation characteristic of sgRNA-I/L@ZS nanosystem was observed through a series of related experiments. By observing the variation of oxidative stress and metabolism, we researched the antibacterial mechanism of sgRNA-I/L@ZS. The crystal violet assay、XTT Staining Assay、confocal laser scanning microscopy and RT-qPCR were analyzed about the effect and mechanism against biofilm. We evaluated the biocompatibility and hemocompatibility of sgRNA-I/L@ZS via MTT assay, LDH cytotoxicity assay，Hemolytic experiment and apoptosis evaluation with flow cytometry. We assessed the sgRNA-I/L@ZS nanosystem influence on bacteria-host interaction by the bacteria count, cell morphology monitoring, apoptosis evaluation with flow cytometry and PI fluorescence assay. In vivo, we analyzed the therapeutic effect of sgRNA-I/L@ZS nanosystem against the mice of carbapenem-resistant A. baumannii Pneumonia and Peritonitis

Results 1. Due to the acid-sensitive response, the sgRNA-I/L@ZS nanosystem could release more imipenem and Zn2+ in acidic infected microenvironment, which was benefit to killing CRAB

2. The ultimate constructed sgRNA-I/L@ZS nanosystem was pH-sensitive and exhibited ROS-reliant release of gaseous NO. Because of the high level of ROS in the bacterial infection tissues and the ROS product of ZnO-SiO2 against bacteria, sgRNA-I/L@ZS was committed to cascade the generation of NO gas.

3. The sgRNA-I/L@ZS nanosystem first induced CRAB to produce ROS, and then sgRNA-I/L@ZS made use of ROS to create and release NO gas. The sgRNA-I/L@ZS nanosystem could generate NO gas via the cascade reaction and induce bacteria to produce ROS; in addition, this platform played a part in promoting proliferation and accelerating infection wound healing

4. The sgRNA-I/L@ZS nanosystem not only induced bacteria to generate ROS and MDA, but also inhibited the enzymatic activity of F-ATPase and the produce of ATP, appearing the phenomenon of DNA damage and protein suppression.

5. The sgRNA-I/L@ZS nanosystem prevented the interaction of CRAB and host cell, which decreased cell death induced by carbapenem-resistant Acinetobacter baumannii infection.

6. Taken together, for pneumonia therapy in vivo, the sgRNA-I/L@ZS nanosystem not only can be devoted to powerfully killing carbapenem-resistant Acinetobacter baumannii and inhibiting inflammatory cytokines and inflammation-related proteins to exert anti-inflammatory, effects but is also able to promote the healing and recovery of infected tissue.

7. SgRNA-I/L@ZS had excellent biocompatibility and hemocompatibility, in addition, it produced fewer side effects.

Conclusion In conclusion, we cleverly combined the advanced technology of CRISPR/Cas9 to structure the multifunctional sgRNA-I/L@ZS ‘nanobomb’, which was committed toreversing drug-resistance to amplify synergistic bactericidal action and exerting a cascade reaction to promote the death of carbapenem-resistant A. baumannii. Imipenem inhibited the formation of the bacterial cell wall, and ZnO-SiO2 nanoparticles destroyed bacteria by various bactericidal mechanisms so that the sgRNA-I/L@ZS nanosystem synergistically killed CRAB. On this basis, genetic mutation targeting blaNDM substituted C to T base through CRISPR/Cas9-sgRNA to prematurely terminate the translation of metallo-β-lactamases, resulting in reversal of the resistance to imipenem amplifying the synergistic bactericidal action of imipenem and ZnO-SiO2. Second, advantageous conditions of high ROS levels (including ROS induced by nanosystem and produced in the infected microenvironment) were utilized by L-arginine to form NO reaction products, which are regarded as antibacterial agents. On the one hand, NO produced in the cascade reaction can further induce CRAB death. On the other hand, NO was beneficial to suppress the inflammatory response and promote proliferation as well as accelerate wound healing in the infected microenvironment. Additionally, the sgRNA-I/L@ZS nanosystem could influence the interaction between carbapenem-resistant A. baumannii and Beas-2B cells to restrain the infection and death of host cells caused by CRAB. In acute pneumonia and peritonitis mouse models, the sgRNA-I/L@ZS nanosystem could damage bacteria, inhibit and alleviate infection, suppress inflammatory reactions, and promote infected tissue repair, revealing excellent bactericidal therapy. Consequently, this work not only reveals a potential multifunctional antibacterial agent against carbapenem-resistant A. baumannii, but also lays the foundation to conquerdrug-resistant strains worldwide

关键字：carbapenem-resistant Acinetobacter baumannii ， CRISPR/Cas9-sgRNA ， nanosystem ， bactericidal，cascade reaction，amplification

MprF Mutations in Methicillin-resistant Staphylococcus Aureus Confer Reduced Susceptibility To Biocides and Daptomycin

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Objective This study aimed to investigate the novel mechanism of daptomycin (DAP) resistance in Staphylococcus aureus provided by Wendel et al

Methods Wild-type MRSA strain SA268 (ST59, spa-type t437) was employed as the foundation for generating mprF mutants. To confirm the correlation between mprF mutations and susceptibility to biocides, we tested the susceptibility to DAP, polyhexamethylene biguanide/polyhexanide (PHMB) , chlorhexidine (CHX), and benzalkonium chloride (BAC) in strains with distinct mprF mutations

Results The mprF mutant strains exhibited lower susceptibility to DAP and PHMB compared to their wild-type counterparts. However, their susceptibility to CHX was comparable, and susceptibility to BAC remained unchanged. Compared with strains carrying wild-type mprF (Δ-pmprFSAZ1, Δ- pmprFSAW1, and Δ-pmprFSAC1), their mprF mutant counterparts (Δ-pmprFS295A, Δ-pmprFI348del, and Δ-pmprFS337L) exhibited a 2–4-fold increase in PHMB MICs, ranging from 2 to 4 μg/ml. For CHX, the strains carrying wild-type mprF (Δ-pmprFSAZ1 and Δ-pmprFSAC1) exhibited similar MICs to strains carrying mutated mprF (Δ-pmprFS295A and Δ-pmprFS337L), ranging from 0.8–1.6 μg/ml

Conclusions Our findings corroborate the hypothesis put forth by Wendel et al. that the decrease in susceptibility to PHMB is correlated with mutations in mprF. The data obtained by Wendel et al. and our study emphasizes the necessity for a deeper examination of the clinical application of antiseptics that takes into consideration their potential influence on antibiotic resistance

关键字：Methicillin-resistant Staphylococcus aureus, Daptomycin, Polyhexamethylene biguanide/polyhexanide, mprF, Antiseptics

Mutation in The Two-component Regulator BaeSR Mediates Cefiderocol Resistance and Enhances Virulence in Acinetobacter Baumannii

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Objective Acinetobacter baumannii has become one of the most challenging pathogens in many countries with limited treatment options available. Cefiderocol is a novel siderophore-conjugated cephalosporin which enters bacteria by an active uptake mechanism via the iron transport system. The compound has excellent in vitro activity against a variety of Gram-negative bacteria, including A. baumannii. To date, few reports on the mechanisms of cefiderocol resistance are available. For most A. baumannii strains, resistance to ceriderocol is mediated by the production of β-lactamases, including NDM (NDM-1, NDM-5) and PER (PER-1, PER-7). Another way to increase resistance is via the reduced expression or mutations of the siderophore receptor genes pirA or piuA, mediating the uptake of ceriderocol. In order to investigate potential mechanisms of cefiderocol resistance in A. baumannii, we performed in vitro evolution experiments at sub-lethal concentrations of the antibiotic

Methods We performed in vitro evolution experiments in which we exposed the reference strain A. baumannii ATCC 17978 to sub-lethal concentrations of cefiderocol. Whole genome sequencing of obtained cefiderocol-resistant strains was performed via Illumina HiSeq, and then the mutations were identified in reference to the parental strain ATCC 17978

Mutations were reconstructed in ATCC 17978 through allelic replacement. To further clarify the regulatory effect of BaeS and BaeR mutations on gene expression, RNA-sequencing of ATCC 17978 and BaeSR mutants was performed. Differentially expressed genes were selected with significance cutoffs of BH adjusted $P < 0.05$ and $|\text{fold-change}| \geq 2$. Gene knockout and overexpression experiments were carried out to verify the role of the high expression of efflux pumps in cefiderocol resistance. Csu pili were observed via Cryo-electron tomography. The virulence of mutants was evaluated by Galleria mellonella infection model.

Results All four cefiderocol-resistant strains obtained harbored mutations in two-component system BaeS-BaeR. When we engineered the mutations of BaeS (D89V) and BaeR (S104N) into the genome of ATCC 17978, these mutations increased cefiderocol minimum inhibitory concentrations (MICs) by 8-fold to 16-fold. Transcriptome analyses showed that the expression of MacAB-TolC and MFS transporters was upregulated in BaeSR mutants. Strains over-expressing MFS transporter and MacAB-TolC displayed higher

MICs and higher median inhibition concentration (IC50) values, while MICs and IC50 decreased when efflux pump genes were knocked out. In a BaeR mutant with up-regulated csu operon, we observed a higher number of pili, enhanced surface motility and increased biofilm formation compared to wild-type ATCC 17978. Using the Galleria mellonella infection model, we found that the BaeS mutant in which paa operon was up-regulated exhibited increased virulence

Conclusion In conclusion, mutations in BaeS (D89V) and BaeR (S104N) decrease the susceptibility to cefiderocol in A. baumannii via the up-regulation of MFS transporters and the efflux pump MacAB-TolC. In addition, the BaeS mutation increases virulence by up-regulating the paa operon. The TCS BaeSR plays a key role in regulating the expression of Csu pili, which affects biofilm formation and swarming motility. This study provides further insights into the role of BaeSR in cefiderocol resistance and virulence in A. baumannii

关键字：BaeSR, cefiderocol resistance, MFS, MacAB-TolC, Csu pili, virulence

中国不同谱系 MRSA 对奥马环素耐药性分析及机制研究

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目的 明确中国不同 MRSA 谱系的奥马环素耐药情况及耐药机制。

方法 通过对收集自全国 22 家医院的 471 株 MRSA 进行肉汤稀释法测定奥马环素的体外药物敏感性；通过生物信息学分析不同谱系的奥马环素 MIC 分布情况及可能耐药机制；通过分子克隆、重叠 PCR 等方法探索其具体耐药机制。

结果 药敏结果显示中国东部、东南部及东北部地区的 MRSA 菌株奥马环素耐药情况明显高于中部及西部地区，其中耐药菌株大部分集中于 CC5 谱系。奥马环素 MIC 为 4mg/L 的 CC5 和 CC239 菌株均携带 tet(M)基因和 rpsJ 基因 57 位点的突变，该突变位于 rpsJ 基因编码的 S10 蛋白的茎环结构中。分子克隆证明核糖体保护蛋白 tet（M）能介导菌株对奥马环素的抗性，编码核糖体蛋白 S10 的 rpsJ 基因突变能降低细菌对奥马环素的敏感性。缩短 S10 蛋白的茎环后发现细菌对奥马环素敏感性下降。

结论 CC5 谱系是中国 MRSA 菌株中主要的奥马环素耐药谱系，tet(M)和 S10 茎环结构改变共同介导 MRSA 对奥马环素的耐药性。

关键字：奥马环素、MRSA、tet(M)、rpsJ

Diversification of Ceftazidime/avibactam-resistance Mechanisms and Dissemination of Multidrug-resistant Pseudomonas Aeruginosa and Klebsiella Pneumoniae in An Intensive Care Unit

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Multidrug-resistant Pseudomonas aeruginosa (MDR-PA) and multidrug-resistant Klebsiella pneumoniae (MDR-KP) are significant threats to human health due to their increased morbidity and mortality in clinical settings. Ceftazidime/avibactam is an important drug for the treatment of MDR-PA and MDR-KP infections. In this study we isolated 32 CZA-resistant strains including 12 MDR-PA strains and 20 MDR-KP strains from an ICU in August 2020-February 2021. 19 MDR-KP strains co-producing KPC-2 and NDM-5 belonged to ST11-KL47 and the other one producing NDM-1 belonged to ST29. Seven MDR-PA isolates belonged to ST275 and three were ST270, while the other two were ST2414 and ST357, respectively. Six ST275 strains carrying blaAFM-2, three ST270 strains carrying blaKPC-87, and one ST357 strain carrying blaPER-1 contributed to CZA resistance. The efflux effect of the efflux pump is the main cause of CZA resistance in the other two strains. Compared to KPC-2, KPC-87 exhibited a 1.5-fold elevation in kcat/Km for ceftazidime, a 7.5-fold increase in Ki for avibactam, and a loss of carbapenem hydrolysis. Insertion of 656 bp ΔblaTEM-1 upstream of blaKPC-87 introduced an additional promoter that increased the expression level of KPC-87. blaKPC-87 was located in the NTEKPC-IIa like element based on the Tn3. blaAFM-2 was located on an In4-like and Tn1403-derived complex class 1 integron. blaPER-1 was located in a Tn1403-derived class 1 intergron. The plasmid carrying blaAFM-2 was an IncP-2 plasmid, while the plasmid carrying blaKPC-87 was similar to the IncP-2 plasmid but lacked the IncP-2 replicon. ST11-KL47-CRKP strains could be divided into three clusters. The cluster 2 and cluster 3 indicated two clones of ST11-KL47-CRKP transmitted among patients, with patient P14 as a center. Phylogenetic analyses revealed that ST275 strains were the main prevalent clone resistant to CZA, which had evolved in a complex manner, whereas ST270 strains exhibited a small-scale dissemination and cross-regional transfer with the referral of a patient. The present study revealed the diversification of resistance mechanisms of MDR-PA to CZA in the ICU and observed the cross-regional transfer of CZA-resistant MRD-PA with the referral of a patient.

关键字：Pseudomonas aeruginosa, Klebsiella pneumoniae, ceftazidime/avibactam, KPC,non-Tn4401 elements, cross-regional transmission

关键字：blaKPC-2, blaGES-5, imipenem/relebactam, high-risk clone, carbapenem-resistant Pseudomonas aeruginosa

BlaKPC-2 Overexpression and BlaGES-5 Carriage As Major Imipenem/relebactam Resistance Mechanisms in Pseudomonas Aeruginosa High-risk Clones ST463 and ST235, Respectively, in China

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Objective Pseudomonas aeruginosa high-risk clones pose severe threats to public health. Here, we characterize the imipenem/relebactam (IR) resistance mechanisms in P. aeruginosa high-risk clones sequence type 235 (ST235) and ST463 in China

Methods Minimum inhibitory concentrations (MICs) were determined, and Illumina short-read sequencing was performed for 1,168 clinical carbapenem-resistant P. aeruginosa (CRPA) isolates. The gene copy number and expression level were analyzed by Illumina sequencing depth and reverse transcription-quantitative PCR, respectively. Resistance conferred by blaGES-5 was evaluated by cloning experiments

Results ST463 and ST235 accounted for 9.8% (115/1,168) and 4.5% (53/1,168) of total isolates, respectively, and showed high frequencies of extensively drug-resistant and difficult-to-treat resistant phenotypes. The overall IR-resistant rate in CRPA was 21.0% (245/1,168). However, the IR resistance rate was 81.7% (94/115) in ST463-PA and 52.8% (28/53) in ST235-PA. Of the ST463 isolates, 92.2% (106/115) were Klebsiella pneumoniae carbapenemase-producing P. aeruginosa (KPC-PA), and all 94 IR-resistant ST463-PA produced KPC-2. Compared to IR-susceptible ST463 KPC-2-PA, IR-resistant ST463 KPC-2-PA exhibited significantly higher blaKPC-2 copy numbers and expression levels. In ST463 KPC-2-PA, 16 mg/L relebactam resulted in additional fourfold reductions in imipenem MIC50/90 values compared to 4 mg/L relebactam. In ST235, 1.9% (1/53) carried blaIMP carbapenemase and 54.7% (29/53) carried blaGES carbapenemase. Other than the IMP producer, all 27 IR-resistant ST235-PA produced GES-5. Cloning experiments revealed that imipenem resistance in blaGES-5-carrying PAO1 transformants was generally unaffected by relebactam

Conclusion In conclusion, IR-resistant CRPA isolates in China were mainly distributed in P. aeruginosa high-risk clones ST463 and ST235. The major underlying IR resistance mechanisms were blaKPC-2 overexpression and blaGES-5 carriage

Combination of Amikacin Or Ceftazidime with Levofloxacin Inhibit Levofloxacin Induced Resistance in Hypervirulent Klebsiella Pneumoniae

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Aims This study aims to investigate the in vitro activity of levofloxacin alone and in combination with amikacin or ceftazidime against clinical hypervirulent Klebsiella pneumoniae (hvKP), with a particular focus on whether levofloxacin-based combinations could suppress levofloxacin-induced drug resistance

Methods A total of 12 clinical hvKP isolates were collected from Huashan Hospital in Shanghai, China between 2019 and 2020. These isolates exhibited hypermucoviscosity and harbored molecular biomarker genes (iroB, iucA, peg-344, rmpA, and rmpA2). Furthermore, they were associated with diagnoses including liver and CNS abscesses, pneumoniae, bacteremia, and endophthalmitis. Antimicrobial susceptibility against 12 hvKP isolates and reference strain NTUH-K2044 were assessed using broth microdilution method and checkboard assay with levofloxacin, amikacin, and ceftazidime alone, as well as levofloxacin-based combinations. Time-kill experiments were conducted against NTUH-K2044 with levofloxacin, amikacin, ceftazidime, and levofloxacin-based combinations with the limit of detection (LOD) set at 100 CFU/mL. Bactericidal activity was defined as ≥3 log10 reduction in initial inoculum CFU/mL at 24th hour, while synergy was considered when there was ≥2 log10 reduction for antibiotic combinations compared to their more active constituent. Additionally, efflux pump inhibition test and wild type oqxR complementation in levofloxacin-resistant NTUH-K2044 derived strains were performed to investigate mechanism of levofloxacin induced drug resistance

Results 1. In vitro activity of levofloxacin alone and in combination

All the 13 hvKP strains were susceptible to levofloxacin, amikacin and ceftazidime. The MIC range of levofloxacin was 0.03 – 0.5 mg/L, amikacin was 0.5 - 2 mg/L, and ceftazidime was 0.125 - 0.5 mg/L. In the checkboard assays, levofloxacin-amikacin combination demonstrated additivity in 10 isolates (79.9%), and indifference in three isolates (23.1%); The levofloxacin-ceftazidime combination showed additivity in six isolates (46.2%), and indifference in seven isolates

(53.8%); No synergy and antagonism were detected.

2. Time-kill experiments

The representative NTUH-K2044 strain was subjected to time-kill experiments to evaluate the bactericidal efficacy of levofloxacin, amikacin, and ceftazidime. The bactericidal activity of levofloxacin at a concentration of 16×MIC (1mg/L) was observed within the first hour, with viable cell counts remaining below the LOD value in subsequent hours. In contrast, exposure to levofloxacin concentrations of 1×MIC, 2×MIC, 4×MIC and 8×MIC resulted in initial bacterial inhibition followed by subsequent regrowth. Notably, the MPC (mutant prevention concentrations) of levofloxacin against NTUH-K2044 was determined to be 1mg/L (16×MIC). Furthermore, 2×MIC concentration of amikacin and ceftazidime demonstrated bactericidal activities at the first and eighth hours respectively, with viable cell counts remaining below the LOD value in subsequent hours. While 1×MIC of amikacin and ceftazidime demonstrated initial inhibition within first four hours and followed subsequent regrowth.

The combination of levofloxacin and amikacin demonstrated a significantly enhanced bactericidal synergy against NTUH-K2044 strain. Regrowth occurred as early as the fourth hour when using levofloxacin at 1/2×MIC concentration combined with amikacin at 1/2×MIC concentration, and viable cell counts reached to about 9 log10 CFU/mL at 24th hours. The combination of levofloxacin at 1×MIC concentration and amikacin at 1/2×MIC concentration effectively inhibited bacterial regrowth within eight hours and followed by regrowth, the viable counts were approximately 5 log10 CFU/mL after 24 hours. Notably, the combination of levofloxacin at 2×MIC concentration and amikacin at 1/2×MIC concentration exhibited bactericidal activity against NTUH-K2044 at the first hour, and viable cell counts remaining below the LOD value in subsequent hours.

Enhanced bactericidal synergy was also observed with the combination of levofloxacin and ceftazidime. The levofloxacin-ceftazidime combinations at a concentration of 1×MIC of both levofloxacin and ceftazidime exhibited bacterial inhibition during the first six hours followed by bacterial regrowth, and viable cell counts reached to about 7 log10 CFU/mL at 24th hours. Furthermore, achieving viable cell counting below LOD value required six hours for a combination of levofloxacin at a concentration of 1×MIC and ceftazidime at a concentration of 2×MIC, whereas it only took one hour when exposed to levofloxacin at a concentration of 2×MIC with ceftazidime at a concentration of 1×MIC.

3. Induced quinolone resistance and mechanisms related to efflux pump OqxAB

An increase in the MIC of levofloxacin was observed in the NTUH-K2044-2A strain when sampling from a tube containing levofloxacin at concentrations of 2×MIC. The sequence analysis was conducted and identified mutations C12G (Tyr 4 stop codon) in OqxAB efflux pump down-regulator oqxR, without mutation in quinoline resistance-related QRDR, drug permeability genes (ompK36), efflux pump systems acrAB-tolC, oqxAB and their regulators. And further sampling from tubes containing levofloxacin with concentrations of 2×MIC and 4×MIC, oqxR mutations G138A (Met 46 Ile) and C295T (Arg 99 Cyx) were detected in derived strains NTUH-K2044-2B and NTUH-K2044-4. And the MIC values of three derived strains for nalidixic acid, norfloxacin, levofloxacin, ciprofloxacin, tetracycline, and chloramphenicol exhibited a significant increase compared to those of the original strain NTUH-K2044. Additionally, we observed that the efflux pump inhibitor PAβN reduced the MIC of levofloxacin by 8-fold to 16-fold. Notably, compared to the self-reference strain NTUH-K2044, three derived strains exhibited significant overexpression in oqxB (349.83-fold, 157.51-fold, 118.82-fold) and rarA (620.86-fold ,31.43-fold ,18.44-fold), while showing no significant difference in transcriptional levels of acrB and ramA.

4. Complementation with the wild-type oqxR gene

The complementation of wild-type oqxR repressed the oqxB and rarA transcriptions remarkably in all three derived strains. In transformative NTUH-K2044-2A/pPuc57oqxR strain, expression of oqxB gene significantly decreased from 349.83 to 1.26. In NTUH-K2044-2B/pPuc57oqxR and NTUH-K2044-4/pPuc57oqxR strains, significant decreases in the expression of oqxB were observed, with levels dropping from 157.51 to 0.66 and from 118.82 to 2.26, respectively. The expression levels of rarA were significantly reduced in NTUH-K2044-2A/pPuc57oqxR (from 620.86 to 5.62), NTUH-K2044-2B/pPuc57oqxR (from 31.43 to 1.23), and NTUH-K2044-4/pPuc57oqxR (from 18.44 to 1.35). Additionally, 2-fold to 4-fold reduction in MICs were observed for levofloxacin, nalidixic acid, ciprofloxacin, norfloxacin, tigecycline, and chloramphenicol after oqxR complementation in NTUH-K2044-2A. However, the decreases in MICs level of certain antibiotics in NTUH-K2044-2A/pPuc57oqxR, NTUH-K2044-4/pPuc57oqxR were unparalleled with their significant oqxB and rarA reduction.

Conclusions Levofloxacin in combination with amikacin or ceftazidime exhibits superior in vitro activities compared to levofloxacin alone against hvKP, which may prevent the inducible levofloxacin resistance related to efflux pump OqxAB

关键字：hypervirulent Klebsiella pneumoniae, levofloxacin, amikacin, ceftazidime, bactericidal activity, oqxR

Genome-wide Analysis of in Vivo-evolved Candida Auris Reveals Multidrug-resistance

Mechanisms

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Candida auris, an emerging and multidrug-resistant fungal pathogen, has led to numerous outbreaks in China. While the resistance mechanisms against azole and amphotericin B have been studied, the development of drug resistance in this pathogen remains poorly understood, particularly in in vivo-generated drug-resistant strains. This study employed pathogen whole-genome sequencing to investigate the epidemiology and drug-resistance mutations of C. auris using 16 strains isolated from two patients. Identification was conducted through Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, and antimicrobial susceptibilities were assessed using broth microdilution and Sensititre YeastOne YO10. Whole-genome sequencing revealed that all isolates belonged to the South Asian lineage, displaying genetic heterogeneity. Despite low genetic variability among patient isolates, notable mutations were identified, including Y132F in ERG11 and A585S in TAC1b, likely linked to increased fluconazole resistance. Strains from patient B also carried F214L in TAC1b, resulting in a consistent voriconazole minimum inhibitory concentration of 4 μg/mL across all isolates. Furthermore, a novel frameshift mutation in the SNG1 gene was observed in amphotericin B-resistant isolates compared to susceptible ones. Our findings suggest the potential transmission of C. auris and emphasize the need to explore variations related to antifungal resistance. This involves analyzing genomic mutations and karyotypes, especially in vivo, to compare sensitive and resistant strains. Further monitoring and validation efforts are crucial for a comprehensive understanding of the mechanisms of drug resistance in C. auris.

关键字：Antifungal susceptibility · Candida auris · Drug resistance mechanisms · ERG11 · Whole genome sequence

ST78 型共产 KPC-2 和 OXA-1 碳青霉烯酶霍氏肠杆菌的耐药特点及全基因组测序分析

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目的 探讨 ST78 型耐碳青霉烯类霍氏肠杆菌的耐药特征和基因组学特征，为其防控与治疗提供理论依据。

方法 收集 2017 年至 2019 年间内蒙古自治区呼和浩特市某三级医院分离的耐碳青霉烯类霍氏肠杆菌，采用基质辅助激光解吸电离-飞行时间质谱仪(MALDI-TOF MS)进行菌种鉴定及复核，应用琼脂稀释法进行药敏试验，采用全基因组测序技术进行耐药相关分子、多位点序列类型（MLST）分析、质粒同源性及全基因组遗传进化分析。

结果 共分离了 7 株耐碳青霉烯类霍氏肠杆菌，MLST 共鉴定出 ST78（6/7）与 ST93（1/7）2 种 ST 序列型。7 株分离株对氨曲南、妥布霉素、头孢他啶、氯霉素、美罗培南、亚胺培南、厄他培南、头孢曲松、头孢噻肟和环丙沙星均耐药，仅对磷霉素和多粘菌素 B 敏感。全基因组测序分析显示，7 株分离株共携带 249 个与抗菌药物相关的耐药基因，其中，最多见的与氯霉素类相关（95/249,38.15%），其次为喹诺酮类（89/249,35.74%）。7 株分离株共携带 44 个编码 β-内酰胺酶的基因，最具优势的为 penA（12/44,27.27%），其次为 blaTEM（11/44,25%）。值得注意的是，仅 4 株 ST78 型霍氏肠杆菌携带了碳青霉烯类耐药基因，包括 blaKPC-2，blaNDM-1 和 blaOXA-1。其中 1 株单独携带了 blaNDM-1，其余 3 株分离株（分别命名为 EH-1，EH-2 与 EH-3）同时携带了 blaKPC-2 和 blaOXA-1。EH-1 与 EH-2 于 2018 年分离自呼吸科，标本来源为痰液；EH-3 于 2019 年分离自肾内科，标本来源为尿液。特别的是，EH-1，EH-2 与 EH-3 均携带 1 个 IncFIb 型耐药质粒，blaKPC-2 和 blaOXA-1 共同位于该质粒上，3 个 IncFIb 型耐药质粒的同源性高达 100%。遗传进化分析结果显示，7 株霍氏肠杆菌分离株之间存在密切的遗传关系，但 EH-1，EH-2 与 EH-3 高度同源。此外，其余 3 株不携带碳青霉烯酶类耐药基因的菌株也对碳青霉烯类耐药，可能与其携带外排泵相关基因 OqxA 和 OqxB 有关。

结论 耐碳青霉烯类霍氏肠杆菌具有泛耐药表型且菌株间的遗传关系较为密切，共产 KPC-2 与 OXA-1 的 ST78 型霍氏肠杆菌可能是由携带 blaKPC-2 和 blaOXA-1 耐药基因的 IncFIb 型质粒在菌株间传播导致的。为防止耐碳青霉烯霍氏肠杆菌暴发流行，应对其加强监测及防控。

关键字：耐碳青霉烯类霍氏肠杆菌，全基因组测序，多位点序列分型，多药耐药

Profiling Daptomycin Resistance Among Diverse Methicillin-resistant Staphylococcus Aureus Lineages in China

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Objective Daptomycin (DAP) is effective against methicillin-resistant Staphylococcus aureus (MRSA). However, reduced susceptibility to DAP in MRSA may lead to treatment failures. We aim to determine the distribution of DAP minimum inhibitory concentrations (MICs) and DAP heteroresistance (hDAP) among MRSA lineages in China

Methods The DAP susceptibility of 472 clinical MRSA isolates collected in 2015-2017 in China was examined via broth microdilution. We compared the clonal complex (CC) distributions, clinical characteristics, and agr mutations in MRSA isolates stratified by the daptomycin MIC. hDAP MRSA isolates were identified using the population analysis profiling (PAP), and agr dysfunction was investigated by δ-haemolysin production. DAP-resistant subpopulation stability was analysed, and mutations were assessed via whole-genome sequencing (WGS)

Results A total of 472 clinical MRSA isolates collected from 2015 to 2017 in China were examined for DAP susceptibility. All isolates (n = 472) were found to be DAP susceptible, but 35.17% (166/472) of them exhibited a high DAP MIC (MIC >0.5 μg/mL). The high DAP MIC group contained a larger proportion of isolates with a higher vancomycin or teicoplanin MIC (>1.5 μg/mL) than the low DAP MIC group (19.3% vs 7.8%, P < 0.001; 22.3% vs 8.2%, P < 0.001). We compared the clonal complex (CC) distributions and clinical characteristics in MRSA isolates stratified by DAP MIC. CC5 isolates were less susceptible to DAP (MIC50= 1 μg/mL) than CC59 isolates (MIC50= 0.5 μg/mL, P < 0.001). Population analysis profiling revealed that 5 of 10 ST5 and ST59 DAP-susceptible MRSA isolates investigated exhibited hDAP. The results also showed that CC5 MRSA with an agrA mutation (I238K) had a higher DAP MIC than those with a wild-type agrA (P < 0.001). The agrA-I238K mutation was found to be associated with agr dysfunction as indicated by the loss of δ-hemolysin production. In addition, agr/psmα defectiveness was associated with hDAP in MRSA. Whole-genome sequencing analysis revealed mutations in mprF and walR/walK in DAP-resistant subpopulations, and most DAP-resistant subpopulations (6/8, 75%) were stable

Conclusion Our study suggests that the increased DAP resistance and hDAP in MRSA may threaten the effectiveness against MRSA infections

关键字：agr; daptomycin; heteroresistance; methicillin-resistant Staphylococcus aureus; mprF; walR/walK.

Genomic Epidemiology Reveals Multiple Mechanisms of Linezolid Resistance in Clinical Enterococci in China

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Background Infections caused by linezolid-resistant enterococci (LRE) are clinically difficult to treat and threaten patient health. However, there is a lack of studies on long time-span LRE strains in China. For this reason, our study comprehensively revealed the resistance mechanisms of LRE strains collected in a Chinese tertiary care hospital from 2011 to 2022

Methods Enterococcal strains were screened and verified after retrospective analysis of microbial data. Subsequently, 65 LRE strains (61 Enterococcus faecalis and 4 Enterococcus faecium, MIC ≥ 8 μg/ml), 1 linezolid-intermediate Enterococcus faecium (MIC = 4 μg/ml) and 1 linezolid-susceptible Enterococcus faecium (MIC = 1.5 μg/ml) were submitted for whole-genome sequencing (WGS) analysis and bioinformatics analysis. The polymerase chain reaction (PCR) assay was used to verify the presence of resistance genes in non-LRE strains

Results The optrA gene was found to be the most common linezolid resistance mechanism in our study. We identified the wild-type optrA and various optrA variants in 98.5% of LRE strains (61 Enterococcus faecalis and 3 Enterococcus faecium). We also found one linezolid-resistant E. faecium strain carried both optrA and cfr(D) gene, while one linezolid-resistant E. faecium only harbored the poxtA gene. Most optrA genes (55/64) were located on plasmids, with transposon Tn554 on the upstream. A minority of optrA genes (9/64) were found on chromosomes with the downstream insertion sequence IS1297. Besides, other linezolid resistance-associated mechanisms [cfr(D), poxtA genes, and mutations in the rplC and rplD genes] were also found in 67 enterococcal strains

Conclusions Our study suggested that multiple mechanisms of linezolid resistance exist among clinical LRE strains in China

关键字：Enterococcus faecalis, Enterococcus faecium, linezolid, optrA, whole-genome sequencing

Global Phylogeography and Genomic Characterization of BlaKPC and BlaNDM-positive

Clinical Klebsiella Aerogenes Isolates From China, 2016-2022.

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Carbapenem-resistant Klebsiella aerogenes (CRKA), being one of the members of Carbapenem-resistant Enterobacteriaceae (CRE), has caused great public health concern, but with fewer studies compared to other CRE members. Furthermore, studies on phylogenetic analysis based on whole genome Single-Nucleotide Polymorphism (SNP) of CRKA were limited. Here, 20 CRKA isolates (11 blaKPC-2-bearing and 9 blaNDM-1/5-harboring) were characterized by antimicrobial susceptibility testing, conjugation assay, whole genome sequencing (WGS) and bioinformatics anlysis. Additionally, the phylogeographic relationships of K. aerogenes were further investigated from public databases. All isolates were multidrug-resistant (MDR) bacteria, and they demonstrated susceptibility to colistin. Most blaKPC-2 or blaNDM-1/5-carrying plasmids were found to be conjugative. Phylogenetic analysis revealed the clonal dissemination of K. aerogenes primarily occurred within clinical settings. Notably, some strains in this study showed the potential for clonal transmission, sharing few SNPs between K. aerogenes and KPC- and/or NDM-positive K. aerogenes isolated from various countries. The STs of K. aerogenes strains had significant diversity. WGS analysis showed that the IncFIIK plasmid was the most prevalent carrier of blaKPC-2, and, blaNDM-1/5 were detected on the IncX3 plasmids. The Tn6296 and Tn3000 transposons were most common vehicles for facilitating the transmission of blaKPC-2 and blaNDM-1/5, respectively. This study highlights the importance of continuous screening and surveillance by WGS for analysis of drug-resistant strains in hospital

关键字：Carbapenem-resistant Klebsiella aerogenes; KPC-2; NDM; phylogeography

Activity of A Combination of Ceftolozane and Tazobactam in Vitro Against ESBL-producing Enterobacterales in China: SMART 2016 – 2019

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This study evaluated ceftolozane/tazobactam (C/T), which is a combination of tazobactam, an inhibitor of ß-lactamase and a new antipseudomonal cephalosporin as medication for extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales isolates. From 2016 to 2019, susceptibilities of 10,545 Enterobacterales isolated from intra-abdominal, urinary tract, respiratory tract, and bloodstream infections to C/T and 11 other antimicrobial agents were analyzed. The majority of isolated Enterobacterales with an ESBL positive rate of 54.6% were E. coli 4,984/10,545, 47.3%) and K. pneumonia (3,606/1,0545, 34.2%), with ESBL positive rates of 59.8% and 51.1%, respectively. Susceptibilities to C/T for all Enterobacterales, E. coli and K. pneumonia were 79.5%, 89.3% and 68.0%, to non-ESBL producers 99.5%, 99.7% and 99.5% and to non-carbapenem resistant (CR) ESBL producers 81.0%, 87.9% and 72.3%, respectively. The isolation rate of ESBL positive and CR-Enterobacterales (CRE), CR-E. coli and CR-K. pneumoniae were 14.3%, 5.6 % and 26.8%, with susceptibilities < 20% for all antimicrobials except for amikacin (AMK) for ESBL-positive CREs (50.4%). The ESBL-positive CR-E. coli susceptibility to C/T was 28.2% which was the fourth highest after 37.1% for imipenem, 38.9% for meropenem and 70.4% for AMK. ESBL-producing CR-K. pneumoniae susceptibilities to all antimicrobials were < 10%, with the exception of AMK which was 37.4%. Our research underscores the viability of C/T as an alternative to carbapenems for ESBL-producing, carbapenem susceptible Enterobacterales. However, the susceptibilities of ESBL-positive CRE to C/T, as well as other studied antimicrobials, were consistently below 20%, with the exception of AMK at 50.4%, emphasizing the pressing need for new innovative treatment strategies.

关键字：Enterobacterales，ceftolozane/tazobactam，ESBL，Carbapenems

Plt-1 Acted As A Novel Virulence Factor by Enhancing Inflammation Level and Macrophage Death in ST11 Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae

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Objective The understanding of the genetic and molecular foundations behind the pathogenicity of ST11 carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKP) remains unclear. While several virulence factors have been identified, some K. pneumoniae lacks the already identified genes that exhibit hypervirulence. Our study introduces the function of a novel gene, plt-1, which plays a significant role in the virulence of K. pneumoniae

Methods and Results The epidemiology of plt-1 was conducted based on two databases containing 239 K. pneumoniae from China and 1,014 K. pneumoniae genomes downloaded from NCBI. Compared to other

sequence types (STs) strains, the plt-1 gene is significantly distributed in the ST11 strains (P<0.0001). Notably, the plt-1 gene is predominantly present in CRKP rather than in carbapenem-susceptible K. pneumoniae (P<0.0001)

Using CRISPR-Cas9, we constructed plt-1 mutants in two typical ST11-K47 and ST11-K64 strains. The plt-1 gene enhances biofilm formation ability and the resistance to serum killing, promotes proliferation within macrophages, and ultimately increases bacterial load in mice organs. Additionally, plt-1 enhances immune responses by intensifying TLR4 activation and causes more severe macrophage death due to increased intracytoplasmic bacterial presence.

Conclusion In conclusion, we identified plt-1 as a marker for ST11 CRKP and enhanced the virulence of K. pneumoniae. This finding underscores the importance of plt-1 in the pathogenicity, indicating its potential as a target for diagnostic and therapeutic strategies

关 键 字： carbapenem-resistant, hypervirulent, Klebsiella pneumoniae, novel virulence factor

抗菌药物的 PK/PD 研究与临床试验

Lefamulin Dosing Optimization Using Population Pharmacokinetic and Pharmacokinetic/pharmacodynamic Assessment in Chinese Patients with Community-acquired Bacterial Pneumonia

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Objective Lefamulin is the first pleuromutilin antibiotic approved for the treatment of community-acquired bacterial pneumonia (CABP). However, the sensitivity of lefamulin to ethnic factors and pharmacokinetic/pharmacodynamic (PK/PD) characteristics in Chinese CABP patients are not fully understood. This study aimed to analyze lefamulin's sensitivity to ethnic factors and conducted PK/PD analysis to assess its microbiological efficacy against Streptococcus pneumoniae and Staphylococcus aureus

Methods The population PK (PopPK) model, initially established with foreign data was validated using data from Chinese CABP patients. PK/PD analysis was conducted for the intravenous administration of 150 mg q12h for 1-h, 1.5-h and extended 2-h infusion. Oral administrations of 600 mg q12h under fasting and fed conditions were assessed, considering original and higher plasma protein binding

Results Lefamulin displayed similar PK characteristics in both Chinese and Western populations. The PopPK model effectively predicted the lefamulin concentrations in Chinese CABP patients. Under the dosage regimen of 150 mg q12h via intravenous infusion for 1/1.5/2h, the probability of target attainments reached 98% at the minimum inhibitory concentration for both 90% Streptococcus pneumoniae and Staphylococcus aureus, considering both original and higher protein binding rates. Regardless of fasting or fed conditions, the probability of target attainments for 600 mg q12h lefamulin via oral administration proved comparable to those for intravenous administration

Conclusion This study proved that intravenous and oral administrations of lefamulin can reach preclinical PK/PD targets of Streptococcus pneumoniae and Staphylococcus aureus. These findings support the optimal use of lefamulin for the safe and effective treatment of Chinese CABP patients

关键字：lefamulin, population pharmacokinetic, pharmacokinetic/pharmacodanamic, ethnic sensitivity

TBAJ-587 对临床相关非结核分枝杆菌的体外抗菌活性研究

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目的 非结核分枝杆菌对很多抗菌药物天然耐药，治疗困难。TBAJ-587 是一种新型二芳基喹啉化合物，其抗菌机制与贝达喹啉相近，但亲脂性更低，对 hERG 钾通道的抑制作用更轻，抗结核活性更强。然而尚未有研究报道 TBAJ-587 对非结核分枝杆菌的抗菌活性。

方法 本研究参考 CLSI M24-A2 指南，使用微量肉汤稀释法检测了 TBAJ-587 对 12 种非结核分枝杆菌标准株、194 株脓肿分枝杆菌临床株、15 株鸟分枝杆菌临床株、28 株胞内分枝杆菌临床株的 MIC。使用感染了脓肿分枝杆菌标准株和临床株的 THP-1 细胞检测了 TBAJ-587 的胞内抗菌活性。

结果 除了耻垢分枝杆菌外，TBAJ-587 对 NTM 标准株的 MIC 均小于等于贝达喹啉。TBAJ-587 对脓肿分枝杆菌临床株的体外抗菌活性（MIC50=0.0625mg/L，MIC90=0.125mg/L）较贝达喹啉（MIC50=0.125mg/L，MIC90=0.25mg/L）更强。TBAJ-587 对鸟胞内分枝杆菌临床株的 MIC 也显著低于贝达喹啉。联合药敏试验显示 TBAJ-587 与常用抗 NTM 药物兼容性良好。TBAJ-587 对巨噬细胞内的脓肿分枝杆菌的抗菌活性与贝达喹啉相近。

结论 TBAJ-587 具有显著的体外抗 NTM 活性，可能具有治疗 NTM 感染的临床应用潜力。

关键字：TBAJ-587，二芳基喹啉，非结核分枝杆菌

单宁酸与不同配比头孢哌酮钠/舒巴坦钠对耐碳青霉烯鲍曼不动杆菌的体外抑菌作用研究

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目的 探究单宁酸与不同配比的头孢哌酮钠/舒巴坦钠对耐碳青霉烯鲍曼不动杆菌（CRAB）的抑菌作用。

方法 采用微量肉汤稀释法测定单宁酸、头孢哌酮钠/舒巴坦钠(1:1)、头孢哌酮钠/舒巴坦钠(2:1)对 6 株 CRAB 最低抑菌浓度（MIC）；采用棋盘稀释法测定单宁酸与头孢哌酮钠/舒巴坦钠联合使用对 CRAB 的 MIC，计算部分抑菌浓度指数（FICI）。

结果 单宁酸对于 6 株 CRAB 的 MIC 范围在 128μg/ ml-256μg/ ml 之间，头孢哌酮钠/舒巴坦钠（1:1）对于 6 株 CRAB 的 MIC 范围在 32μg/ ml-128μg/ ml 之间，头孢哌酮钠/舒巴坦钠（2:1）对于 6 株 CRAB 的 MIC 范围在 64μg/ ml-256μg/ ml 之间。单宁酸联合头孢哌酮钠/舒巴坦钠 FICI 在 0.375～0.75 之间，表现为协同和相加作用。

结论 对于 CRAB，头孢哌酮钠/舒巴坦钠(1:1)抑菌效果比头孢哌酮钠/舒巴坦钠(2:1)抑菌效果更好。单宁酸与头孢哌酮钠/舒巴坦钠联用表现为协同和相加作用，有望成为中西药联合抗 CRAB 的一部分。

关键字：单宁酸；头孢哌酮舒巴坦；碳青霉烯；鲍曼不动杆菌；联合抑菌；舒巴坦

Clinical Efficacy and Drug Resistance of Ceftazidime-avibactam in The Treatment of Carbapenem-resistant Gram-negative Bacilli Infection

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Objective To examine the clinical efficacy, safety, and resistance of CeftazidimeAvibactam (CAZ-AVI) in patients with Carbapenem-resistant Gram-negative bacilli (CR-GNB) infections

Methods We retrospectively analyzed relevant data of CR-GNB infected patients receiving CAZ-AVI treatment, analyzed relevant factors affecting drug efficacy, and compared the efficacy and safety with patients receiving Polymyxin B treatment

Results A total of 139 patients were included. Agranulocytosis, septic shock, SOFA score, and CAZ-AVI treatment course were independent risk factors affecting the prognosis of patients with CR-GNB infection treated with CAZ-AVI while prolonging the treatment course of CAZ-AVI was the only protective factor for bacterial clearance. The fundamental indicators showed no statistically significant differences between CAZ-AVI and Polymyxin B treatment groups. At the same time, the proportion of patients treated with monotherapy was significantly higher in the CAZ-AVI group than in the Polymyxin B group (37.2% vs. 8.9%, $p < 0.05$), the 30-day mortality rate of the CAZ-AVI treatment group (27.7% vs. 46.7%, $p = 0.027$) was lower than that of the Polymyxin B treatment group. The 30-day clinical cure rate (59.6% vs. 40% $p = 0.030$) and 14-day microbiological clearance rate (42.6% vs. 24.4%, $p = 0.038$) were significantly higher in the CAZ-AVI than in the Polymyxin B treatment group.

Eighty nine patients were monitored for CAZ-AVI resistance, and the total resistance rate was 14.6% (13/89). The resistance rates of Carbapenem-resistant Klebsiella pneumoniae (CRKP) and Carbapenem-resistant Pseudomonas aeruginosa (CRPA) to CAZ-AVI were 13.5 and 15.4%, respectively

Conclusion CAZ-AVI has shown high clinical efficacy and bacterial clearance in treating CR-GNB infections. Compared with Polymyxin B, CAZ-AVI significantly improved the outcome of mechanical ventilation in patients with septic shock, agranulocytosis, Intensive Care Unit (ICU) patients, bloodstream infection, and patients with SOFA score > 6, and had a lower incidence of adverse events. We monitored the emergence of CAZ-AVI resistance and should strengthen the monitoring of drug susceptibility in clinical practice and the rational selection of antibiotic regimens to delay the onset of resistance

关键字：ceftazidime-avibactam, Polymyxin B, carbapenem-resistant gram-negative bacilli, clinical efficacy, drug resistance

Concentration Analysis, Population Pharmacokinetic Modeling and Optimization of Administration Regimens of Meropenem in Septic Patients in Chinese Intensive Care Units

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Objective Sepsis, a severe organ dysfunction due to a dysregulated response to infection, requires early identification and prompt treatment. Patients with sepsis experience changes in the pharmacokinetic parameters of antimicrobial drugs due to the need for fluid resuscitation, increased capillary leakage, self-regulation of the autonomic nervous system, and alterations in organ function. Meropenem is a broad-spectrum water-soluble antibiotic commonly used in the treatment of sepsis. However, the use of this agent in such patients poses significant challenges due to the influence of renal clearance on its elimination and the influence of factors such as fluid leakage on drug distribution. Individualized dosing is required based on the specific conditions of the patient. Although many meropenem population pharmacokinetic (PK) models have been published, there is no large prospective population PK study with rich sampling focusing on critically patients most at risk of sub-therapy pharmacokinetic/pharmacodynamic (PK/PD) target attainment. This study aims to describe meropenem's PK/PD in severe sepsis, simulate dosage regimens, and identify optimal initial dosage for critically septic patients with different renal clearance

Method This was a single-center prospective observational PK study in the intensive care unit (ICU) of a tertiary A hospital from China. Patients with sepsis and treated with meropenem were screened for inclusion. Record patient clinical information and regularly collect and measure serum drug concentrations of meropenem. Population PK modelling and dosage simulation was performed with Pmetrics in R-package. Successful PK/PD target attainment was defined as the probability of target attachment is above than 100%fT>MIC and 100%fT>4MIC

Result This study included 42 eligible patients, with a total of 98 cases tested for serum drug concentration of meropenem. A one-compartment model with first-order elimination best described the meropenem concentration-time profiles. The model adopts multiplication proportional error, and the drug clearance rate is related to the creatinine clearance rate. Goodness-of-fit plots indicated that the fit of the final model was reasonably good. Patients with renal hypofunction included in the study had significantly higher serum trough concentrations than those with normal renal function and those with hyperactive renal function. Regimen simulations at CrCl=60mL/min showed 0.5g Q8h and Q6h achieved 90% PTA at MIC=2mg/L; 1g Q8h reached 90% PTA at MIC=4mg/L. 2g Q12h achieved 90% PTA only at MIC=1mg/L. At 100%fT>4MIC, only 1g Q6h reached 90% PTA. At CrCl=90mL/min and 120 mL/min, various regimens achieved 90% PTA at MIC=2mg/L. At CrCl=150mg/L, 0.5g Q6h, 1g Q6h, 2g Q8h achieved 90% PTA at MIC=2mg/L. Only 1g Q6h achieved 90% PTA at MIC=4mg/L

Conclusion In this study, a PPK model was established to understand the pharmacokinetics of meropenem in patients with severe sepsis. Renal function is associated with the clearance rate of meropenem. Clearance increased with increasing creatinine clearance. Patients were grouped according to renal function. Renal hypofunction results in higher and more variable serum concentrations. Evaluation of patients on admission is essential. Treatment options should consider infectious, physiological, and biochemical factors. TDM and protocol modifications are critical. The drug administration simulation experiment showed that increasing the frequency and duration of infusion could improve the compliance rate. In patients with severe sepsis and ARC, prolonged infusion duration and increased dose may be necessary to achieve advanced goals

关键字：Population pharmacokinetics, Pharmacodynamics, Sepsis, Meropenem, Monte Carlo simulation, Intensive care unit

Repurposing CD5789 As An Antimicrobial Against MRSA and Its High Resistant Phonotypes

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Abstract Methicillin-resistant Staphylococcus aureus (MRSA) poses a great threat to human health, and the formation of biofilm and persister cells make the situation even worse. Drug repurposing is an effective way to solve this problem by shortening the drug development times and reducing the research costs. In this study, CD5789 (trifarotene), a fourth-generation retinoid to be approved by the FDA in 2019 for the topical acne vulgaris regimens, was exhibited significant bactericidal activity against MRSA type strains and its clinical isolates with the minimal concentration (MIC) of 2-4 μg/mL and 4-16 μg/mL, respectively in a dose-dependent manner. By crystal violet staining, we found that CD5789 could significantly inhibit the biofilm formation by MRSA and could further eradicate the preformed biofilm at the concentration of 8 μg/mL. By checkerboard dilution assay, sub-MIC of CD5789 showed significant synergistic antimicrobial effects with sub-MIC gentamycin against MRSA type strains as well as clinical isolates. In addition, CD5789 also exhibited effective bactericidal activity against MRSA persister cells at the concentration of 8~16 μg/mL. Extremely low cytotoxicity of CD5789 was observed by CCK-8 assay indicated the well tolerability to human body. In all, CD5789 has the potential to be an alternative for refractory MRSA-related infections.

关键字：Methicillin-resistant Staphylococcus aureus; CD5789; repurposing; biofilm; persister cell

幽门螺杆菌体外药敏试验 (K-B) 法折点研究及确认

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目的 对幽门螺杆菌体外药敏试验纸片扩散法（K-B 法）折点标准化研究及确认，为临床幽门螺杆菌体外药敏试验提供依据。

方法 我们从临床分离出幽门螺杆菌 100 株，进行传代培养，利用纸片扩散法检测对阿莫西林、甲硝唑、克拉霉素、左氧氟沙星、利福平、四环素检测各菌株所获得的抑菌圈直径为变量，绘制 ROC 曲线，同时评价约登指数，利用已注册上市的幽门螺杆菌药敏试剂盒（琼脂稀释法）做参比试验，以最佳灵敏度和特异性作为幽门螺杆菌药敏纸片扩散法抑菌圈直径值折点确定的标准。参考 EUCAST 发布的针对幽门螺杆菌的 6 种抗生素 MIC 折点，采用更加准确可靠的琼脂稀释法对纸片扩散法确定的抑菌圈直径进行验证，使用共识推荐的误率分析法来确定纸片扩散法（K-B 法）的折点设置的准确性。为了验证纸片扩散法所采纳的阳性判断值的正确性和可靠性，我们进一步对药敏检测折点依据上述阳性判断值获得的药敏结果同琼脂稀释法药敏检测结果进行了一致性分析。

结果 根据约登指数，得到阿莫西林纸片扩散法的折点为耐药（R）≦13mm，中介（I）14-17mm，敏感（S）≧18mm；甲硝唑折点为耐药（R）≦15mm，中介（I）16-21mm，敏感（S）≧22mm；克拉霉素折点为耐药（R）≦10mm，中介（I）11-12mm，敏感（S）≧13mm；左氧氟沙星折点为耐药（R）≦13mm，中介（I）14-16mm，敏感（S）≧17mm；利福平折点为耐药（R）≦16mm，中介（I）17-19mm，敏感（S）≧20mm；四环素折点为耐药（R）≦14mm，中介（I）15-18mm，敏感（S）≧19mm。纸片扩散法阳性判断值获得的药敏结果同琼脂稀释法获得的药敏结果相比，在不同 MIC 范围的 ME 及 VME 比率均在容许范围内，显示纸片扩散法的阳性判断值是可靠和准确的，且具有良好的一致性。

结论 本实验利用 ROC 曲线分析方法确立了幽门螺杆菌体外药敏试验纸片扩散法（K-B 法）的折点并进行确认，为临床实验室选择药敏试验提供依据，为临床幽门螺杆菌精准治疗用药提供帮助。

关键字：幽门螺杆菌，纸片扩增法，折点确认

基于主成分分析法的危重症患者万古霉素浓度过度暴露危险因素研究

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目的 由于万古霉素在危重患者中出现浓度过度暴露现象，本研究拟探索危重症患者万古霉素谷浓度过度暴露的危险因素并进行临床评价，为后期临床应用提供数据参考。

方法 回顾性分析 2021 年 1 月至 2022 年 11 月我院收治的 110 例危重症患者，基于主成分分析法的多连续变量因素降维处理、单因素分析初步筛选出多个主要影响因素，继而二元多因素 Logistics 回归分析，最终筛选出影响急危重症患者万古霉素谷浓度过度暴露的危险因素，利用 ROC 曲线作相关评价。

结果 主成分分析法结果表明：年龄、体重、肌酐清除率、尿素氮和白蛋白为主要影响因素。单因素分析结果表明：感染性休克、血管活性药物、合并有心脏病和 ALT 对急危重症患者万古霉素谷浓度影响均有统计学差异（P 值分别为 0.008、0.043、0.037，

P<0.05 和 0.024，P<0.05），但肝功能不全对急危重症患者万古霉素谷浓度影响没有统计学差异（P=0.61，P<0.05）。Logistics 回归分析表明肌酐清除率(OR=1.009, P=0.002)和感染性休克(OR=3.408, P=0.014)可能是导致危重症患者万古霉素过度暴露的危险因素。ROC 曲线对应的 ROC 曲线下面积(The area under the ROC curve， AUC) 0.7859 (95%CI=[0.6965，0.8753]，P<0.0001)。说明 CrCL 对危重症患者万古霉素过度暴露的准确性的判断有意义，约登指数（Youden index）的最大值为 0.5314，当 CrCL 的最佳临界值为 59.91mL/min 时，其敏感度为 76%，特异度为 22.86%，说明当 CrCL<59.91mL/min 时，二元 Logistics 回归预测万古霉素过度暴露的风险增加。

结论 肌酐清除率和感染性休克可能是影响急危重症患者谷浓度过度暴露的危险因素。

关键字：主成分分析法，万古霉素，过度暴露，二元 Logistics 回归，危险因素

预防性使用抗菌药物方案对老年植入永久性心脏起搏器术后感染的预防效果

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目的 分析老年植入永久性心脏起搏器患者采取预防性使用抗菌药物方案对感染的预防效果。

方法 将院内近 1 年（2023.1-2023.12）收治的需植入永久性心脏起搏器的老年患者 80 例作为本次观察对象，根据患者抗菌药物使用方案的不同分组，即 A 组（术前 3d 预防性使用抗菌药物方案，30 例）、B 组（术前 1d 预防性使用抗菌药物方案，30 例）、C 组（术前不应用抗菌管理，20 例），比较三组治疗后术后感染发生率（囊袋感染、切口感染、呼吸道感染）、抗菌药物成本、治疗前病原学送检率，比较三组管理前后炎症因子水平（白细胞计数（White blood cell count，WBC）、C 反应蛋白（C-reactive protein，CRP）、白细胞介素-1（interleukin-1，IL-1））、心功能（左室收缩末期内径(LV end-systolic inner diameter，LVESd)、左室舒张末期内径(Left ventricular end-diastolic inner diameter，LVEDd)、左心室射血分数（Left ventricular ejection fraction，LVEF））。

结果 A 组抗菌药物成本高于 B 组、C 组，治疗前病原学送检率高于 B 组、C 组，对比有统计学意义（P＜0.05）；三组治疗前比较炎症因子水平与心功能可见差异较小，无统计学意义（P＞0.05），治疗后比较三组各项功能指标可见 A 组各项指标改善效果更优于 B 组、C 组，对比有统计学意义（P＜0.05）；A 组术后感染发生率低于 B 组、C 组，对比有统计学意义（P＜0.05）。

结论 在老年患者植入永久性心脏起搏器治疗中给予预防性使用抗菌药物方案可提高治疗前病原学送检率，合理控制病菌感染以降低术后感染发生率，减轻体内炎症水平，术前早期开展抗菌药物管理还能有助于提高心功能恢复效果，可在临床中推广。

关键字：预防性使用抗菌药物，老年，植入永久性心脏起搏器，术后感染

Hematological Adverse Events Associated with Antimicrobials for MRSA Infections: A Real-World Analysis Based on FAERS

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Objective This study investigated the patterns of hematological adverse events related to daptomycin (DAP), tigecycline (TIG), vancomycin (VAN) and linezolid (LIN) in the FDA Adverse Event Reporting System (FAERS)。

Methods Adverse event associations were analyzed through calculating reporting odds ratio (ROR), proportional reporting ratio (PRR), multiple gamma Poisson shrinkage (MGPS), and Bayesian confidence propagation neural network (BCPNN). A comprehensive descriptive analysis was also conducted considering factors such as age, gender, daily dose, cumulative dose, and time to onset

Results The leading hematologic adverse events were eosinophilia for daptomycin, coagulation abnormalities and thrombocytopenia for tigecycline, thrombocytopenia, neutropenia, and anemia for linezolid, and thrombocytopenia, eosinophilia, and neutropenia for vancomycin. Most of the affected patients were over 55 years old. Daily doses for the tigecycline and daptomycin groups exceeded the standard daily dose. The times to onset were 14.00 days for daptomycin (interquartile range [IQR], 4.00-21.00), 6.00 days for tigecycline (IQR, 2.00-9.00), 10.00 days for linezolid (IQR, 4.00-16.5), and 10.00 days for vancomycin (IQR,5.00-20.00)

Conclusion It is essential to intensify early monitoring and identification of these adverse events, especially in the context of off-label dosages and for elderly patients and individuals taking medication for over one week

关键字：Pharmacovigilance, Data mining, Anti-MRSA agents, Hematological adverse events, FAERS.

头孢哌酮/舒巴坦（2:1）治疗革兰阴性菌血流感染给药方案评估：基于全国血流感染细菌耐药监测联盟的蒙特卡洛模拟研究

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目的 通过蒙特卡洛模拟评价头孢哌酮/舒巴坦 (CSL, 2:1) 对不同肾功能患者革兰阴性菌血流感染给药方案的合理性。

方法 应用琼脂稀释法测定 CSL 对革兰阴性菌的最低抑制浓度(MIC)，并通过蒙特卡洛模拟(MCS)计算不同肾功能患者 CSL 不同给药方案对不同敏感性细菌的达标概率(PTA)和累积反应分数(CFR)，评估给药方案的合理性。

结果 CSL 对血流感染来源肠杆菌、鲍曼不动杆菌和铜绿假单胞菌的 MIC90 分别为 32/16、128/64 和 64/32mg/L。对 MIC＞16mg/L 的肠杆菌，对不同肾功能患者即使 CSL 以 4.5g q6h 15 分钟输注，获得的 PTA 仍低于 90%， CFR 最高为 77.82%，对产 ESBL 肠杆菌血流感染 CFR 仍低于 80%。对 ESBL 阴性肠杆菌感染患者，CLCR＞60ml/min 时，CSL 3.0g q6h（说明书最大剂量）、3.0g q8h、4.5g q6h 和 4.5g q8h 四种给药方案获得的 CFR 分别为 90.2%、83.15%、91.4%和 87.09%；CLCR≤60ml/min 时，所有给药方案均可使 CFR 大于 80%。对鲍曼不动杆菌感染患者，当 CLCR＞60ml/min，CSL 各给药方案所获 CFR 均低于 40%；CLCR 为 31-60ml/min，CSL 4.5g q6h 给药获得 CFR 为 85.27%；CLCR 为 10-30ml/min，3.0g q6h、4.5g q6h 和 4.5g q8h 获得的 CFR 分别为 88.05%、91.86%和 82.61%；CLCR＜10ml/min 时（非透析患者），各给药方案所获得 CFR 均大于 80%。对铜绿假单胞菌感染患者，当患者 CLCR 在 10-30 或≤10ml/min 时，CSL 以 4.5g q6h 给药所获得的 CFR 分别为 80.09%和 81.68%。

结论 CSL 治疗革兰阴性菌血流感染时，需要根据细菌敏感性和患者肾功能等情况制定个体化给药方案，目前推荐的给药方案可能存在剂量不足情况。针对鲍曼不动杆菌敏感性折点可能需要进一步调整。

关键字：头孢哌酮/舒巴坦, 血流感染, 蒙特卡洛模拟

Therapeutic Drug Monitoring of Ceftazidime/avibactam and Pharmacokinetic/pharmacodynamic Target Assessment in Infected Patients: A Single-centre Retrospective Observational Study

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Objective This study aimed to 1) describe the distribution characteristics and its influencing factors of ceftazidime/avibactam trough concentrations (Cmin); 2) analyze the pharmacokinetic/pharmacodynamic (PK/PD) target assessment of ceftazidime/avibactam; 3) evaluate the clinical outcome of patients infected with multidrug-resistant gram-negative bacteria (MDRGNB)

Methods We conducted a single-centre retrospective observational study. Cmin and its influencing factors were studied in 39 infected patients treated with ceftazidime/avibactam. The PK/PD of ceftazidime and avibactam were 100% of time during the dosing interval that free drug concentrations remained above minimal inhibitory concentrations (i.e., fCmin/MIC > 1) and 100% of time during the dosing interval that free drug concentrations remained above threshold concentration (i.e., fCmin/CT > 1). The optimal joint PK/PD was defined as that ceftazidime and avibactam reached the PK/PD target simultaneously. Finally, the clinical outcome of ceftazidime/avibactam in infected patients was as antly correlated with cystatin C. The Cmin of avibactam was 6.0 ± 4.4 mg/L, and significantly correlated with cystatin C and the presence or absence of continuous renal replacement therapy. Totally, the joint PK/PD target of ceftazidime/avibactam were 82.6%. Then 76.92% (30/39) patients were clinically cured

Results Eighty-two plasma samples from 39 infected patients were analyzed. The results showed Cmin of ceftazidime was 24.1 ± 14.3 mg/L, which was significantly correlated with cystatin C. The Cmin of avibactam was 6.0 ± 4.4 mg/L, and significantly correlated with cystatin C and the presence or absence of continuous renal replacement therapy. Totally, the joint PK/PD target of ceftazidime/avibactam were 82.6%. Then 76.92% (30/39) patients were clinically cured

Conclusion These results suggested the Cmin of ceftazidime and avibactam vary widely and were affected by renal function. The current administration regimen can achieve excellent clinical results

关键字：ceftazidime/avibactam; drug-resistant gram-negative bacterial; therapeutic drug monitoring; pharmacokinetic/pharmacodynamic

体外动态 PK/PD 优化新药 MRX-8 与美罗培南抗多重耐药鲍曼不动杆菌的联合用药方案研究

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目的 建立体外动态 PK/PD 模型，优化对多重耐药鲍曼不动杆菌（MDRAB）有效的 MRX-8 体外联合用药方案。

方法 选取临床分离 MDRAB 菌株 2 株，通过最低抑菌浓度（MIC）测定、棋盘法联合药敏、静态杀菌曲线实验初步评估 MRX-8 与美罗培南的协同效果，通过动态杀菌曲线实验进一步研究 MRX-8 与美罗培南组合在临床用药方案下的杀菌效果。

结果 两株 MDRAB 的多位点序列分型（MLST）均为 ST2 型，对 MRX-8、美罗培南的 MIC 数值相等，分别为 0.5 mg/L 和 64 mg/L。在棋盘法联合药敏中 MRX-8 联合美罗培南对 AB 21-3759 有协同作用，AB 21-3881 有相加作用。静态杀菌曲线实验中，对于 AB 21-3759，MRX-8 0.25~1 mg/L 单药能使细菌数目暂时下降，至 24 h 出现反跳，1 mg/L MRX-8 联合 1 mg/L 美罗培南可在 24 h 内完全抑制细菌的生长。对于 AB 21-3881，1 mg/L MRX-8 单药可在 24 h 内完全抑制细菌的生长。动态杀菌曲线实验中，对于 AB 21-3759，相较于 MRX-8 单药，联合美罗培南方案（MRX-8 0.75 mg/kg q8h 稳态浓度联合美罗培南 1g q6h 持续输注稳态浓度）可更好的杀灭细菌，联合美罗培南能使耐药性的出现延迟 12~24 h。对于 AB 21-3881，仅 MRX-8 单药 1 mg/kg q12h 给药方案即可维持 72 h 内静息杀菌状态。

结论 本研究中 MRX-8 0.75 mg/kg q8h 稳态浓度联合美罗培南 1g q6h 持续输注稳态浓度在体外可使 MDRAB 在 72h 菌落数维持静息杀菌水平，对于难治的鲍曼不动杆菌感染，推荐 MRX-8 联合美罗培南并尽快达到稳态。

关键字：MRX-8，美罗培南，革兰氏阴性菌，体外药动学/药效学

甘草酸可抑制 QS 系统表达降低沙门菌的耐药性：潜在的抗菌增效剂

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目的 沙门菌广泛分布于人、动物和环境中，既能感染人，也能感染动物及污染动物性肉品。目前，抗生素仍是主要防控手段，但耐药（AMR）沙门菌的出现及传播，使其成为公共健康的潜在威胁而更加难以防控。前期，我们证实沙门菌 LuxS/AI-2 型群体感应（Quorum sensing, QS）系统可通过调控外排泵 AcrAB-TolC 调控其 AMR。所以基于抑制 QS 系统表达为基础寻找高效、绿色的新型抗菌药物对 AMR 沙门菌的防控至关重要。

方法 本研究以 LuxS 蛋白为靶标，利用分子对接技术筛选能够抑制 LuxS 蛋白表达的中药单体分子，并进行分子动力学分析；同时利用筛选的中药单体分子进行体外抑菌实验及与抗生素的联合抑菌作用，并通过 qPCR 检测中药单体分子对沙门菌 luxS 基因 mRNA 转录水平的影响，利用 WB 检测中药单体分子对 LuxS 蛋白表达水平的影响，并测定 AI-2 的活性。

结果 结果显示，根据结合能大小、中药单体分子的溶解性、应用广泛性、价格等因素，最终选定具有与 LuxS 蛋白多个氨基酸残基形成氢键及疏水作用力的中药单体甘草酸（Glycyrrhizic acid, GA）作为 LuxS 蛋白表达的抑制剂；体外抑菌试验显示，32 mg/mL GA 可有效抑制沙门菌的生长，说明 GA 有一定的抑菌能力。亚抑菌浓度的 GA 可以显著抑制 luxS 基因 mRNA 的表达和 LuxS 蛋白的表达及 AI-2 的活性及外排泵基因 acrA 和 acrB 的表达，且呈现剂量依赖性；另外，GA 与 AMC、CTX、SIZ、CIP 四种抗生素进行联合应用均表明有协同抑菌作用。

结论 GA 作为 LuxS 蛋白表达抑制剂可与抗生素联合应用产生了协同抑菌作用，有效地降低沙门菌的耐药性，具有研发成为抗菌增效剂的潜质。

关键字：甘草酸，沙门菌，多重耐药，QS 系统抑制剂，抗菌增效剂

Population Pharmacokinetics and Dosing Optimization of Biapenem in Patients with Sepsis

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Objective Biapenem is a carbapenem antibiotic, which can be used for the treatment of adults and children with infections due to susceptible bacteria. Although biapenem is utilized in the treatment of different bacterial infections, current pharmacokinetic data in septic populations remain limited

Methods In this study, we characterized the pharmacokinetics of biapenem in septic patients using a population pharmacokinetic (PPK) approach. The clinical PK data to develop the PPK model were obtained from 317 septic patients admitted to Nanjing Drum Tower Hospital between 2018 and 2022. All patients were randomized to the modeling and external validation groups at a 3:1 ratio, with PPK modeling and validation performed utilizing the NONMEM software.The PPK model was then used to perform Monte Carlo simulations to evaluate the probability of attaining 70% of the time that the free antimicrobial drug concentration exceeds the MIC (fT>MIC)

Results The model found to best describe the

available data was a two-compartment PPK model with first-order elimination characterized by the parameters clearance (CL), central volume (V1), peripheral volume (V2), and intercompartmental clearance (Q). A covariate analysis identified that creatinine clearance (CLCR) was a significant covariate influencing biapenem CL, while blood urea nitrogen (BUN) was a significant covariate influencing biapenem Q

Conclusion The current daily dosage regimen of 1.2g may insufficient to achieve 70% fT>MIC in septic patients. Conclusions The dosage regimen of 600mg every 6 hours appears to be the optimal choice

关键字：biapenem; pharmacokinetics; dosing regimen; sepsis

奈诺沙星在尿路感染体外模型中对大肠埃希菌的药代动力学/药效学研究

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目的 建立尿路感染体外药动学/药效学（PK/PD）模型并利用该模型探索奈诺沙星与大肠埃希菌的体外药效学关系，对其尿路感染给药方案进行评价。

方法 收集泌尿道标本来源大肠埃希菌共 12 株，分别采用 CLSI 规定的微量肉汤稀释法和人工尿合成培养基测定其抑菌浓度 MIC 和 MICSHU。基于奈诺沙星口服 500mg qd I 期临床试验所获得的健康受试者血药浓度与尿药浓度，模拟奈诺沙星不同药物暴露量下对大肠埃希菌的杀菌效果，其中 Cmax 分别为 5.70 mg/L（血药组）、147 mg/L（尿药低暴露组）、476 mg/L（尿药高暴露组）。采用阳离子调节肉汤培养基（CAMHB）与人工合成尿培养基（SHU）作为细菌生长液体环境，其中 CAMHB 用于血药组和尿药低暴露组的研究，SHU 用于尿药不同暴露组的研究。根据 10 株受试菌在不同培养基中的 MIC 选择合适的菌株进行体外 PK/PD 研究，在给药前及给药后 0-24h 内不同时间点分别进行菌落计数，绘制动态时间-杀菌曲线。药效学指标为 0-24h 内细菌数量变化（Δlog10CFU/mL），使用蒙特卡洛模拟计算达标概率（PTA）与累积响应百分数（CFR）。

结果 体外药敏结果显示，MICSHU 显著高于 MIC，且受 pH 值影响。体外 PK/PD 结果显示，血药组中，奈诺沙星仅对 1 株菌（MIC = 0.5mg/L）具有良好杀菌效果（Δlog10CFU/mL < -2）。尿药低暴露组中，奈诺沙星在 CAMHB 培养环境中对 MIC = 8-32 mg/L 的三株受试菌株均效果良好（Δlog10CFU/mL < -1），在 SHU 培养环境中仅对 MIC 为 2-8 mg/L 三株受试菌株效果良好，而奈诺沙星尿药高暴露组可以覆盖 MIC ≤ 16mg/L 的菌株。奈诺沙星 CAMHB 与 SHU 中与 Δlog10CFU/mL 最相关的 PK/PD 指数均为 fAUC/MIC，相应靶值分别为 41.7 、 165 （ Δlog10CFU/mL = 0 ）， 46.5 、 198（Δlog10CFU/mL = -1）。以 CAMHB 靶值计算 PTA，结果显示口服奈诺沙星 500mg qd 对 MIC ≤ 32 mg/L 的大肠埃希菌具有杀菌作用，CFR 达 94.9%；以 SHU 靶值计算 PTA，口服奈诺沙星 500mg qd 仅对 MIC ≤ 8 mg/L 的大肠埃希菌具有抑菌作用，CFR 为 83.4%。

结论 尿路感染体外 PK/PD 模型显示，口服奈诺沙星 500mg qd 在不同细菌生长环境中对大肠埃希菌的活性不同，在尿液环境对 MIC ≤ 8 mg/L 的大肠埃希菌具有较好的杀菌效果。

关键字：体外药代动力学/药效学，尿路感染，大肠埃希菌，奈诺沙星，人工合成尿培养基

抗菌药物管理与院感防控

回顾性分析 203 例头孢菌素类抗菌药物的不良反应

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目的 了解头孢菌素类药物相关药品不良反应(Adverse drug reactions，ADR)发生的特点、规律及相关因素，为临床合理用药提供参考。

方法 采用回顾性分析的方法，调取我院 2012 年 1 月 1 日～2021 年 12 月 31 日上报国家药品不良反应监测系统的头孢菌素类药物 ADR 报告 214 例，其中排除 11 例皮试阳性报告，剩余 203 例纳入分析。对患者的年龄、性别、怀疑药品的给药方式、药品不良反应的临床表现等进行统计分析。

结果 研究共纳入头孢菌素的 ADR 报告 203 例。患者年龄 5 个月～85 岁，男性 97 例，女性 106 例。通过统计，18 岁以下未成年人以及≥65 岁的老年人是严重 ADR 的易发人群，静脉滴注相对于口服给药更易引起严重 ADR，差异有统计学意义（P ＜ 0.05）；而患者的性别、之前是否有药物过敏史、药物类型、给药剂量以及给药时长对于头孢菌素不良反应类型，无统计学意义（P ＞0.05）。引起不良反应的主要药物为三代头孢菌素如注射用头孢他啶（25.12%）、注射用头孢噻肟钠（20.69%）、注射用头孢哌酮钠舒巴坦钠（13.79%）、注射用头孢曲松钠（8.87%）。ADR 的临床表现包括皮肤及其附件损害、消化系统损害、心血管系统损害、神经系统损害等。以皮肤及其附件损害（60.82%）最为常见。

结论 合理使用头孢菌素类药物,加强 ADR 监测,对合理使用该类药物，保障用药安全具有积极的意义。

关键字：头孢菌素，抗菌药物，药品不良反应，合理用药

住院患者抗菌药物过敏史评估的最佳证据总结

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目的 检索、评价和汇总抗菌药物过敏史评估的最佳证据，为住院患者抗菌药物过敏评估护理实践提供循证支持。

方法 系统检索 UpToDate、BMJ Best Practice、美国国立指南库、国际指南协作网、BSACI 指南网、AAAAI 指南网、中国医脉通指南网、JBI Evidence Synthesis、Cochrane Library、CINAHL、EMBASE、PubMed、Web of Science、中国知网、万方数据库、维普、中国生物医学文献数据库中抗菌药物过敏评估相关的临床决策、指南、专家共识、证据总结、系统评价和 Meta 分析，检索时限均为建库至 2023 年 7 月。由 2 名研究员独立筛选文献并进行质量评价，经循证研究小组讨论，对符合标准的文献进行资料提取和证据整合。

结果 最终纳入 8 篇文献，包括指南 6 篇，系统评价 2 篇。总结出抗菌药物过敏评估重要性、过敏评估对象、过敏评估人员、过敏评估内容、过敏史记录、评估注意要点 6 个方面 25 条证据。

结论 本研究总结了住院患者抗菌药物过敏史评估的最佳证据，可为医护人员制定抗菌药物过敏评估方案提供循证依据，建议护理人员在应用和转化证据时，充分考虑临床实际情况，探索具有本土特色的住院患者抗菌药物过敏史评估方案。

关键字：抗菌药物；过敏评估；护理评估；证据总结；循证护理学

我院碳青霉烯类抗菌药物管理实践与效果分析

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目的 本研究旨在评估我院碳青霉烯类抗菌药物的全程管理体系，特别是跨学科合作与信息化技术相结合的效果。通过这一研究，我们希望提升抗菌药物使用合理性，减少耐药菌的发展，降低医疗成本，并提高患者治疗效果。

方法 本研究采取了多维度的管理策略，包括组织建设、信息化管理、在线会诊审核系统和处方点评干预等。我们对管理实施前后的碳青霉烯类抗菌药物使用强度、使用率、处方合理性、医保违规情况和耐药菌检出率进行了详尽分析。此外，还对医护人员进行了相关培训，提高了他们的药物使用意识和能力。

结果 我院实行碳青霉烯类抗菌药物管理后，碳青霉烯类抗菌药物的使用强度由 2.54 降至 1.63，使用率从 2.64%降至 1.64%；处方合理性从 73.60%上升至 91.80%；医保筛查扣费金额减少。然而，耐药菌的检出率仍呈现上升趋势。

结论 本研究表明，跨学科合作与信息化技术的结合能够有效提升我院碳青霉烯类抗菌药物的管理效果。我们的管理策略在提高药物使用合理性、经济效益以及患者安全方面均取得了显著成效。然

而，耐药性问题的增加提示我们在未来的工作中需要更加注重持续教育、监测系统的完善和医保政策的优化。希望这一研究能够为其他医疗机构提供有价值的参考，共同提升抗菌药物的合理使用水平，为公共健康事业做出更大的贡献。

关键字：碳青霉烯类, 抗菌药物管理, 跨学科合作, 信息化技术, 细菌耐药

头孢菌素类注射剂皮试的规范化管理及分析

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目的 分析西藏自治区人民政府驻成都办事处医院（以下简称“我院”）规范头孢菌素类注射剂皮试对临床抗菌药物使用的安全性和合理性影响及其经济学价值，为头孢菌素皮试的规范化管理提供参考和依据。

方法 回顾性分析我院规范头孢菌素类注射剂皮试前后的皮试筛查情况、药物过敏情况和换药情况等数据，同时从药品费用、耗材费用和护理劳动时间等方面对规范头孢菌素皮试进行经济性研究。

结果 我院规范头孢菌素皮试之前，皮试率高达 95.14%，皮试阳性率约为 2.19%，皮试阴性的患者过敏反应发生率为 0.35%，其中包含 0.03%危及生命的严重过敏反应。规范头孢菌素皮试后，皮试率下降至 15.84%，皮试阳性率为 3.91%，患者用药后过敏反应的发生率降低至 0.29%，且均表现为I度或II度过敏反应。经济性方面，规范头孢菌素皮试后，患者角度的人均皮试成本下降 70.64%，医疗机构角度的人均成本下降 76.30%。

结论 不规范的头孢菌素皮试不仅不能预测过敏，还可能增加其他抗菌药物的滥用风险以及造成医务人员对过敏反应的忽视，也给患者、医保和全社会带来不必要的经济负担。因此规范头孢菌素皮试是有效保障医疗质量和安全的一项重要工作，亟待推进，同时也需要多部门共同参与、共同协作。

关键字：头孢菌素；皮试；合理用药；药物经济学

PDCA 循环与多学科协作管理模式在减少多重耐药菌医院感染中的应用效果评价

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目的 多重耐药菌在医院内的迅速传播是威胁人类健康的世界性公共卫生问题，而多重耐药菌医院感染控制需要临床、药学、微生物学及医院感染控制等多学科共同协作，本研究旨在探讨 PDCA 循环联合多学科协作（Multi-disciplinary team,MDT）管理模式在降低我院多重耐药菌医院感染中的应用效果，为医疗机构 MDRO 的医院感染管理提供参考。

方法 我院从 2023 年开始采取 PDCA 循环联合多学科协作管理模式对 MDRO 的医院感染防控进行干预，包括计划阶段、实施阶段、检查阶段和改进阶段，实施阶段包括成立多学科协作小组、强化培训、建立风险预警机制、建立信息互通渠道等措施。本研究将 2023 年 1 月-12 月收治的 72659 例实施 PDCA 联合多学科协作管理模式的住院患者作为干预后组，将 2022 年 1 月-12 月收治的 60902 例实施常规院内感染防控管理的住院患者作为干预前组，对两组的 MDRO 医院感染发病情况、检出情况及各项感染防控措施执行情况等进行比较。

结果 干预后组的多重耐药菌医院感染发病率明显低于干预前组（$p < 0.001$），干预后组多重耐药菌医院感染例数在多重耐药菌检出总例数的占比明显低于干预前组（$p<0.001$），干预后组医护人员对 MDRO 感染防控措施依从率高于干预前组。

结论 采用 PDCA 联合多学科协作管理的多重耐药菌院感防控管理模式可以有效降低多重耐药菌医院感染发生率，提高多重耐药菌医院感染核心防控措施的依从性。

关键字：多学科协作，多重耐药菌，医院感染

难治性耐药铜绿假单胞菌肺部感染的危险因素及预后

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目的 探讨医院难治性耐药铜绿假单胞菌(difficult-to-treat resistance Pseudomonas aeruginosa,DTR-PA)肺部感染的临床特征、感染危险因素和预后情况，为尽早防控 DTR-PA 肺部感染提供理论依据。

方法 收集 2018 年 1 月至 2022 年 12 月广东省人民医院确诊的由 DTR-PA 所致的肺部感染患者临床资料 80 例(DTR-PA 感染组)，另外按照年龄相近、

性别相同、同期住院、入住病区一致等原则，随机选取由非DTR-PA所致肺部感染的患者80例(对照组)。运用单因素和多因素 logistic 回归方法，分析 DTR-PA 肺部感染的危险因素，应用 χ2 检验评估患者预后。

结果 DTR-PA 导致的肺部感染具有多种危险因素，其中患者伴有肺部疾病(OR=0.394,95%CI 0.172 ～ 0.903,P=0.028) 、神经系统疾病(OR=0.312,95%CI 0.118～0.826,P=0.019)、存在≥3 种抗菌药物联用 (OR=0.215,95%CI 0.066 ～ 0.701,P=0.011)可能是其感染的重要危险因素。DTR-PA 感染组的肺部感染的病死率高于对照组(P<0.001)。

结论 患者伴有肺部和神经系统疾病、存在≥3 种抗菌药物联用可能是 DTR-PA 肺部感染的重要危险因素，且 DTR-PA 肺部感染患者的病死率高。因此，临床应对 DTR-PA 所致的肺部感染危险因素进行综合评估，采取积极的防范措施，以改善患者预后。

关键字：难治性耐药铜绿假单胞菌；肺部感染；临床特征；危险因素；临床预后

耐碳青霉烯类铜绿假单胞菌感染的临床特征及相关危险因素研究

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目的 探讨医院耐碳青霉烯类铜绿假单胞菌(CRPA)感染的临床特征及相关危险因素，为有效防控 CRPA 感染提供科学依据。

方法 收集 2020 年 1 月至 2022 年 6 月，广东省人民医院分离的 CRPA 所致感染的患者病例资料 60 例，采用 1∶2 病例-对照研究方法，随机收集由碳青霉烯类敏感铜绿假单胞菌(CSPA)所致感染患者资料 120 例作为对照，分析 CRPA 感染的临床特征、感染危险因素及患者预后。

结果 60 株 CRPA 主要来源于下呼吸道分泌物(30 株，50.0%)和中段尿标本(10 株，16.7%),集中于重症监护室(26 株，43.3%)和心血管外科(13 株，21.7%)。经单因素分析，多种因素可能会导致 CRPA 感染的发生，其中患者应用过氨基糖苷类药物(OR=0.339,95%CI:0.146～0.790,P=0.012)及应用过≥3 种抗菌药物 (OR=0.247,95%CI:0.068 ～ 0.898,P=0.034)可能是导致 CRPA 感染发生的重要危险因素。CRPA 感染的死亡率高于 CSPA 感染(P=0.003)。

结论 CRPA 所致感染严重影响患者预后，临床需采取积极措施提升对 CRPA 的防控能力，同时需加强对各类抗菌药物的管理，做好环境卫生学监测，以减少 CRPA 感染的发生与院内流行。

关键字：耐碳青霉烯类铜绿假单胞菌;临床特征;危险因素;预后;抗菌药物

ICU 与非 ICU 病区 MDRO 患者管理现状对比研究

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目的 将重症监护病房（Intensive Care Unit,ICU）和非 ICU 对多重耐药菌（Multidrug-resistant Organisms,MDRO）患者管理现状进行对比分析,为加强 ICU 病区 MDRO 管理工作,提供有效防控和干预措施改进的方向。

方法 使用问卷星自行设计问卷，对所有在院的 MDRO 患者防控措施执行情况进行调查，对比 ICU 和非 ICU 的 MDRO 种类分布、知晓率、隔离措施落实、环境的消毒与物品的专用及转出或外出检查的交接情况。

结果 共调查 88 名 MDRO 患者，其中有 34 名患者来自 ICU。ICU 中的 CRAB 比例高于非 ICU，ICU 的工作人员对 MDRO 患者的知晓率高于非 ICU，相邻病床存在易感患者的比例 ICU 高于非 ICU，97% 的 ICU 对 MDRO 患者的周围物品环境和医疗器械消毒频次 2 次以上，外出检查的 MDRO 患者多于非 ICU，交接方式主要为口头交接。

结论 对比 ICU 和非 ICU 的 MDRO 防控措施执行情况，对 ICU 采取有针对性的干预措施，提高医务人员对 MDRO 患者管理的知晓率和实践能力，加强 ICU 环境消毒和物品专用管理，改进 MDRO 患者转出或外出检查时的交接方式等，可以有效降低多重耐药菌医院感染的发生率，提高医疗质量和安全水平。

关键字：ICU；多重耐药菌；现状研究

某三级医院感染控制和抗菌药物管理对遏制细菌耐药的效果评价

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目的 在医疗领域，感染控制和抗菌药物管理是遏制细菌耐药性的关键因素。本文旨在探讨和分析某三级医院在感染控制和抗菌药物管理方面的实践，发现存在的问题，提出相应的改进措施，不断优化管控方案，遏制细菌耐药。

方法 该三级医院将抗菌药物临床应用管理和感染控制纳入医院核心管理内容，通过多元化的研究方法，包括文献检索和归纳、数据分析、临床观察，结合本院感染控制和抗菌药物管理的现状，总结出了系列管控措施，并在实践中严格执行。

结果 通过系列的管控措施，我院多重耐药菌检出率呈下降趋势。抗菌药物管理各项指标基本控制良好，但仍存在一类切口预防使用率和预防用药疗程不达标的问题，因此未来仍需要进一步加强和完善管理措施，以遏制细菌耐药性的蔓延。

结论 综上所述，该三级医院的感染控制和抗菌药物管理在遏制细菌耐药性中起到了良好的作用。为了应对日益严重的细菌耐药性问题，医护人员需要进一步加强这两个方面的工作，并采取综合性措施，不断改进和优化自身的感染控制和抗菌药物管理工作。

关键字：感染控制，抗菌药物管理，遏制细菌耐药

Risk Factors and Prognostic Model of Carbapenem-resistant Klebsiella Pneumoniae in Patients with Bloodstream Infection

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Objective Infections caused by Carbapenem-resistant Klebsiella pneumoniae (CRKP) are increasing annually, with bloodstream infection (BSI) being a significant outcome associated with CRKP, resulting in higher mortality rates. The objective of this investigation was to explore the risk factors for bloodstream infection with carbapenem-resistant Klebsiella pneumoniae and the factors linked to poor patient prognosis, and to formulate a forecast model for infection and prognosis

Methods 758 patients with Klebsiella pneumoniae (KP) bloodstream infections were collected from September 2017 to June 2022. Using SPSS.25 and R 3.6.1 software, we analysed the data to identify the independent influencing factors of CRKP-BSI in hospitalised patients. Based on the identified risk factors, we constructed a prediction model and visualised the results as a column line graph. The predictive model's discrimination was assessed using the Receiver Operating Characteristic (ROC) curve's area under the curve (AUC), while its calibration was assessed through the calibration plot

Results Nosocomial infection (OR=4.257, 95% CI 2.479-7.308), ICU admission (OR=4.070, 95% CI 2.479-6.682), shock (OR=2.733, 95% CI 1.488-5.019), APTT (OR=1.032, 95% CI 1.002-1.063), PTA (OR=0.984, 95% CI 0.973-0.996), FBG (OR=1. 301, 95% CI 1.096-1.545), carbapenems (OR=2.812, 95% CI 1.766-4.479), aminoglycosides (OR=5.536, 95% CI 2.091-14.654), and beta-lactam (OR=2.241, 95% CI 1.378-3.621) antibiotic usage had an impact on CRKP bloodstream infections. The model demonstrated an area under the ROC curve of 0.834 in the modelling group, with the calibration curve indicating favourable alignment between the model's predictions and actual observations. The model exhibited significant differentiation in the validation group, with the calibration curve reinforcing its efficacy. The model's efficacy was influenced by admission to ICU (OR=8.172, 95% CI 4.389-15.216), shock (OR=3.081, 95% CI 1.836-5.172), and haemodialysis (OR=3.788, 95% CI 1.337-10.). 738), The study developed a prognostic model for CRKP-BSI patients using blood glucose (OR=1.133, 95% CI 1.034-1.242) and PTA (OR=0.977, 95% CI 0.961-0.993). The model's ROC curve had an area of 0.869 and the calibration curve indicated satisfactory predictive accuracy. The external validation group's predictive model ROC curve had an area of 0.826. The calibration curve demonstrated that the predictive and actual value curves of the model corresponded well

Conclusion Following the outbreak of CRKP-BSI, healthcare staff must efficiently manage risk factors and recognize high-risk patients with a poor prognosis at the earliest opportunity, and implement suitable interventions to enhance patient prognosis

关键字：Carbapenem-resistant Klebsiella pneumoniae; Bloodstream infection; Risk factors; Prediction model; Prognosis.

导管冲洗用生理盐水微生物污染的监测研究

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目的 检测多家医院常用于手工配置导管冲洗液的已开封、多剂量生理盐水袋（瓶）中污染菌存在的情况，调查手工配制导管冲洗液的污染率，探究临床手工配制盐水过程中可能存在的污染因素。

方法 随机抽取西安市四家三级甲等医院 32 个临床科室，用于手工配制导管冲洗液的已开封无菌生理盐水袋（瓶）共 604 份样本，将盐水袋（瓶）的生理盐水进行过滤，将过滤膜进行培养，如发现

在过滤膜上有细菌生长，则用 MOLDI-TOF MS 质谱仪进行菌种鉴定并统计结果。

结果 来自四家医院不同科室的盐水样本中均检出微生物，收集 604 份临床盐水样本，共发现 145 例样本有污染菌生长，总体污染率为 24%。经鉴定，共发现 37 种污染菌，其中 4 种为临床常见致病菌。A、B、C、D 四家医院的污染率分别为 26.3%、25.6%、20.0%、23.0%，检出微生物种类分别为 18、29、13、14 种，四家医院均检出藤黄微球菌、人葡萄球菌。检出率前三位的微生物分别为藤黄微球菌、人葡萄球菌、气囊水栖菌。

结论 临床常用于手工配置导管冲洗液的已开封生理盐水存在很大的污染风险，可检出多种致病菌，是引起患者血流感染的潜在危险因素，污染情况在不同医院中普遍存在，消毒、手卫生不彻底，以及多剂量盐水被反复抽吸是导致盐水污染的可能因素。

关键字：盐水， 污染，微生物

Antimicrobial Resistance Changes of Multidrug-resistant Organisms Among Critically Ill Patients During The COVID-19 Pandemic: An Interrupted Time Series Analysis in A Teaching Hospital in Guangzhou, China

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Objective Multidrug-resistant organisms (MDROs) have emerged as an important cause of poor prognoses of patients in the intensive care unit (ICU). In this study, we aimed to investigate the changes in MDROs in the ICU during the COVID-19 pandemic and provide a scientific basis for antimicrobial stewardship and infection control

Methods In this study, an interrupted time series model was used to evaluate the change in MDROs in the ICU before and after the outbreak of COVID-19 in Guangzhou. The data were extracted from the antimicrobial surveillance system of a large tertiary hospital from April 2018 to September 2021. Quasi-Poisson regression was used to fit the interrupted time-series model and selected based on their AIC values

Results After the outbreak of COVID-19, the risk of resistance to carbapenems and meticillin in Klebsiella pneumoniae decreased (RR=0.890, RR=0.915, $P < 0.05$); the risk of resistance to the carbapenems and third/fourth generations cephalosporins in Pseudomonas aeruginosa decreased (RR=0.927, RR=0.888, $P < 0.05$), while the risk of resistance to the carbapenems in Escherichia coli increased (RR=2.267, $P < 0.05$)

Conclusion After the outbreak of COVID-19, the risk of multi-drug resistance in Klebsiella pneumoniae and Pseudomonas aeruginosa decreased significantly, while the resistance to the carbapenems in Escherichia coli showed an upward trend, suggesting that during the COVID-19 pandemic, continuous control and surveillance of hospital infections caused by MDROs deserved great concern, especially Escherichia coli and the rational use of carbapenems

关键字：multidrug-resistant organisms, intensive care unit, nosocomial infection, COVID-19, interrupted time series

基于 SWOT 分析的医院 MDROs 感染防控 PDCA 管理方法及效果分析

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目的 通过 SWOT 法分析常州某三甲中医院多重耐药菌感染防控管理流程，并结合 PDCA 管理模式对医院多重耐药防控措施执行情况进行干预，以提升该院多耐防控能力，为大型综合医院多重耐药菌感染防控提供可靠的依据和参考。

方法 于 2023 年 1 月至 2023 年 12 月，先通过 SWOT 分析法分析出常州市某三甲中医院多重耐药菌感染防控的劣势和威胁，然后通过 PDCA 管理模式找到对策并干预，调取数据分析干预前后多重耐药菌检出率、多重耐药菌医院感染率、医生隔离医嘱开具及时率、多耐防控措施落实率等的相关性。

结果 干预前（2022 年 1 月-2022 年 12 月）住院人数为 58000 人，总检出 MDROs 株数 431 株，总 MDROs 检出率为 35.10%，其中医院感染 46 株，MDROs 医院感染率为 0.26%，干预后（2023 年 1 月到 2023 年 12 月）住院人数为 62268 人，总检出 MDROs 株数 1249 株，总 MDROs 检出率为 33.71%，其中医院感染 421 株，MDROs 医院感染率为 0.15%，院内感染的肠杆菌科的 CRKP、CRE 以及 CRPA 在干预后均有降低；干预后隔离医嘱开具及时性、各项预防控制措施的落实率和管床医护及保洁人员知晓率均有提升。

结论 结合 SWOT 法的 PDCA 管理方法可有效提高 MDROs 预防控制措施落实的效率，强化医护及保洁等 MDROs 的防控意识，从而有效降低 MDROs 在医院感染率。

关键字：SWOT，PDCA，多重耐药菌（MDROs），医院感染防控，干预，感染率

COVID-19 大流行对抗生素抗菌药物使用和微生物分离耐药的影响——一项基于 25 家综合医院的横断面研究

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目的 本研究旨在了解山西地区 COVID-19 大流行期间住院患者抗菌药物使用、微生物分离及耐药情况，分析合并用抗菌药物对 COVID-19 患者结局指标的影响，为 COVID-19 常态化管理中抗菌药物的合理使用提供数据支持和参考。

方法 本研究由山西省药事质控中心发起，遴选 3 家省级医院，13 家地市级三级医院，9 家地市级二级医院，采取分层等比随机抽样的方法抽取出院时间在 2022 年 12 月 1 日至 2023 年 1 月 31 日期间的非手术住院病例，从中提取患者的一般人口学资料、新冠检测结果、有关共病和疾病严重程度、相关实验室检查、住院期间感染和微生物培养结果、抗菌药物和新冠治疗用药、住院天数、不良反应和费用等信息。

通过 ICD-10 诊断代码进行细菌感染诊断，采用 SPSS 软件进行结果分析。

结果 纳入 2064 名患者，其中新冠阴性（n=1053）、新冠阳性（亚组：使用抗菌药物（n=511）、未使用抗菌药物（n=190））和新冠未知组（n=310）。新冠阳性组患者年龄较高，但查尔森合并症评分低于其余两组，所有患者抗菌药物医嘱条目数、DOT 排名前三位的为第三代头孢菌素、喹诺酮类、头孢菌素复合制剂。新冠阳性组抗菌药物使用强度 84.28DDDS/100pd，抗菌药物使用时长为 811.06DOT/1000pd，使用限制使用级抗菌药物的人数明显高于其余两组。在所有患者中，共有 1176（57.0%）例患者接受了抗菌药物治疗，其中 744（63.2%）例患者有细菌感染诊断，只有 121（10.3%）例患者有微生物培养阳性结果。新冠阳性患者抗菌药物使用率 72.9%，使用抗菌药物亚组中有细菌感染诊断的 363（71.0%）例，未使用抗菌药物组有细菌感染诊断的为 19（10.0%）例。分析抗菌药物处方时间，967（82.2%）例在一入院就使用了抗菌药物，其中有 65（6.7%）例没有细菌感染。在新冠阳性使用抗菌药物组的住院天数在 11-20 天的患者显著多于其余三组，住院费用及使用药品的总费用也显著高于其余三组。在不良反应方面，在用药总数＞20 种的组别中，发生肝损伤和中性粒细胞减少症的患者要多于用药较少的组。

结论 合并新冠病毒感染以及提高了重症非 COVID-19 患者的收治率，是导致 25 家医院抗菌药物使用率增加的客观原因。新冠阳性患者抗菌药物使用率、抗菌药物使用强度、DOT/1000pd、抗菌药物的级别、费用要明显高于新冠阴性组和新冠未知组。新冠患者合并用抗菌药物并不能缩短其住院天数，且住院总费用和药品总费用要明显增加。

关键字：COVID-19，抗菌药物管理，横断面研究，合并细菌感染

基于灰色关联分析的某医院医疗组长 AUD 与 CMI 相关性探讨

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目的 探讨四川省某大型三级甲等医院医疗组长层级抗菌药物使用强度（Antibiotics Use Density，AUD）与病 例组合指数（Case Mix Index，CMI）的相关性，为实现公立医院 AUD 的精细化管理提供实证依据。

方法 运用灰色关联分 析法探讨医疗组长层级 AUD 与 CMI 的相关性，并对比分析精细化管理的实施效果。

结果 医疗组长及其所在亚专业 CMI 与 AUD 关联系数分别为 0.96 和 0.94，共 361 名医疗组长 CMI 与 AUD 的关联系数大于 0.9。精细化管理实施后，截至 2022 年 5 月，全院 AUD 降至 34.58，医疗组长 AUD 下降幅度前 5 位的灰色关联系数均小于 0.9，最低仅为 0.754。

结论 CMI 是 AUD 的重要影响因素，应重点关注高 AUD、低 CMI 的医疗组长，实现公立医院抗菌药物的医院层级、科室层级和医疗组长层 级的精细化管理。

关键字：抗菌药物使用强度，病例组合指数，灰色关联分析，医疗组长，医院

其他微生物及其感染

多粘菌素 B 吸附柱治疗成人脓毒症和感染性休克患者的疗效和安全性的系统评价与荟萃分析

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目的 多粘菌素 B 吸附柱（Polymyxin B-immobilized hemoperfusion, PMX-HP）是一种去除脓毒症患者循环内毒素的治疗策略。然而既往研究中，有报告结论为 PMX-HP 治疗对脓毒症和感染性休克患者有生存益处，也有报告结论为 PMX-HP 治疗没有生存获益。因此，我们再次进行了一项最新的荟萃分析，以确定 PMX-HP 治疗对脓毒症和感染性休克患者死亡率的影响，同时评价 PMX-HP 治疗的安全性。

方法 我们在 PubMed、EMBASE 和 Cochrane 对照试验中心注册库中检索了从开始到 2023 年 06 月 30 日的所有符合条件的对照试验。所有研究多粘菌素 B 血液灌流对脓毒症/感染性休克患者 28 天死亡率影响的临床试验均符合条件。采用 Cochrane 偏倚风险评估工具和 ROBINS-I 工具评估偏倚风险。

结果 共纳入了 30 项研究，包括 25680 名成人患者。使用 PMX-HP 可以降低脓毒症/感染性休克患者 28 天死亡率(OR 0.77, 95% CI 0.66-0.90, p = 0.0006)。亚组分析显示，在混合感染部位组和年龄＜70 岁组中，PMX-HP 治疗后 28 天死亡率显著降低。PMX-HP 还可以降低内毒素水平(MD -1.22, 95% CI -1.62 - 0.81, p <0.00001)，改善 SOFA 评分(MD -2.11, 95% CI -3.80- 0.43, p =0.01)。PMX-HP 组和标准治疗组之间的严重不良事件没有显着差异（(p=0.05)。

结论 本研究表明，使用 PMX-HP 治疗可降低脓毒症和感染性休克患者的 28 天死亡率。使用 PMX-HP 治疗脓毒症患者可以降低 28 天死亡率并且是安全的，治疗效果可能是因为 PMX-HP 可以降低内毒素水平和改善血流动力学。不过仍然需要更多高质量的随机对照试验研究来进一步评估 PMX-HP 对脓毒症或感染性休克的临床作用。

关键字：多粘菌素 B 吸附柱, 脓毒症, 感染性休克, 系统评价，荟萃分析

Burkholderia Thailandensis Isolated From Infected Wound, Southwest China, 2022

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Objective A 61-year-old male farmer, who had untreated type 2 diabetes mellitus, reported a one-month history of pain and swelling in his left knee. He had injured the middle toe of his left foot with a plow a month earlier, which later developed redness, swelling, and pain below the left knee joint. Despite a week of antibiotic treatment at a local community health centre, his symptoms did not improve. In December 2022, the patient began to experience weakness in his left and right upper limbs, and he later fell, sustaining an injury to his left lower limb. During this period, he experienced lower limb weakness and exhibited symptoms related to the central nervous system. Initially, he was admitted to the Orthopedic Department of Dazhu County People's Hospital for treatment of a "left lower-limb injury", and a "left-foot diabetic foot infection". However, due to the worsening of his central nervous system symptoms, he was later transferred to the neurology department where he was diagnosed with osteomyelitis and a demyelinating disease. In this study, we report another clinical isolate of B. thailandensis 2022DZh, obtained from a patient with an infected wound resulting from a cut inflicted by a farm tool in a field in Dazhu, Sichuan, Southwest China, in 2022

Methods We extracted DNA from the isolate 2022DZh for confirmation and further characterization, and 16S rRNA gene sequencing of 2022DZh using nucleotide BLAST (https://blast.ncbi.nlm.nih.gov/Blast.cgi) was performed, revealing 100% similarity with B. thailandensis BPM. For the single-copy gene phylogenetic tree analysis, we compared the genome of B. thailandensis 2022DZh with a reference panel of publicly available Burkholderia species genomes. For the average nucleotide identity (ANI) Heatmap analysis, we compared the genome of B. thailandensis 2022DZh and 9 other isolates from various Burkholderia species. Based on our phenotypic and molecular data, isolate 2022DZh was conclusively identified as B. thailandensis

Results Strain 2022DZh was obtained from a deep tissue specimen during surgical debridement of the infected wound on the left foot (Figure 1). The single-copy gene phylogenetic tree analysis indicated that B. thailandensis 2022DZh clusters with B. thailandensis BPM (Figure 2A). The results of average nucleotide identity (ANI) revealed that B. thailandensis 2022DZh also clusters with B. thailandensis BPM, with a genome identity of 99.85%. However, when compared to B. pseudomallei BPC006, the genome identity was only 92.31% (Figure 2B), consistent with the commonly used 95% threshold for distinguishing species. Through multilocus sequence type analysis (available at https://pubmlst.org/organisms/burkholderia-pseudomallei), it was determined that B. thailandensis

2022DZh and B. thailandensis BPM are all both belong to sequence type (ST) 76. Genomic analysis indicates that this isolate clusters with B. thailandensis BPM, a human isolate from Chongqing

Conclusion In conclusion, our findings underscore B. thailandensis can cause serious infections, and clinical practitioners should increase their awareness of this type of infection. Therefore, we strongly recommend enhancing monitoring and surveillance for B. thailandensis infection in both humans and livestock

关键字：Burkholderia thailandensis；infected wound；the single-copy gene phylogenetic tree analysis；average nucleotide identity (ANI) analysis

Comprehensive Analysis of Myeloid Nuclear Differentiation Antigen in Urinary Tract Infection and Urosepsis

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Objective Urinary tract infections (UTIs) are characterized by a broad clinical phenotype ranging from uncomplicated cystitis to septic shock. Upper urinary tract obstructions are critical contributors to the onset of urosepsis, and UTIs also significantly contribute to its progression . Research has shown that around 12% of patients diagnosed with hospital-acquired UTIs ultimately developed urosepsis. Another prospective study discovered that among patients with UTIscan lead to fever in approximately half of patients, with approximately 30% of these progressing to UTIs-induced sepsis and 2% to severe sepsis. According to the third iteration of the International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) in 2016, sepsis is redefined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, affecting millions of people each year with a mortality rate that can reach up to 40%. Moreover, there is growing recognition that sepsis survivors often experience long-term physical, psychological, and cognitive impairments with significant health care and social implications. Urosepsis, often overlooked by inexperienced clinicians, constitutes approximately 9-31% of all sepsis cases, following sepsis induced by lung and abdominal infections. It is important to note that urosepsis has an insidious onset and rapid progression, with a UTIs patient's condition potentially deteriorating from a seemingly harmless state to severe sepsis in a very short time if not promptly diagnosed and effectively treated. Therefore, early recognize the urosepsis and determine its severity are of great significance in improving the prognosis of urosepsis patients

Methods TMT Sequencing in UTI Rat Bladders: The study employed Tandem Mass Tag (TMT) sequencing to analyze UTI rat bladders

Machine Learning Algorithms: Two machine learning algorithms were utilized to evaluate the diagnostic efficacy of MNDA in UTIs and its correlation with disease severity.

Urosepsis Rat Model: A novel rat model of urosepsis was developed to assess MNDA expression at different stages and severity levels of urosepsis, as well as its correlation with disease severity.

Human Serum Sample Analysis: Serum samples from patients across multiple centers were collected to evaluate MNDA expression in various infectious diseases.

Single-Cell Sequencing and Immunofluorescence: Peripheral blood single-cell sequencing in humans and multicolor immunofluorescence techniques were used to reveal the early diagnostic capability of MNDA and its specific mechanisms.

Results MNDA Upregulation in UTIs: Significant upregulation of MNDA was observed in UTIs, showing a correlation with the severity of the infection

Validation of Urosepsis Rat Model: The modified urosepsis rat model proved robust across three different batches and was not affected by surgical procedures.

MNDA Expression in Urosepsis Progression: Rapid elevation of MNDA expression was noted within an hour of urosepsis progression, correlating with factors like bacterial load, sepsis markers, and the extent of organ damage (assessed by H&E staining and PET/CT imaging).

Elevated MNDA Levels in Human Patients: Patients from Chinese hospitals with UTIs, urosepsis, and non-urinary sourced sepsis exhibited higher MNDA levels compared to healthy controls.

MNDA Expression in Urosepsis and Sepsis Patients in the U.S.: Significant early increase in MNDA expression was found in monocytes of urosepsis and sepsis patients in the United States. A notable rise in MNDA expression was also observed during the transition of dendritic cells as urosepsis progressed.

Conclusion The research underscores the significant upregulation of MNDA in UTIs and urosepsis, endorsing its potential as an early diagnostic marker and a therapeutic target. These findings provide critical insights into the mechanisms of urosepsis and pave the way for novel diagnostic and therapeutic approaches in managing this severe infection

关键字：Dendritic cell, Early diagnosis, MNDA, Urinary tract infection, Urosepsis.

非 HIV 感染人群 PCP 危险因素分析及预测模型构建

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目的 随着抗逆转录病毒疗法在 HIV 感染者中的广泛应用，HIV 患肺孢子菌肺炎(PCP)的风险明显降低，而非 HIV 人群 PCP 的发生数量却逐年上升，且病情进展更快，病死率更高，早期识别非 HIV 人群中的 PCP 是临床急需。本研究采用病例对照研究，筛选出 PCP 的独立危险因素，构建预测模型和可视化的风险预测工具，以期在临床中早期识别 PCP。

方法 此研究为前瞻性多中心研究，根据相应的纳入及排除标准，在 2018 年 9 月至 2021 年 1 月国内 9 家医院筛选病例，根据 PCP 诊断标准分为 PCP 组与非 PCP 组，以单因素回归分析比较 PCP 组与非 PCP 组之间的人口学、临床特征、实验室检查及影像学表现等信息的差异是否存在相关性，再运用 R 软件采用多因素 logistic 回归分析独立危险因素，建立预测模型方程并绘制列线图，构建诊断预测模型并进行验证。

结果 共纳入 191 例病例，其中 PCP 组 27 例，非 PCP 组 164 例。单因素分析两组在年龄、心率、吸氧浓度、PCO2、LDH、APTT、呼吸困难、使用类固醇激素超过 4 周、过去 90 天应用免疫抑制剂、吸氧、COPD 中度以上、脏器骨髓移植、结缔组织病、慢性肾衰竭需透析治疗、结节影、渗出影、入院时场所、住院场所、机械通气、死亡的差异具有统计学意义。多因素回归分析显示与 PCP 的独立危险因素包括：LDH 水平($p < 0.05$，OR:1.005，95%CI:1.002-1.008)，CT 表现为渗出影($p < 0.05$，OR:56.035，95%CI: 5.001-1940.865)，行机械通气($p < 0.05$，OR:13.101，95%CI: 1.901-117.711)。建立 logistic 回归模型，其方程式为 log(p) = 0.004718 * LDH + 4.025968 *渗出影有无 + 2.572701 *是否机械通气。根据多因素回归结果构建了可预测 PCP 感染发生风险的可视化列线图模型（图 1）。该列线图模型 ROC 曲线下面积(AUC)=0.9695（图 2），用内部数据对该预测模型进行验证，绘制混淆矩阵，该模型的特异度 70.4%，灵敏度 98.2%，阳性预测值 95.3%，阴性预测值 13.6%，总正确率 94.2%，预测风险接近于实际风险。

结论 血清 LDH 水平、影像渗出影、机械通气是非 HIV 人群 PCP 的独立危险因素，此研究构建的可视化诊断预测列线图能较好的预测 PCP 发病风险，且所纳入变量简单易获取，具有良好的操作性，有较好的临床应用前景。但仍需进一步以多中心、大样本外部数据对该预测模型进行验证。

关键字：肺孢子菌肺炎；危险因素；非 HIV 人群；诊断预测模型

NagZ Modulates The Virulence of E. Cloacae by Acting Through The Gene of Unknown Function, ECL_03795

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Objective β-N-acetylglucosaminidase (NagZ) plays a critical role in peptidoglycan recycling. In our previous study, we demonstrated that NagZ knockout significantly abolished AmpC-dependent β–lactam resistance in Enterobacter cloacae (E. cloacae). However, it remains unclear whether NagZ also influences the virulence of E. cloacae

Methods We utilized wild-type E. cloacae clinical isolates, nagZ knockout strains, and NagZ complementation strains to establish infection models in RAW264.7 cells, Galleria mellonella larvae, and mice. Mortality rates, inflammation markers, and histopathological examinations were employed to assess the virulence of these strains

Results Our study, incorporating data on mouse and Galleria mellonella larval mortality rates, inflammation markers, and histopathological examinations, revealed a substantial reduction in the virulence of E. cloacae following NagZ knockout. Transcriptome sequencing uncovered differential gene expression between NagZ knockout and wild-type strains, particularly in nucleotide metabolism pathways. Further investigation demonstrated that NagZ deletion led to a significant increase in cyclic diguanosine monophosphate (c-di-GMP) levels. Additionally, transcriptome sequencing and RT-qPCR confirmed significant differences in the expression of ECL_03795, a gene with an unknown function but speculated to be involved in c-di-GMP metabolism due to its EAL domain known for phosphodiesterase activity. Interestingly, in ECL_03795 knockout strains, a notable reduction in the virulence was observed, and virulence was rescued upon complementation with ECL_03795

Conclusion Our study suggests that NagZ's function on virulence is partially mediated through the ECL_03795→c-di-GMP pathway, providing insight into the development of novel therapies and strongly supporting the interest in creating highly efficient NagZ inhibitors

关键字： E. cloacae, NagZ, virulence; ECL_03795, c-di-GMP.

敲低 lincRNA-COX2 抑制单核细胞增生李斯特菌感染相关的巨噬细胞的凋亡和 M1 型极

化

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目的 探讨长链基因间非编码 RNA 环加氧酶 2(lincRNA-COX2)在单核细胞增生李斯特菌(Lm)感染所致 RAW264.7 细胞凋亡和细胞极化中的作用.

方法 体外培养 RAW264.7 细胞,分为未感染对照组、Lm 感染组、小干扰 RNA 阴性对照(si-NC)组、si-NC 联合 Lm 组、lincRNA-COX2 小干扰 RNA(si-lincRNA-COX2)组、si-lincRNA-COX2 联合 Lm 组.Lm 感染复数(MOI)=10 感染 RAW264.7 细胞,细菌感染 6 h 后收集细胞,倒置荧光显微镜和实时定量 PCR 检测 siRNA 转染抑制效率,Western blot 法检测细胞中裂解型胱天蛋白酶 3(c-caspase-3)、caspase-3、B 细胞淋巴瘤因子 2(Bcl2)、Bcl2 相关 X 蛋白(BAX)、精氨酸酶 1(Arg1)和诱导型一氧化氮合酶(iNOS)蛋白水平.

结果 Lm 感染 RAW264.7 细胞后,c-caspase-3/caspase-3、BAX/Bcl2 比值、iNOS 蛋白水平较对照组显著上调,而 Arg1 水平较对照组下调.敲低 lincRNA-COX2 可抑制 Lm 感染引起的 RAW264.7 细胞中 BAX/Bcl2、c-caspase-3/caspase-3 及 iNOS 蛋白的升高,上调 Lm 感染后 RAW264.7 细胞中的 Arg1 蛋白.

结论 敲低 lincRNA-COX2 抑制 Lm 感染引起的 RAW264.7 细胞凋亡并抑制其向 M1 型极化.

关键字：单核细胞增生李斯特菌；RAW264.7 细胞；长链基因间非编码 RNA 环加氧酶 2(lincRNA-COX2)；细胞凋亡；细胞极化

广州地区 259 例丙型肝炎病毒患者 HCV 基因分型研究

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目的 了解广州地区丙型肝炎病毒患者的 HCV 基因型分布情况，为该地区丙型肝炎病毒的预防和诊疗提供依据。

方法 选择自 2019 年 9 月至 2023 年 4 月共 259 例丙型肝炎病毒患者的 HCV 基因分型的结果，分析比较不同年龄、性别和年度各基因型感染率的差异。

结果 共纳入 259 例患者，最常见的基因型为 6a 型和 1b 型，占 42.47%和 42.08%，与其它亚型差异有统计学意义（P＜0.05）。其余依次为 3a 型占 6.18%，2a 型占 4.63%，3b 型占 4.25%，2b 型占 0.39%，未发现亚型混合感染。1b 型，青年人群（41.86%）、中年人群（31.447%）分别低于老年人群的 71.93%；6a 型，青年人群（44.186%）、中年人群（51.572%）分别高于老年人群的 15.789%，有统计学差异（P＜0.05）。女性 1b 型 63.077%、2a 型 10.769%分别高于男性的 35.052%和 2.577%，女性 6a 型 18.462%低于男性的 50.516%，有统计学差异（P＜0.05）。不同年度各基因型感染率无统计学差异。

结论 广州地区丙型肝炎病毒患者 HCV 基因分型以 6a 型、1b 型为主。1b 型多见于 60 岁以上的老年人群和女性，6a 型多见于中青年人群及男性。

关键字：HCV，基因分型，RT-PCR，广州

2020-2022 年广州地区 2182 例儿童 7 种呼吸道病原体流行态势分析

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目的 对 2020-2022 年广州地区 2182 例儿童 7 种呼吸道病原体流行态势进行分析并探讨原因。

方法 选择自 2020 年 1 月 1 日至 2022 年 11 月 30 日共 2182 例儿童患者的呼吸道病原体检查结果，即甲型流感病毒（FluA）、乙型流感病毒（FluB）、呼吸道合胞病毒（RSV）、人副流感病毒（PIV）、腺病毒（AdV）、肺炎支原体（MP）和肺炎衣原体（Cpn），分析不同年度、年龄、性别、季节间各病原体阳性构成比和检出率的差异。

结果 RSV 在 2020-2022 年、各个年龄段、男童/女童、春季/夏季/秋季中成为阳性病原体构成比排名第一的优势毒株，2022 年和 FluA 并列第一，冬季则被 PIV 所取代。RSV 检出率（5.42%）高于 PIV（1.86%）、FluA（0.93%）、AdV（0.44%）、MP（0.36%）、FluB（0.19%）和 Cpn（0.05%），差异具有统计学意义。2022 年度 FluA 检出率（3.27%）与 2021 年（0%）、2020 年（0.75%）比较均具有统计学差异。2021 年度 PIV 检出率（3.31%）与 2020 年（0.98%）比较具有统计学差异。0-28d 新生儿 RSV 检出率（0.90%）与 1-12m 婴儿（8.50%）和 1-3y 幼儿（7.25%）比较差异有统计学意义。1-12m 婴儿 RSV 检出率（8.50%）和>6y 儿童（2.94%）比较差异有统计学意义。0-28d 新生儿 PIV 检出率（0%）与 1-12m 婴儿（3%）和 1-3y 幼儿（2.59%）比较差异有统计学意义。女性 PIV 检出率 2.93%高于男性的 1.05%，差异有统计学意义。FluA、RSV 和 PIV 检出率有季节差异。FluA 夏季检出率（2.54%）与春季、秋季比较差异有统计学意义，春秋两季均为 0%。RSV 检出率春秋、夏秋、夏冬与秋冬季节比较差异有统计学意义，秋季最高为 10.38%，夏季次之为 5.49%，春

季和冬季较低，分别为 2.52%和 1.96%。PIV 检出率秋季（0.72%）与冬季（3.92%）比较差异有统计学意义。单一病原体感染为主，RSV 检出率最高占 4.85%。

结论 2020-2022 年广州地区儿童 7 种呼吸道病原体感染以 RSV 较为普遍，Cpn 少见，优势毒株以 RSV 为主。FluA 和 PIV 检出率存在年度差异。RSV 在 1-12m 婴儿中检出率最高，PIV 在 0-28d 新生儿中检出率最低。女性 PIV 检出率高于男性。FluA、RSV 和 PIV 检出率存在季节差异，FluA 检出率夏季最高，RSV 检出率秋季最高，PIV 检出率冬季最高。感染模式以单种病原体感染多见。

关键字：广州，儿童，呼吸道病原体，季节，感染模式。

Clinical Characteristics of Patients with Pulmonary NTM in Fuyang, China: A Retrospective Study

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Infections caused by nontuberculous mycobacteria (NTM) are increasing worldwide, and they are very difficult to treat because they are inherently resistant to many common antibiotics. Notably, the distribution of NTM pathogenic bacteria is geographically specific.We retrospectively reviewed consecutive cases of NTM pulmonary disease reported from a designated hospital for infectious diseases in Fuyang district of China to determine the clinical characteristics of 234 patients with NTM pulmonary disease were included in this study between March 2018 to May 2023. Seventy-three (31.20%) patients had a history of previous tuberculosis or tuberculosis exposure and bronchiectasis. A total of 217 patients were tested for C-reactive protein, most of whom had levels above the normal range. A total of 132 strains (49.62%) were Mycobacterium intracellulare. Women were susceptible to bronchiectasis. Female cases were dominated by Mycobacterium avium, and male cases were dominated by Mycobacterium abscessus. Mycobacterium avium (34.21%) and Mycobacterium abscessus (33.33%) were most common in people with previous tuberculosis or tuberculosis exposure history. Among respiratory tract-related diseases, patients with bronchiectasis had the highest isolation rate of Mycobacterium avium (55.36%). The PNI of patients with a history of tuberculosis or tuberculosis exposure was lower than that of patients without a history of tuberculosis (P value=0.021).Clinical symptoms of the disease were not species specific. Previous tuberculosis or tuberculosis exposure history immensely enhanced the risk of NTM disease.

关键字：NTM, clinical symptoms, tuberculosis exposure history, bronchiectasis

Transverse Comparison of Clinical Characteristics and Prognostic Factors in HIV Infected Patients with Cytomegalovirus Encephalitis in Guangdong, China

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Background Cytomegalovirus encephalitis (CME) is one of the serious opportunistic complications in human immunodeficiency virus (HIV) infected patients, characterized by a rapid onset, poor prognosis and high mortality. Until now, there have been limited comprehensive research on the clinical and prognostic characteristics of HIV/CME patients reported in China

Methods We conducted a retrospective enrollment of 43 patients diagnosed with CME among individuals infected with HIV from 2015 to 2023 in Guangzhou eighth people’s hospital. Among them, 27 patients experienced favorable prognosis and 16 patients experienced unfavorable prognosis (which includes death, ineffectiveness of treatment, or aggravated condition) as determined by clinical diagnosis. Statistics of clinical symptoms and laboratory examinations between two groups were analyzed. Multivariate analysis and nomogram were developed using statistical variables

Results HIV/CME patients with unfavorable prognosis represented more consciousness disorder and nuchal rigidity than those with favorable prognosis. There were no identifiable differences between the two groups in terms of clinical characteristics such as hemiparalysis, meningeal irritation, cerebrospinal fluid (CSF) pressure, and other relevant factors. In the CSF, the level of chloride (Cl) was obviously higher in HIV/CME patients with favorable prognosis, while the Cytomegalovirus (CMV)-DNA showed the opposite trend. A multivariate analysis of fever, nuchal rigidity, consciousness disorder, and CSF CMV-DNA can be used to predict prognosis in HIV/CME patients, with C-index of 0.83 (95% CI: 0.64-1.00). The log CSF CMV-DNA copies/mL emerged as an independent risk factor for prognosis. High CSF CMV-DNA (≥ 300,000 copies/mL) indicated unfavorable prognosis

Conclusion HIV/CME patients with unfavorable prognosis usually showed obvious signs and symptoms of central nervous system infection, lower CSF Cl level, and higher CSF CMV-DNA compared to favorable prognosis patients. Recognizing these indicators early and administering timely antivirus therapy before the disease progresses to CME are of great value in improving the survival rate of patients

关 键 字：HIV, Cytomegalovirus, Encephalitis, Prognosis, CSF CMV-DNA

新型肠炎沙门氏菌菌影候选疫苗在小鼠免疫应答和保护功效的评估

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目的 比较肠炎沙门氏菌制备的菌影（SE-ghost）通过肌肉注射（im）和口服（oral）不同免疫途径接种雌性 BALB / c 小鼠产生体液和细胞免疫应答的功效。

方法 用 SE-ghost 接种 BALB/c 小鼠，间接 ELISA 检测小鼠血清中 IgG 抗体水平和阴道灌洗液 IgA 抗体水平；流式检测小鼠脾脏 CD3+CD4+T、CD3+ CD8+T 细胞百分比变化和脾脏内细胞因子 IL-4、IFN-γ 分泌；三免后所有小鼠口服强毒攻击半数致死量肠炎沙门氏菌。用 SE-ghost 刺激 BMDCs ，流式细胞仪检测表面分子抗体 APC-CD11c、 FITC-MHC Class II、 PE-CD40、 FITC- CD86、PE-CD80 表达量；双抗体夹心 ELISA 测定 BMDCs 上清液 IL-1β、IL-6、IL-10 和 IL-12 P70 的产量。

结果 与 PBS 组相比，SE-ghost（oral）和 SE-ghost（im）免疫组小鼠体内肠炎沙门氏菌特异性抗体 IgG 和 IgA 水平明显增高；脾脏 CD3+CD4+T 细胞百分比上调、高分泌细胞因子 IL-4 、IFN-γ；致病菌肠炎沙门氏菌强毒攻击后，SE-ghost（oral）和 SE-ghost（im）免疫组生存率高达 80%。与对照组相比，SE-ghost 刺激 BMDC 后高表达表面成熟分子抗体 CD86、CD80、CD40、MHC-II；高分泌细胞因子 IL-1β、IL-6、IL-10、IL-12P70。

结论 通过肌肉注射 SE-ghost 进行免疫，可在小鼠中引发更强大的抗原特异性免疫反应，以防止沙门氏菌感染。SE-ghost 是一种有用的沙门氏菌候选疫苗。

关键字：肠炎沙门氏菌；细菌菌影；灭活疫苗；免疫应答；保护功效

Efficacy, Safety, and Cost-effectiveness Analysis of Antiviral Agents for Cytomegalovirus Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplantation Recipients

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Background Cytomegalovirus (CMV) infection is associated with higher non-relapse mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). But the preferred drug for preventing cytomegalovirus infection is still controversial. We evaluate the efficacy, safety, and cost-effectiveness of antiviral agents based on the most recent studies

Methods A pairwise and network meta-analysis was conducted to obtain direct and indirect evidence of antivirals. The cost of allo-HSCT recipients in a teaching hospital was collected, and a cost-effectiveness analysis using a decision tree combined with Markov model was completed from the perspective of allo-HSCT recipients over a lifetime horizon

Results A total of 19 RCTs involving 3565 patients (8 antivirals) were included. In the network meta-analysis, relative to placebo, letermovir, valacyclovir, and ganciclovir significantly reduced CMV infection incidence; ganciclovir significantly reduced CMV disease incidence; ganciclovir significantly increased the incidence of serious adverse event; none of antivirals significantly reduced all-cause mortality. Based on meta-analysis and Chinese medical data, the incremental cost-effectiveness ratios (ICER) per quality-adjusted life year (QALY) saved for maribavir, acyclovir, valacyclovir, ganciclovir, and letermovir relative to placebo corresponded to US$216 635.70, US$11 590.20, US$11 816.40, US$13 049.90, and US$12 189.40, respectively. One-way sensitivity analysis showed the most influential parameter was discount rate. The probabilistic sensitivity analysis indicated a 53.0% probability of letermovir producing an ICER below the willingness-to-pay threshold of US$38 824.23/QALY. The scenario analysis demonstrated prophylaxis with letermovir is considered cost-effective in the United States

Conclusion Currently, letermovir is an effective and well-tolerated treatment for preventing CMV infection, and it might be a cost-effective choice in allo-HSCT recipients in China

关键字：allogeneic hematopoietic stem cell transplantation, antiviral agent, cytomegalovirus, prophylaxis, cost-effectiveness analysis

Viral Shedding Pattern of Severe Fever with Thrombocytopenia Syndrome Virus in Severely Ill Patients: A Prospective, Multicenter Study

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Background Severe fever with thrombocytopenia syndrome (SFTS) is spreading rapidly in Asia. The

pathway of SFTS virus shedding from patient and specific use of personal protective equipments (PPEs) against viral transmission have rarely been reported

Methods A multicenter cohort study was performed to determine SFTS virus (SFTSV) level from blood, throat swabs, fecal/ anal swabs, urine and bedside environment swabs of SFTS patients by qRT-PCR in three sentinel hospitals for SFTS in Anhui province from April 2020 to October 2022. Specific PPEs were applied in healthcare workers contacting with the patients who had oropharyngeal virus shedding and hemorrhagic signs

Results A total of 189 SFTSV-confirmed patients were included in the study, 54 patients died (case fatality rate, 28.57%). Positive SFTSV in throat swabs (T-SFTSV), fecal /anal swabs (F-SFTSV) and urine (U-SFTSV) were detected in 121 (64.02%), 91 (48.15%) and 65 (34.4%) severely ill patients, respectively. The levels of T-SFTSV, F-SFTSV and U-SFTSV were positively correlated with the load of SFTSV in blood. We firstly revealed that SFTSV positive rate of throat swabs were correlated with occurrence of pneumonia and case fatality rate of patients (P< 0.0001). Specific precaution measures were applied by healthcare workers in participating cardiopulmonary resuscitation and orotracheal intubation for severely ill patients with positive T-SFTSV, no event of SFTSV human-to-human transmission occurred after application of effective PPEs

Conclusions Our research demonstrated SFTSV could shed out from blood, oropharynx, feces and urine in severely ill patients. The excretion of SFTSV from these parts was positively correlated with viral load in the blood. Effective prevention measures against SFTSV human-to-human transmission are needed

关键字：Severe fever with thrombocytopenia syndrome virus, Dabie bandavirus, Shedding, Precaution measures, Multicenter study, Human-to-human

发热伴血小板减少综合征病例血细胞胞内病毒含量的检测方法研究

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目的 拟构建发热伴血小板减少综合征（severe fever with thrombocytopenia syndrome，SFTS）病例外周血各群白细胞中发热伴血小板减少综合征病毒（severe fever with thrombocytopenia syndrome virus，SFTSV）感染率的流式细胞检测方法，为临床评估病例预后，靶细胞和相关机制研究提供新工具。

方法 建立检测非洲绿猴肾细胞系（VERO-E6）和人单核白血病细胞系（THP-1）细胞 SFTSV 感染率的流式方法，并与定量逆转录 PCR（qRT-PCR）方法比较验证。应用流式细胞术检测 SFTS 病例外周血各亚群白细胞胞内 SFTSV 含量，并与单细胞测序比较验证，流式细胞检测结果与病例相关临床数据进行独立样本 T 检验。

结果 qRT-PCR 和流式细胞检测结果一致。经斯皮尔曼相关分析，SFTSV 胞内病毒流式检测和 qRT-PCR 检测结果有显著的相关性（rs=0.9240，P ＜ 0.01）。qRT-PCR 结果显示，感染后 3d 内 VERO-E6 细胞内 SFTSV mRNA 每天平均相对表达量 24h、48h 和 72h 分别为：493±30，2718±170，5377±595，而 THP-1 为 1.00±0.10，1.07±0.25，1.81±0.18SFTSV。感染后 3d 内 VERO-E6 内病毒含量显著梯度升高，24h、48h 和 72h 的平均阳性率为（38.0±3.6）%，（63.7±7.5）%,（97.6±0.6）%。而 THP-1 内病毒含量变化不明显，流式细胞胞内染色检测 SFTSV 感染 THP-1 均小于 1%。流式细胞技术在部分 SFTS 病例的 B 淋巴细胞检测出 SFTSV 阳性，与单细胞测序结果一致。

结论 流式细胞检测胞内 SFTSV，相对于 qRT-PCR 更适用于混合细胞样本，相对于单细胞测序周期短、成本低、实用性强；SFTSV 感染 B 淋巴与血清病毒高拷贝数相关，提示预后不良。

关键字：发热伴血小板减少综合征病毒，发热伴血小板减少综合征，流式细胞术

尿路感染相关指标对尿路合并血流感染的预测作用

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目的 评估尿路感染合并血流感染的相关因素对指导临床决策具有重要的意义。通过尿培养和血培养结果监测尿路感染合并血流感染病原菌及耐药情况来预测尿路感染合并血流感染的发生以指导临床用药。

方法 本研究对 2018 年-2023 年间泉州市第一医院尿培养菌落计数阳性的患者尿培养和血培养的结果进行回顾性分析。

结果 根据我们的研究结果，在 449 例 UTI-BSI（33.5%）中，中老年男性发热、休克、口肌痛、尿路刺激、或合并糖尿病、恶性肿瘤、脑梗死、低蛋白血症、肾输尿管成像（结石、积液、脓肿、囊肿）更容易合并 BSI，合并 BSI 白细胞（WBC）、中性粒细胞（NEU）、c 反应蛋白（CRP）、降钙素原（PCT）升高更明显，预后更差。372 例患者(82.9%)血培养结果与尿培养一致，大肠埃希菌有 238 株(64.0%)对

头孢唑林、头孢他啶、头孢噻肟、头孢吡肟、头孢呋辛、氨苄西林、哌拉西林和氨曲南的耐药率高于单纯 UTI，而对环丙沙星的耐药率较低。因此，本研究有助于寻找更有效的生物指标来评估风险 BSI 并指导临床经验性用药。

结论 1）在尿路感染患者中，临床表现为发热、休克、有尿路刺激症状、腰痛，患有糖尿病、恶性肿瘤、脑梗死、低蛋白血症的患者应警惕其发生血流感染的可能。建议此类患者在送中段尿进行尿培养时，抽取静脉血进行血培养。（2）当尿路感染的患者当血常规出现 WBC、N、NLR、CRP、PCT 水平显著升高时，特别是 CRP 大于 48.305mg/L，PCT 大于 0.335ng/mL 时应高度关注其已经合并血流感染的可能。（3）分离菌株结果一致的 UTI-BSI 最主要的致病菌为大肠埃希菌，其次是肺炎克雷伯氏菌。（4）患者尿路感染合并血流感染并有上述特征，当血培养药敏结果未出而尿培养药敏结果已出可以使用尿培养药敏结果预测血培养药敏结果的易感性，可以根据尿培养结果由经验性治疗转为精确治疗，更好更快的指导临床合理利用抗生素治疗。(5) 当发现 UTI-BSI 致病菌为大肠埃希菌时，临床应谨慎考虑尽量减少使用环丙沙星以及三代头孢类抗菌药物经验性治疗 UTI-BSI 患者。

关键字：尿路感染，血流感染，预测作用

1 例由 COVID-19 感染引发的急性生殖器溃疡的罕见病例报告

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目的 急性生殖器溃疡（AGU）已被证实与各种病原体有关，如埃波斯坦-巴尔病毒（EBV）和巨细胞病毒（CMV）等。然而，与 2019 年新型冠状病毒疾病（COVID-19）相关的 AGU 病例非常罕见。本案例通过报告一例 37 岁女性因 COVID-19 感染引起的 AGU，来探讨 AGU 和 COVID-19 之间的潜在联系。

方法 对一名 37 岁的女性病人进行病例分析。该病人因 5 天的持续发热与疼痛性生殖器溃疡来我院就诊。一月前，她经历了一次未经治疗自我恢复的 COVID-19 感染历史。体格检查结果显示，小阴唇上存在多个不对称的溃疡，溃疡底部坏死，上面覆盖白色渗出物。

结果 实验室检查排除了其他可能触发 AGU 的常见因素，如单纯疱疹病毒、梅毒、EB 病毒、人类免疫缺陷病毒和巨细胞病毒，所有血清学试验结果均为阴性。此外，该患者并无高风险的性行为，也无个人或家族自身免疫疾病或炎症性肠病的病史。最终诊断为由 COVID-19 引发的 AGU。使用糖皮质激素治疗后，病人在 24 小时内体温恢复正常，经过 14 天的治疗，阴部水肿及溃疡症状得到了显著的改善。

结论 该病例报告了一例由 COVID-19 感染引发的 AGU，突显了 COVID-19 感染与 AGU 之间可能存在的关联。鉴于全球 COVID-19 疫情尚未结束，临床医生对疑似 COVID-19 感染引发的生殖器溃疡症状应保持高度警觉，这可能有助于避免病人延误治疗，并避免不必要的干预。诊断后，及时给予类固醇治疗可能是一种有效的治疗方法，能有效缓解病人症状和改善病程。

关键字：COVID-19，SARS-CoV-2，急性生殖器溃疡，发热

Bloodstream Infections by Nontuberculous Mycobacteria and Antimicrobial Susceptibility of The Isolates in Quanzhou, China

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Objective This study aimed to investigate the clinical characteristics of patients treated for Nontuberculous mycobacteria (NTM) bacteremia. The etiology and drug resistance characteristics of NTM were analyzed to provide reference for clinical diagnosis and treatment

Material and Methods The study retrospectively analyzed the Clinical data of patients with NTM bloodstream infection in Quanzhou, China during January 2020 and March 2023. Isolates were identified to species level by rpoB and Hsp65 sequencing. The drug sensitivity testing of the successfully resuscitated strains were carried out by the minimum inhibitory concentration (MIC) method.

Results Among 14 patients with bacteremia due to NTM, 92.9% patients were considered infection, the majority (n=11) had immunocompromised diseases, including human immunodeficiency virus (HIV) infected and hematologic tumors. Of the 14 isolates, 3 were Mycobacterium intracellulare，2 were Mycobacterium colombiense，2 were Mycobacterium avium，2 were Mycobacterium abscessus. The Others, such as Mycobacterium paraintracellulare, Mycobacterium sherrisii, Mycobacterium simiae, Mycobacterium chelonae and Mycobacterium canariasense were one, respectively. With the Anti-NTM therapy, clinical symptoms improved in most patients. In HIV-infected patients, all isolates were

slow-growing mycobacteria (SGM), which were susceptible to clarithromycin and rifabutin besides the Mycobacterium simiae. Other antibiotics showed different resistance in different strains. Rapid-growing mycobacteria (RGM) were mainly found in HIV-negative patients and sensitive to most antibiotics

Conclusions We described the prevalence and clinical characteristics of NTM bloodstream infections in this region, which provides meaningful reference value for clinical treatment. Due to the richness of the detection strains, rapid identification of strains and susceptibility testing are very necessary

关键字：Nontuberculous mycobacteria (NTM); bloodstream infection (BSI); antimicrobial susceptibility; Mcobacterium intracellulare; Mycobacterium sherrisii; Mycobacterium simiae

Alteration of The Airway Microbiota Is Associated with The Progression of Post-COVID-19 Chronic Cough in Adults: A Prospective Study

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Objective Cough is one of the most common symptoms observed in patients presenting with COVID-19, persisting for an extended duration following SARS-CoV-2 infection. We hypothesized that dynamic alterations in the airway microbiota could lead to the progression of post-COVID-19 chronic cough

Methods We prospectively recruited 57 patients experiencing persistent cough after infection during the Omicron wave of SARS-CoV-2 in China following the abandonment of the Zero-COVID-19 policy. Detailed clinical data was obtained, and airway microbiota profiling was assessed in nasopharyngeal swab, nasal lavage, and induced sputum samples collected from them at 4 and 8 weeks after SARS-CoV-2 infection, respectively

Results Our findings revealed that the Staphylococcaceae, Corynebacteriaceae, and Enterobacteriaceae bacterial family were the most prevalent in the upper airway, while Streptococcaceae, Lachnospiraceae, and Prevotellaceae emerged as the most prevalent bacterial family in the lower airway. An increase in the abundance of Staphylococcus in nasopharyngeal swab samples and of Streptococcus in induced sputum samples was observed after a month. Furthermore, a discernible panel of microbial features, including the abundance of Staphylococcus identified in nasopharyngeal swab samples at baseline period, emerged as insightful predictors for improvement in cough severity

Conclusions In conclusion, dynamic alterations in the airway microbial composition may contribute to the post-COVID-19 chronic cough progression, while the compositional signatures of nasopharyngeal microbiota could reflect the improvement of this disease

关键字：Airway microbiota, COVID-19, Airway dysbiosis, Chronic cough, Staphylococcus

Klebsiella Oxytoca Subgroup KO5: Highly Resistant and Superior Immune Evasion Capability

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Objective Klebsiella oxytoca complex is a member of the normal gut microflora and also an important human pathogen causing antibiotic-associated hemorrhagic colitis and a variety of other infections. In a previous nationwide multicenter study, we identified a highly drug-resistant subgroup, KO5, which demonstrated resistance to multiple drugs and exhibited a higher prevalence of drug resistance genes. Additionally, our previous research revealed a crucial virulence gene, mgtB, exclusively present in the KO5 subgroup. In this paper, we aim to investigate the differences in virulence and pathogenicity of the highly resistant subgroup KO5 compared to the other subgroups

Methods Each subgroup was represented by three selected strains to conduct macrophage survival assay. The observation of bacterial survival within macrophages was conducted using transmission electron microscopy. Various assays were performed to analyze the cellular responses following bacterial infection. This included the detection of reactive oxygen species (ROS), nitric oxide synthase (NOS), nitric oxide (NO), 11 inflammatory factors, and the lysosomal activity of macrophages

Results Our results revealed that KO5 had a higher survival rate against macrophages than isolates of other subgroups. Transmission electron microscopy results confirm that more KO5 strains could survival within macrophage. After infected by KO5, the macrophage resulted in higher cellular respiratory storm products ROS, NO, NOS, as well as elevated inflammatory factors IL-6, IL-8, and INF-γ than other subgroups. However, it exhibited lower lysosomal enzyme activity in macrophages. The results identified that the highly resistant subgroup KO5 is capable of activating macrophages, enabling itself been taken into the host organism, but wouldn't be eliminated by the macrophages

Conclusion In conclusion, the study identified a highly resistant subgroup KO5 and have stronger immune evasion capabilities, which could be a contributing factor to enter the host organism and establish persistent infections. Clinical should pay more attention to

it as it's a noticeable superbug and could cause a severe challenge to public health

关键字：klebsiella oxytoca, Highly resistant, Immune evasion capability

IS26 Mediated Recombination Poses Contribution To The Formation of BlaKPC and BlaNDM Hybrid Plasmid

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Emergence and epidemic of carbapenem-resistance Enterobacterale producing double carbapenemases, like KPC-2 and NDM-1, have aroused worldwide attention while less is focused on its formation and evolution mechanisms. Recently, two strains of Citrobacter freundii carrying both blaKPC-2 and blaNDM-1 genes were isolated from an teaching hospital, which provided us with valuable research samples to further explore the mystery of carbapenem-resistant Enterobacteriaceae (CRE).

Two Citrobacter freundii isolates (C. freundii WYM and C. freundii ZGQ) were separated from clinical specimens and identified through the MALDI-TOF MS system. Antimicrobial susceptibility testing was conducted using the Vitek COMPACT 2 system. The presence of carbapenemases was confirmed through the colloidal gold immunoassay (CGI) test, and polymerase chain reaction (PCR) followed by sequencing. Subsequent investigations included S1-PFGE, southern blot analysis, and filter mating conjugation experiment to ascertain gene location and the transferability of carbapenem-resistant plasmids. A passage experiment was determined the stability of the plasmids under antibiotic and antibiotic-free conditions. Growth rate determination was performed to explore the fitness cost of transconjugants. Whole-genome sequencing (WGS) was carried out using the HiSeq 2000 and PacBio RSII platforms. Ceftazidime-avibactam, administered either alone or in combination with aztreonam, was employed in bactericidal activity tests to assess combination efficiency in vitro, and bactericidal experiments evaluated the potential for therapy.

C. freundii WYM and C. freundii ZGQ co-produce blaKPC-2 and blaNDM-1, which makes Citrobacter freundiihighly resistant to carbapenem drugs. Conjugation assay proved that the plasmids were capable of transconjugation, and the hybrid plasmids containing blaNDM-1 and KPC-2 could be transferred to the recipient Escherichia coli J53, and both were located on the same transconjugant according to S1-PFGE with Southern blot experiments. WGS and bioinformatics analysis revealed that the IS26 mediated recombination poses contribution to the formation of plasmid co-producing KPC and NDM carbapenemase. In vitro evolution experiments showed that transconjugant E. coli J53 (pZGQ_NDM_KPC) in the conjugates could be stably inherited after 10 days of passage.

Our research not only reveal a new plasma created by blaKPC-2 and blaNDM-1, but also confirmed that it was very valuable for renewable genes and homological recombination studies to improve the understanding of Carbapenem resistant Enterobacteriaceae (CRE). The aim of this study was to characterize the IS26 mediated recombination poses contribution to the formation of plasmid co-producing KPC and NDM carbapenemase

关键字：IS26, NDM-1, KPC-2, Citrobacter freundii, carbapenem resistance, plasmids recombination

Evaluation of The Synergy of Aztreonam in Combination with Ceftazidime/ Avibactam, Meropenem/vaborbactam and Imipenem/relebactam Against Dual-carbapenemase-producing Enterobacterales

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Objective We aimed to identify the location and combination patterns of the carbapenemase-encoding genes in dual-carbapenemase-producing Enterobacterale strains. The synergistic activity and bactericidal activity of aztreonam in combination with ceftazidime/avibactam(CZA), meropenem/vaborbactam(MEV) and imipenem/relebactam(IMR) against these strains was evaluated

Method 12 dual-carbapenemase-producing Enterobacterale strains were sequenced on Illumina and MinION platforms. The sizes of plasmids and the location of carbapenemase genes were verified by S1-PFGE followed by southern blot using gene specific probes. Conjugation abilities of plasmids harboring carbapenemase genes were evaluated by filter mating experiment. In vitro efficacy of the combination of aztreonam and CZA, MEV and IMR against strains were determined using checkerboard assay and time kill experiment

Result Among 12 isolates, they were K. pneumoniae (n=9), P. rettgeri (n=2) and E. hormaechei (n=1). Almost all strains exhibited resistance to β-lactams including carbapenems, CZA, MEV, and IMR. But the majority were susceptible to tigecycline and colistin. The most common dual-carbapenemase genes pattern of

CRE strains was bla(KPC+NDM) (n=6), followed by blaKPC+IMP (n=4), bla(KPC-2+NDM-5) (n=4), bla(KPC-2+IMP-26) (n=3), bla(KPC-2+NDM-1) (n=2), bla(KPC-2+KPC-2) (n=1), bla(KPC-2+IMP-4) (n=1) and bla(NDM-1+IMP-4) (n=1). In each strain, the carbapenemase genes were all located on different plasmids. Six carbapenemase-encoding plasmids were able to conjugate from the original strain to the receipt strain E.coli J53. The results of the checkerboard synergy analysis consistently revealed good synergistic effects of the combination of ATM and CZA, ATM and MEV, ATM and IMR. The results of the kill-time curves showed that, all strains, except for strain I, exhibited significant synergistic activity and bactericidal activity between 2-8 hours

Conclusion Dual-carbapenemase-producing Enterobacterale is a potential threat to clinical infection treatment as it could be resistant to first-line antibiotics and new antibiotics. For strains producing dual carbapenemases, especially those with both KPC and MBL enzymes, ATM combined with novel β-lactam/β-lactamase inhibitor combinations were an effective treatment options.

关键字：Dual-carbapenemase-producing Enterobacterales; Beta-lactam/beta-lactamase inhibitor combinations; Aztreonam; Checkerboard assay; Time-kill curve

Effects of Heterogeneous Nuclear Ribonucleoprotein K and E Combined with Human Papillomavirus 16 Infection in Cervical Cancerization

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Objective As important members of the RNA binding proteins (RBPs), heterogeneous nuclear ribonucleoprotein K and E (hnRNP K/E) are involved in various tumor progression. Human papillomavirus (HPV) gene expression is closely linked to RBPs and is tightly regulated at the RNA processing level. However, the comprehensive role of hnRNP K/E combined with HPV16 infection in cervical cancerization remain unclear. Our study investigated the effects of hnRNP K/E combined with HPV 16 infection in cervical cancerization

Methods A total of 244 participants, including 177 with different grades of cervical lesions and 67 with normal cervix, were enrolled from a community-based cohort and hospital cohort established in Shanxi Province, China. Western blotting was used to detect the expression of hnRNP K/E, HPV16 E2 and E6 proteins. Additive model was used to analyze interaction between hnRNP K/E and HPV16 infection. Bayesian kernel machine regression (BKMR) was used to explore the comprehensive effects of hnRNP K/E, HPV16 E2 and E6 in cervical cancerization

Results HPV16 E6 protein high expression (H=20.809, P<0.001) and HPV16 E2 protein low expression (H=19.061, P<0.001) were associated with increased risk of cervical carcinogenesis. hnRNP K high expression (odds ratio [OR]=8.649, 95% confidence interval [CI]: 3.100~24.130) could increase the risk of cervical intraepithelial neoplasia of grade 2 or worse (CIN2+), while hnRNP E1(OR=0.269, 95% CI: 0.107~0.685) and hnRNP E2 (OR=0.271, 95% CI: 0.107~0.685) high expression reduced the risk of CIN2+. Additionally, we observed that there was a synergic effect between hnRNP K high expression, hnRNP E1/E2 low expression and HPV16 infection on CIN2+. It was worth noting that there was a significantly negative overall effect of hnRNP K/E, HPV16 E2 and E6 on CIN2+

Conclusion There was a negative correlation between hnRNP E1/E2 and cervical carcinogenesis, while hnRNP K was positively associated with CIN2+, especially, there was a stronger risk when it combined with HPV16 infection. Notably, combination of hnRNP K/E with HPV16 E2 and E6 could reduce the risk of CIN2+ occurrence. Our results provide new insights into the combination of HPV infection control and RBPs measures to prevent cervical cancerization

关键字：heterogeneous nuclear ribonucleoprotein K and E, Cervical cancerization, Human papillomavirus 16, Comprehensive effects

The Identification and Validation of Crucial Ferroptosis-related Genes in Pulmonary Tuberculosis Based on Bioinformatics Analysis

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Objective To study and screen the genes related to ferroptosis of pulmonary tuberculosis, and to provide potential molecular markers for the subsequent diagnosis, treatment and prognosis of pulmonary tuberculosis

Methods he purpose of this study was to screen the differential genes by using the transcriptome sequencing data collected from patients with tuberculosis through the combination of transcriptome sequencing and bioinformatics. The ferroptosis genes related to tuberculosis were screened by Ferrdb for bioinformatics

analysis, and the key genes of ferroptosis of tuberculosis were discovered. By collecting a certain number of whole blood samples from patients with tuberculosis, the key gene was verified by fluorescence quantitative PCR (qRT-PCR), which provided scientific basis for the early diagnosis and clinical treatment of tuberculosis

Results 20 differential genes related to ferroptosis were selected through the database. Gene ontology (GO) functional enrichment analysis showed that they were mainly involved in the biological processes such as hypoxia response, enzyme activity and autophagy. The protein interaction network was constructed by string and combined with enrichment analysis, the key genes of ferroptosis in pulmonary tuberculosis including HRAS, ATF3, MAPK8, ATM, IDH1 and HIF1A were further screened. The qRT-PCR test on the whole blood of 10 patients with tuberculosis and 10 pairs of healthy volunteers showed that the expression of ATF3 and MAPK8 in the whole blood of tuberculosis patients was significantly higher than that of healthy volunteers, and the difference was statistically significant (P<0.05)

Conclusion ATF3 and MAPK8 are the key genes of ferroptosis in pulmonary tuberculosis, and may be used as molecular markers for diagnosis and treatment of pulmonary tuberculosis

关键字：tuberculosis; ferroptosis; bioinformatics; ATF3; MAPK8

铁死亡相关长链非编码 RNA 在结核病中的研究：基于生物信息学分析及实验验证

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目的 基于转录组测序及生物信息学技术筛选结核病患者血液中铁死亡相关长链非编码 RNA，分析其免疫浸润情况及诊断价值并进行实验验证。

方法 利用 limma 包对 3 例 TB 患者全血样本和 3 例健康志愿者全血样本全基因组转录测序数据进行数据分析，筛选差异表达基因，采用 R 软件的 ggplot2 包和 pheatmap 包绘制火山图和热图，然后从 FerrDb 数据库下载 259 个铁死亡基因，Venn 软件在线工具绘制韦恩图，筛选结核病铁死亡相关基因，并进行基因功能富集分析，蛋白质互作网络分析，然后采用 CIBERSORT 分析结核病患者血液样本中免疫细胞浸润情况，采用 pearson 相关性评估 lncRNA 与铁死亡相关基因的表达水平，以确定铁死亡相关 lncRNA，在分析结核病铁死亡相关 lncRNA 与免疫细胞的相关性，随后采用外部数据集 GSE54992 验证，最后对收集的临床样本进行荧光定量 PCR 试验（qRT-PCR）进行验证。

结果 通过对 3 例 TB 患者，3 例健康对照者全血样本进行全基因转录组测序，共得到 9071 个有差异的基因，其中 636 个差异 lncRNA，有 330 个 lncRNA 表达上调，306 个 lncRNA 表达下调。1530 个差异 mRNA，有 813 个 mRNA 表达上调，717 个 mRNA 表达下调，与铁死亡基因取交集，共得到 133 个差异基因，GO 富集中，生物学过程主要集中在细胞对化学应激的反应，抗氧化反应等，细胞组分中，主要作用于噬菌体组装位点，自噬，吞噬体组装部位膜，分子功能主要为氧化还原酶活性，RNA 聚合酶II特异性 dna 结合。KEGG 通路富集显示差异基因主要富集于铁死亡，自噬，有丝分裂等通路。在线数据库 STRING 筛选出 10 个 TB 铁死亡关键基因，采取 pearson 相关系数计算 lncRNA 与 TB 铁死亡相关基因的相关系数，以阈值 (|Cor| 大于 0.3 且 pvalue<0.05 为标准，选出铁死亡相关的 lncRNA 分别是 MALAT1、MIATNB、LINC01465。将筛选 lncRNA 与免疫细胞进行相关性分析发现 MIATNB 与记忆细胞 B、单核细胞呈正相关性，LINC01465 与记忆细胞 B 呈正相关性，LINC00667 与幼稚 B 细胞呈负相关性。外部数据集 GSE54992 和临床样本 qRT-PCR 验证显示 MIATNB 在结核病患者血液中基因表达高于对照组，差异有统计学意义（P<0.05）。

结论 通过转录组测序技术联合生物信息学技术筛选出结核病铁死亡相关的长链非编码 RNA:MIATNB，该基因在结核病患者中高表达，与细胞免疫浸润密切相关，可能是结核病诊断治疗的潜在分子生物标志物。

关键字：结核病，铁死亡，长链非编码 RNA，生物信息学

Antimicrobial Susceptibility and Molecular Mechanisms of Resistance for Macrolide From Mycobacterium Abscessus Complex

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Objective To provide a reference basis for the clinical selection of an effective starting regimen by investigating the minimum inhibitory concentrations (MIC) of 16 antimicrobial agents from Mycobacterium abscessus complex (MABC) strains and their molecular mechanisms of macrolide resistance

Methods The Mycobacterium abscessus complex isolated in Quanzhou, Fujian Province from 2020

to 2022 were collected, and the subspecies were identified by PCR and gene sequencing. The drug sensitivity test of the strains from the infected cases were carried out by the minimum inhibitory concentration (MIC) method. PCR was used to detect erm(41) and rrl resistance related genes in clarithromycin resistant strains

Results A total of 51 MABC were collected, including 45 (88.2%) M. abscessus and 6 (11.8%) M. massiliense, while no M. bolletii isolate was detected. Among them, 33 cases (64.7%, 33/51) were infected. The clarithromycin sensitivity decreased from 87.88% to 15.15% after incubated 14 days. Amikacin and tigecycline were susceptible in 91.6% and 87.8% respectively. MABC showed the lowest resistance rates to cefoxitin (9.09%), but the intermediary rate was the majority, up to 63.64%. Additionally, linezolid was close to half rate(48.49%) susceptible. The intermediated and resistant rate of imipenem were 45.46% and 54.55% respectively. Others were overwhelmingly drug resistant (>85%). The erm(41) of M. abscessus subsp. abscessus were predominated on T28, accounting for 93.3%(28/30) and the erm(41) gene sequevar type showed genetic polymorphism and dominated by type8. One acquired resistance strain contained an A2058G point mutation in rrl gene, the other had no point mutation

Conclusion In Quanzhou. M. abscessus subsp. sbscessus and the erm (41) sequevar type8 were the major epidemic strains. MABC were resistant to most antibiotics, most of had induced resistance to clarithromycin. However, amikacin, tigecycline and cefoxitin had strong antibacterial activity against it. There is important to detect the MICs of MABC for clinical medication guidelines.

关键字：Mycobacterium abscessus；molecular mechanisms；Drug resistance

The Status Quo of Genital Chlamydia Trachomatis Infection Based on Cervical Swab and Serum Tests Among Women Attending Infertility and Gynecology Clinics in Hunan, China

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Objective Genital infection with Chlamydia trachomatis (C. trachomatis) is a major public health issue worldwide. It can lead to cervicitis, urethritis, and infertility. This study was conducted to determine the characteristics of genital C. trachomatis infection among women attending to the infertility and gynecology clinics

Methods Endocervical swabs were collected from 8,221 women for C. trachomatis nucleotide screening and genotyping, while serum samples were collected for C. trachomatis pgp3 antibody determination using luciferase immunosorbent assays

Results High C. trachomatis DNA prevalence (3.76%) and seroprevalence (47.46%) rates were found, with genotype E (27.5%) being the most prevalent. C. trachomatis omp1 sense mutation was associated with cervical intraepithelial neoplasia (CIN) (odds ratio [OR] = 6.033, 95% confidence interval [CI] = 1.219–39.185, $p = 0.045$). No significant differences in C. trachomatis seroprevalence rates were observed between women with detectable C. trachomatis DNA in the infertility and routine physical examination groups (86.67% vs. 95%, $p > 0.05$); however, among women with negative C. trachomatis DNA, the former group had a markedly higher seroprevalence than the latter group (56.74% vs. 20.17%, $p < 0.001$). C. trachomatis DNA, but not pgp3 antibody, was significantly associated with CIN (OR = 4.087, 95% CI = 2.284–7.315, $p < 0.001$)

Conclusion Our results revealed a high prevalence, particularly seroprevalence, of C. trachomatis among women with infertility. Furthermore, we found an association between C. trachomatis omp1 sense mutations and CIN. Therefore, C. trachomatis serves as a risk factor for CIN

关键字：Chlamydia trachomatis, genotype, seroprevalence, luciferase immunosorbent assays, cervical intraepithelial neoplasia

Investigation of in Vitro Susceptibility and Resistance Mechanisms To Amikacin Among Diverse Carbapenemase-producing Enterobacteriaceae

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Objective This study aims to assess the in vitro drug susceptibility of various Carbapenemase-Producing Enterobacteriaceae (CPE) genotypes and elucidate the underlying mechanisms of amikacin resistance

Methods A total of 72 unique CPE strains were collected from the Second Hospital of Jiaxing between 2019 and 2022, including 51 strains of Klebsiella. pneumoniae, 11 strains of Escherichia coli, 6 strains of Enterobacter cloacae, 2 strains of Klebsiella aerogenes, 1 strain of Citrobacter freundii, and 1strain of Citrobacter werkmanii. Among these strains, 24 carried blaKPC gene, 20 carried blaNDM gene, 23 carried blaOXA-48 gene, and 5 carried both blaKPC and blaNDM. We measured the in vitro activity of amikacin and other common antibiotics. Strains carrying blaOXA-48-like gene were selected for whole genome sequencing (WGS) via next-generation sequencing to identify genes related to antimicrobial resistance (AMR) and virulence factor (VF)

Results Out of the 72 carbapenemase-producing Enterobacteria strains tested, 41.7% exhibited resistance to amikacin. The drug resistance rates for K. pneumoniae, E. coli, and Enterobacter spp. were 51.0%, 27.3%, and 10.0%, respectively.The majority of the CPE strains (>90%) displayed resistance to cephalosporins and carbapenems, while most of them were sensitive to polymyxin B and tigecycline (97.2% and 94.4%). The amikacin resistance rate was 100% for strains carrying blaOXA-48, 20.8% for those with blaKPC, 5.0% for those with blaNDM, and 20.0% for those with both blaKPC and blaNDM. These differences were statistically significant ($P < 0.05$). Through sequencing, we detected aminoglycoside resistance genes RmtF and AAC(6')-Ib, VF genes iucABCD and rmpA2 in OXA-48-producing multidrug resistance and highly virulent strains. These genes were located on a IncFIB- and IncHI1B-type plasmid, respectively. Both plasmids were highly homologous to the plasmid from OXA-232 strains in Zhejiang province and Shanghai province. Integration of these resistance genes into the lncFIB plasmid, facilitated by the IS6 and/or Tn3 transposons, resulted in OXA232-producing K. pneumoniae with amikacin resistance

Conclusion The in vitro susceptibility of Carbapenemase-producing Enterobacteriaceae strains to amikacin varied based on their drug-resistant genotypes. Amikacin demonstrated potent antibacterial activity against Enterobacteriaceae strains carrying blaNDM. The non-transferrable lncFIB plasmid, carrying AAC(6')-Ib and RmtF genes, was likely responsible for the extremely high level of in vitro drug resistance of blaOXA-48-like K. pneumoniae. Given the high MIC values, resistance phenotype, and the type of carbapenemase carried, we suggest that clinical attention be given to the 16S rRNA methylase gene

关键字：Carbapenemase-producing Enterobacteriaceae；Drug Resistance Genes；Amikacin； Whole Genome Sequencing

新冠变异株 Omicron 患者合并多重耐药菌感染危险因素及风险预测模型构建

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目的 分析新冠变异株 Omicron 患者合并感染 MDROs（多重耐药菌）的患者资料，研究该 MDROs 的流行特征及其危险因素，构建风险预测模型。为新冠病毒感染患者合并多重耐药菌感染的预防控制提供依据。

方法 回顾性分析某大型三甲医院 2022 年 12 月 8 日-2023 年 3 月 31 日期间全院新冠感染患者资料，选取合并多重耐药菌感染的患者为病例组，同时根据患者所住病区按 1:2 频数随机匹配未合并多重耐药菌感染的患者为对照组。使用电子数据库和 WHONET5.6 软件收集基线信息、临床特征和培养结果，并在两组之间进行比较。采用多因素 logistic 回归建立耐药菌风险预测模型。

结果 45 例新冠感染合并 MDROs 感染患者作为病例组，90 例未合并多重耐药菌的新冠感染患者为对照组被纳入研究，检出 MDROs 株数为 52 株，分离率较高的菌株分别为鲍曼不动杆菌（n=20，38.46%）、肺炎克雷伯菌（n=12，23.08%）和金黄色葡萄球菌（n=9，17.31%）。单因素分析显示，侵入性操作（有创呼吸机、中心静脉置管）、是否使用抗菌药物、抗菌药物使用种类、抗菌药物使用日数、抗菌药物的联合使用、白蛋白、血红蛋白、PCT、CRP、白介素-6 和白介素-10 在两组间差异有统计学意义（$P<0.05$）。最终，预测模型包含抗菌药物使用种类、有创呼吸机的使用、白蛋白>30g/L 及 PCT>0.5ng/mL。(Logit (P) =抗菌药物种类 2-3×1.99＋抗菌药物种类≥4×2.638+有创呼吸机×1.670－白蛋白>30g/L×1.344＋PCT＞0.5ng/mL×1.520)，模型的 ROC 预测曲线下 AUC=83.2%。

结论 抗菌药物使用种类、有创呼吸机的使用、白蛋白<30g/L 及 PCT>0.5ng/mL 是耐药细菌感染的独立危险因素，风险预测模型的建立有利于早期识别 Omicron 患者合并感染 MDROs 的高危因素，及时采取防控措施，从而降低 MDROs 医院感染率。

关键字：新冠变异株 Omicron，合并感染，MDROs（多重耐药菌），危险因素

肺炎衣原体与新冠病毒共感染患者炎症因子风暴的临床特征分析

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目的 明确不同严重程度、年龄肺炎衣原体与新冠病毒共感染患者炎症因子风暴的临床特征。

方法 研究对象为 2022 年 12 月 20 日-2023 年 1 月 20 日期间于郴州市第一人民医院就诊的 102 名新冠肺炎患者，其中成人 71 名，儿童 31 名，收集患者肺泡灌洗液、咽拭子、及血清标本。应用荧光 PCR 法检测新冠病毒核酸，ELISA 法检测肺炎衣原体 IgG/IgM 抗体，流式细胞术检测肺泡灌洗液中 IL-5 、IFN-α 、IL-2 、IL-6 、IL-1β、IL-10、TNF-α、IL-12、IL-4、IL-17 、IFN-γ 及 IL-8 水平。

结果 采用倾向性评分对各组年龄、性别、基础疾病进行 1：1 匹配，容差设置为 0.4，肺炎衣原体 IgM 阳性新冠重症患者比率为 50%（2/4），与 IgM 阴性组（52.86%，37/70）比较无显著性差异（p>0.05），肺炎衣原体 IgG 阳性与阴性新冠重症患者比率也无显著差异（46.67% vs 52.17，p>0.05）。成人重症肺炎衣原体 IgG 阳性患者肺泡灌洗液 IFN-α 分泌高于 IgG 阴性患者（2.35±1.63 pg/mL vs 1.71±1.45, p=0.037），两组其他细胞因子比较均无显著性差异（p>0.05）；成人非重症肺炎衣原体 IgG 阳性患者 IL-8 和 IL-17 水平均高于 IgG 阴性患者（p=0.044、p=0.039）；成人重症、非重症肺炎衣原体 IgM 阳性与阴性组患者肺泡灌洗液细胞因子比较均无显著性差异（p>0.05）。未成年人非重症组 IgM 阳性患者肺泡灌洗液 IL-8 水平高于 IgM 阴性患者（p=0.046）。

结论 肺炎衣原体 IgG 或 IgM 与新冠肺炎重症程度不存在关联；机体处于新冠病毒导致的炎症因子风暴的背景下，肺炎衣原体感染引起的炎症因子的改变十分轻微。

关键字：肺炎衣原体，新冠病毒

Early Prediction of Central Venous Catheter-related Bloodstream Infection in ICU Patients Using XGboost Machine Learning

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Objective Central line catheters are widely used in intensive care units (icus) as a treatment tool for critically ill patients. However, centerline associated bloodstream infections (CLABSIs) has been increasing year by year, becoming one of the main causes of bloodstream infections in ICU patients. To this end, we attempted to develop a machine learning algorithm to provide clinical decision support

Methods A predictive model was developed using retrospective data from MIMIC-IV dataset. Patients' catheterization was extracted according to the ICD10 code of the International Statistical Classification of Diseases and Related Health Problems.We created three machine learning models and trained and validated them using 70:30 split training and test data

Results 4136 patients were included in our study with a central line, the rate of CLABSI was 1.6%. The mortality rate was 49.23% while the mortality rate for patients with CLABSI was 63.24% and patients without CLABSI had a 48.99% mortality rate (p<0.001). XGboost had the highest AUC (0.782; 0.733,0.832), followed by decision tree (0.726; 0.657,0.794) and logistic regression (0.705; 0.646,0.764) on the testing dataset

Conclusion In the study of prediction models for CLABSI in ICU patients, the prediction model based on XGboost algorithm may have better prediction efficiency. Our model may be an effective clinical decision support tool for the assessment of CLABSI risk and warrants further exploration

关键字：Machine learning, XGboost, MIMIC IV, ICU, central venous catheter-related bloodstream infection

腺病毒肺炎和鹦鹉热衣原体肺炎的临床特征比较

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目的 提高发热门诊临床医生对腺病毒肺炎和鹦鹉热衣原体肺炎的早期鉴别能力。

方法 回顾性分析就诊于北京大学第三医院发热门诊，并采用宏基因组高通量测序（mNGS）或 PCR 确诊的 18 例腺病毒肺炎患者和 19 例鹦鹉热患者，收集患者禽类接触史、发热及伴随症状、血液化验和胸部 CT 影像。

结果 腺病毒肺炎患者和鹦鹉热衣原体肺炎患者报告有明确禽类（鹦鹉或鸽子）接触史者有 2 例（11%）和 13 例（68%）（P<0.05）。腺病毒肺炎患者和鹦鹉热肺炎患者均高热，体温峰值分别为（39.3℃±0.3℃）和（39.5℃±0.5℃）（P>0.05）。大部分患者伴有咳嗽，但腺病毒患者咳嗽有痰比例高达 78%，而鹦鹉热衣原体肺炎患者干咳占 84%（P<0.05）。两组患者伴明显头痛、全身肌肉关节痛比例无统计学差异（P>0.05）。两组患者血常规白细胞计数、中性粒细胞比例、C 反应蛋白水平均无明显差异(P>0.05)，但腺病毒肺炎患者的 PCT 高于正常值比例明显超过鹦鹉热衣原体肺炎患者（61% vs 32%，P<0.05）。两组患者的胸部影像绝大多数（83% vs 85%）均为下叶和肺外带受累（83% vs 84%），形态以肺部实变最为常见（89%vs 63%），其次为肿块（31% vs 42%）和结节（15% vs 26%），常同时伴周围磨玻璃影（89% vs 85%）和内部支气管充气征（83% vs 85%）。但相比于鹦鹉热衣原体肺炎患者，腺病毒肺炎患者的胸部影像肺炎病灶多发更为常见（61 % vs 32%，P<0.05）。

结论 腺病毒和鹦鹉热衣原体肺炎临床、化验和影像学存在很多相似，详细询问禽类接触史和血 PCT 水平有助于二者鉴别。

关键字：腺病毒肺炎；鹦鹉热衣原体肺炎；社区获得性肺炎

高毒力碳青霉烯耐药肺炎克雷伯菌噬菌体分离表征 及其解聚酶研究

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目的 肺炎克雷伯菌（Klebsiella pneumoniae, Kp）是医院感染最为常见的重要病原体，常感染免疫低下患者，导致血液感染、呼吸道感染、尿路感染等疾病。近年来，随着广谱抗菌药物的大规模临床应用，多重耐药和泛耐药菌检出率逐年上升，给临床感染治疗带来了巨大的挑战。由于高毒力碳青霉烯耐药肺炎克雷伯菌（CR-hvKp）同时具有高毒力和多耐药的双重致病性，对公共卫生及临床抗感染治疗造成严重威胁。噬菌体疗法是目前解决多重耐药菌感染的重点及趋势，受到国内外研究者的广泛关注。然而，目前靶向 CR-hvKp 的噬菌体类群研究还较为匮乏。

方法 本文利用 CR-hvKp 菌株作为宿主，分离获得了靶向 CR-hvKp 的多个噬菌体。对杀伤效果最好的噬菌体进行了详细表征以及基因组测序；同时，对其所属的噬菌体类群进行了比较基因组分析以及解聚酶序列研究。

结果 噬菌体 Kpph1 和 Kpph9 能在双层平板上形成清晰透亮的噬菌斑，对 CR-hvKp 具有较强的杀菌活性。噬菌斑外圈存在明显的晕环结构，表明均具有产能裂解宿主荚膜多糖的解聚酶的潜能。同时，Kpph1 和 Kpph9 能有效抑制 CR-hvKp 生物膜的形成，并对成熟生物膜具有清除作用。两个噬菌体均为裂解型噬菌体，具有较好的酸碱和温度适应性，其基因组上未存在已知的抗性基因、毒力因子以及移动元件，因此在基于噬菌体疗法治疗 CR-hvKp 感染中具有良好的临床应用前景。

基因组测序及系统进化分析表明，Kpph1 隶属于 Drexlerviridae 科 Webervirus 属，而 Kpph9 则为 Autographiviridae 科 Drulisvirus 属新种。Kpph1 和 Kpph9 均具有两个潜在的解聚酶序列，且该序列是比较分析中变异度最高的区域。Kpph1 ORF20 与 GH-K3 噬菌体解聚酶序列相似性最高，结构预测表明其为 K2 特异性解聚酶。Kpph1 ORF19 序列在该属所有噬菌体中都保守存在。该序列注释为基板蛋白，可能在噬菌体与宿主互作过程中起到重要作用。Kpph9 的 ORF48 和 ORF56 均预测为尾纤蛋白，在该属噬菌体中序列差异均较大。在该噬菌体中具有的两个潜在解聚酶序列是否宿主特异性具有差异，或者在噬菌体侵染不同时期起到作用目前尚不清楚。

结论 本研究分离表征了两株靶向 CR-hvKp，具有良好的抗菌及抗生物膜活性的裂解型噬菌体。对 Kpph1 和 Kpph9 及其编码的解聚酶序列进行深入研究，将对了解噬菌体及其宿主相互作用，构建靶向 CR-hvKp 噬菌体库，开发噬菌体源药物具有重要意义。

关键字：高毒力多重耐药肺炎克雷伯菌，噬菌体，比较基因组分析，解聚酶，临床应用

异基因造血干细胞移植后 EBV 感染类型及代谢特征

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目的 探讨血液病患者行异基因造血干细胞移植（allo-HSCT）术后 EB 病毒（EBV）的感染类型和再激活的代谢特征。

方法 纳入 2022 年 11 月至 2023 年 5 月期间于某医院血液科行 allo-HSCT 的患者，通过实时荧光定量聚合酶链式反应（PCR）分析血浆及外周血单个核细胞（PBMC）对 EBV 感染的监测效果，通过分析 LMP1、EBNA1、EBNA2 和 BALF2 基因表达探讨 EBV 潜伏感染类型，利用超高效液相色谱串联质谱（UPLC-MS/MS）方法分析 EBV 再激活过程的非靶向代谢组学特征。

结果 29 例 allo-HSCT 术后患者共 39 份样本的 PBMC EBV DNA 均为阳性，血浆 EBV 的检出率为 69.23%（27/39）（P＝0.014），其 LMP1、EBNA1、EBNA2 和 BALF2 基因的阳性率分别为 35.90%（14/39）、100%（39/39）、100%（39/39）和 15.38%（6/39），大部分符合 EBV 潜伏感染 III 型的基因表达模式。EBV 再激活组（n=30）和 EBV 阴性组（n=30）血浆非靶向代谢组学筛选出 39 种特征代谢物，EBV 再激活可能与丁酸代谢、谷氨酰胺及谷氨酸代谢密切相关。

结论 针对 allo-HSCT 术后血液病患者的 EBV 感染监测，PBMC 比血浆对 EBV DNA 载量具有更佳的检出率，潜伏感染大部分为 III 型，EBV 再激活患者血浆具有脂质代谢和氨基酸代谢产物的显著改变。

关键字：造血干细胞移植，EB 病毒，潜伏感染，聚合酶链式反应，代谢组学

Genomic Analysis of Three Hepatitis B Virus-related Liver Diseases Reveals Intrahepatic Immune Cell Infiltration Characteristics

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Objective Hepatitis B virus (HBV) infection has become a great challenge to the global health and is a common cause of a series of liver diseases, even leading to hepatocellular carcinoma. The interplay between virus and host immune response is related to the outcome of HBV infection, it is essential to clarify the intrahepatic immunological characteristics of HBV infected populations

Methods Here, microarray data of three hepatitis B virus-related liver diseases including HBV-associated acute liver failure (HBV-ALF) (n=38), chronic hepatitis B virus infection (CHB) (n=340), and hepatitis B virus-associated hepatocellular carcinoma (HBV-HCC) (n=134) were retrieved from NCBI Gene Expression Omnibus (GEO). The intrahepatic immune cell infiltration percentages were calculated using CIBERSORTx deconvolution

Results Compared with health control (HC) (n=34), plasma cells, naïve CD4+ T cells, and activated memory CD4+ T cells were exclusively elevated in HBV-ALF, while resting memory CD4+ T cells and regulatory T cells were decreased. With the development of liver fibrosis, M0 and M1 macrophages in the liver tissues of CHB patients tended to increase while M2 macrophages became exhausted. Resting NK cells and resting mast cells tended to gradually decrease with the degree of intrahepatic inflammatory activity. Multivariate Cox proportional regression analysis suggested M0 macrophages, resting dendritic cells and eosinophils were independent risk factors related to the prognosis of HBV-HCC. LASSO regression revealed the higher the Riskscore (0.0389 M0 macrophages + 0.09518 resting dendritic cells + 0.412 eosinophils), the lower the overall survival rate of HBV-HCC patients (HR = 2.4376, P < 0.0001). Differential genes between the high and low risk groups were involved in interaction of cytokines and receptors, cytokines and receptors interacted with viral proteins, and chemokine signaling pathways

Conclusion In conclusion, this study provided valuable information about intrahepatic immune cell infiltration landscape of various HBV-infected diseases by deconvolution of genomic data

关键字：Hepatitis B virus, Immune cell infiltration, CIBERSORTx

Metabolomics Analysis of BEAS-2B Cells with SFTS Virus Infection Based on LC-MS/MS

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Objective Severe fever with thrombocytopenia syndrome virus (SFTSV) is an emerging tick-borne virus that can cause severe mortality. Severely ill patients often develop secondary pulmonary infections including invasive pulmonary aspergillosis (IPA), which increases the fatality rate. The pathogenesis of pulmonary infections in SFTS patients remains unclear. The aim of this study is to explore the metabolic alterations in BEAS-2B cells with SFTSV infection and provide new understanding of its pathogenesis

Methods Metabolic profiles in human bronchial epithelial BEAS-2B cells infected with SFTSV were analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS)

Results BEAS-2B cells were successfully demonstrated to be infected with SFTSV by Immunofluorescence assay(IFA). The PCA score plot showed that all samples were within the 95% confidence interval, with satisfactory separation between groups and aggregation within groups. OPLS-DA model were analyzed and the key parameters including R2Y and Q2 were both above 0.5, indicating the data were reliable and applicable. The study identified 1189 differential metabolites, of which 126 were significantly up-regulated and 148 were significantly down-regulated. These metabolites were mainly classified into super classes, including organoheterocyclic compounds (19.5%), lipids and lipid-like molecules (13.0%), benzenoids (10.3%), organic acids and derivatives (9.8%), amino acids and peptides (5.3%), and fatty acids (5%). According to the KEGG analysis, these metabolites were primarily involved in choline metabolism in cancer; glycine, serine, and threonine metabolism; tryptophan metabolism; ABC transporters; arginine and proline metabolism. Choline and alpha-Acylglycerophosphocholine were the remarkable increasing metabolites in choline metabolism in cancer, whereas glycerophosphocholine and phosphatidylcholine were the decreased metabolites

Conclusion The results suggested that SFTSV infection induces metabolic reprogramming in BEAS-2B cells, with significant changes in choline metabolism in cancer.Understanding this metabolic reprogramming might provide new insights into the mechanism of pulmonary infections in SFTS patients and lead to the discovery of new therapeutic targets

关键字：Severe fever with thrombocytopenia syndrome, pulmonary infections, BEAS-2B, metabolomics

铜绿假单胞菌转座子突变文库的构建及毒力基因的筛选鉴定研究

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目的 铜绿假单胞菌（Pseudomonas aeruginosa，PA）是一种常见的条件致病菌，能够引起多种感染。目前随着抗菌药物的广泛使用，PA 的耐药性日趋严重，急需开发新的治疗方法。而 PA 能够分泌大量的毒力因子，在多种宿主中引起广泛的感染。目前抗毒力疗法已成为传统抗生素治疗铜绿假单胞菌感染的一种有吸引力的替代策略。为了筛选铜绿假单胞菌中与毒力相关的基因，在本研究中，我们利用随机插入转座子的方法，使插入部位的基因失活，构建了铜绿假单胞菌的转座子随机突变体文库，通过筛选与铜绿假单胞菌的毒力表型相关的突变体，经过转座子整合位点鉴定，发现了与铜绿假单胞菌的毒力相关的基因。为进一步发掘铜绿假单胞菌潜在的毒力因子调控方式奠定基础，同时也为开发新型药物靶标并为临床抗感染治疗提供新的方向和思路。

方法 1. 采用随机突变技术构建铜绿假单胞菌的转座子突变体文库；通过随机挑取单克隆转座突变株，进行转座子整合位点鉴定，验证铜绿假单胞菌转座子突变文库是否构建成功；

2. 通过氯仿提取绿脓素，得到铜绿假单胞菌突变文库中与野生株的绿脓菌素差异较大的突变菌株，共筛选得到 20 株绿脓菌素合成能力改变的突变菌株；

3. 采用 Cubes-seq 方法对筛选出的 20 株突变菌株进行转座子整合位点测序鉴定；

结果 1. 以本实验室前期收集一株碳青霉烯类耐药的铜绿假单胞菌为 WT 菌株，采用随机突变技术共构建 22000 多株铜绿假单胞菌的转座子突变体文库；随机挑取 24 株单克隆转座突变株，进行转座子整合位点鉴定，测序结果显示 24 株突变菌株成功插入铜绿假单胞菌基因组，并且转座子插入随机性良好，24 株分别插入到不同的基因位点。

2. 经过表型筛选，共筛选得到 20 株绿脓素合成能力改变的突变菌株，其中 10 株突变株较野生株的绿脓素合成能力较高，差异具有统计学意义（$P<0.05$）。

3. 筛选出的 20 株突变菌株进行转座子整合位点鉴定，分别插入 sdiA、rhlR、pqsE、PA0328、PA2678、PilX、hmgA、PA3370、PA4906、PA4838 等基因位点。

结论 1. 采用随机突变技术共构建 22000 多株铜绿假单胞菌的转座子突变体文库，转座子插入随机性良好，可用于筛选铜绿假单胞菌相关毒力基因。

2. 通过表型筛选及测序鉴定，发现了 PA0328 基因与铜绿假单胞菌的绿脓素合成能力相关；

关键字：铜绿假单胞菌；转座子；突变体文库；毒力因子；

中国西部汉族人群维生素 D 受体基因 SNP 与结核病发生发展的相关性研究

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目的 以中国西部汉族成人为研究对象，分析筛选的维生素 D 受体（VDR）基因单核苷酸多态性（SNP）是否影响结核病的发生发展，以及治疗药物的选择性。

方法 回顾性收集在四川大学华西医院就诊的 597 例结核病患者为病例组，901 例健康受试者为对照组。从数据库筛选出 VDR 的 21 个候选 SNP 位点进行检测，结合临床症状、实验室指标、治疗药物毒副作用等要素，采用 SNP 统计软件（Plink）分析 VDR 基因多态性与结核病发生发展的相关性。

结果 实验共检测 21 个候选 SNP，其中 rs58379944，rs11574012 的“G”等位基因，rs12581281 的“A”等位基因，对结核病具有防御作用。患者组中阳性 SNP 显性遗传模型中的分组对比显示：痰涂片阴性率、GLO、CHOL、LDL、CD8、N 计数均有统计学差异。接受抗结核治疗患者在抗结核药物性肝损伤的差异有统计学意义。

结论 在中国西部汉族成人中，VDR 基因多态性与结核病感染风险之间存在密切联系。VDR 的 rs58379944、rs11574012、rs12581281 位点的多态性变异可能改变了 VDR 在结核病发生发展中细胞免疫、体液免疫、脂代谢中靶细胞的表达效率；这些 SNP 可能成为预测抗结核药物性肝损伤的潜在生物学标志物。

关键字：结核病；维生素 D 受体；单核苷酸多态性；感染风险；药物性肝损伤

2021 年成都地区肺炎支原体感染流行病学分析

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目的 探讨分析 2021 年度成都地区肺炎支原体(MP)的流行特征及变化趋势,为临床提供参考依据。

方法 选取四川省成都市 2021 年度由于呼吸道感染而进行 MP 抗体检测的患者 10012 例,采用 MP 抗体被动凝集法进行检测,观察不同年龄阶段、不同季节以及不同性别下感染情况的差异。

结果 呼吸道感染患者标本中, MP 阳性患者 3084 例,总阳性率为 30.80% ;从性别差异来看,男性患者阳性率(25. 84%)低于女性(36. 12%),差异有统计学意义(χ2 =124.00 , P <0. 05);从年龄阶段区分,未成年 MP 阳性率为 43. 53% ,高于成人(33. 83%)和中老年人(14. 03%),各年龄组间 MP 阳性率差异有统计学意义(χ2 =790.13 , P <0. 05); 0~18 岁 MP 感染患者中呈现阳性率随年龄增长而升高的趋势, MP 阳性率最高的是 15~17 岁青少年(61. 61%), MP 阳性率最低是 <1 岁组的婴儿(4. 08%),各未成年年龄组 MP 阳性率差异有统计学意义(χ2 =388.27 , P <0. 05);从不同季节比较, MP 阳性率最高的季节是秋季(33. 67%),夏季是阳性率最低的季节(27. 01%),冬季和春季之间 MP 阳性率比较差异无统计学意义(χ2 =1.16 , P >0. 05),其余组别间 MP 阳性率比较差异有统计学意义(χ2 =28.23 , P <0. 05);从月份比较, 11 月是一整年中 MP 阳性率最高的月份(35. 85%),最低是 2 月(21. 79%)。

结论 MP 阳性率中女性大于男性;学龄前期、学龄期和青少年人群是 MP 易感人群。秋季和秋冬交替季,即 9 月至 12 月, MP 感染高发。 MP 是引起 2021 年度成都市呼吸道感染的重要病原体之一,应针对 MP 感染的流行病学特征对易感人群采取有针对性的防治措施,加强健康卫生宣教工作的开展,以预防和控制疾病的发生。

关键字：肺炎支原体;流行病学;成都市

血液病患者肠道定植 CRE 后感染的危险因素分析

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目的 耐碳青霉烯类肠杆菌科细菌(carbapenem-res1stant Enterobacter1aceae,CRE)检出率日渐上升，已引起广泛的国际关注，并对全球公共卫生安全带来严峻挑战。目前针对血液病患者肠道定植 CRE 后发生感染的相关研究在国内国外均较少。本研究旨在探究血液病患者肠道定植 CRE 与后续发生感染的相关性及其危险因素。

方法 筛选出 2017 年 1 月 1 日至 2021 年 4 月 26 日血液科送检至中南大学湘雅医院检验科微生物室的耐碳青霉烯肠杆菌筛查标本共 2304 例，其中检出肠道定植 CRE 的 146 例。去除同一患者重复送检的标本后，送检的血液病患者标本共 599 例，筛查出肠道定植 CRE 的 75 例。以其中检测出肠道定植 CRE 的患者为实验研究对象(共 75 例)，其中 17 例检出 CRE 定植后发生由同种菌属细菌引起感染的病例为实验组，58 例检出 CRE 定植后未发生由同种菌属引起感染的病例为对照组，回顾性比较两组病例在临床数据上的差异，以卡方检验进行单因素分析，以 Logistic 回归分析进行多因素分析。并比较不同类型血液病的定植率和各类病原菌的定植率。

结果 血液科患者 CRE 定植率为 12.52%(75/599)。各类血液病中淋巴瘤定植率最高(16/62，25.81%)，其次是急性髓细胞性白血病(29/197，14.72%)，而后依次是骨髓增生异常综合征(5/35，14.29%)、急性淋巴细胞性白血病(13/143，9.09%)、红细胞相关疾病(7/93，7.53%)，最后是其他类型血液病(5/69， 7.25%)；在各类定植的 CRE 中，最常见的是肺炎克雷伯菌(34/75，45.3%)，其次是大肠埃希菌(19/75，25.3%)，而后依次是阴沟肠杆菌(7/75，9.3%)、枸橼酸杆菌(2/75， 2.6%)、产气克雷伯菌(2/75，2.6%)、产酸克雷伯菌(1/75，1.3%)、克氏枸橼酸杆 菌(1/75， 1.3%)，其他未分类的肠杆菌科细菌占 12%(9/75)；单因素分析结果显示， 血液病患者肠道定植 CRE 后发生感染与肝脏疾病、腹泻和休克有关(P<0.05)；多因 素分析结果显示是否患有肝脏疾病、入院期间是否发生腹泻和休克是血液病患者肠道定植 CRE 后发生感染的独立危险因素(P<0.05)。

结论 血液病患者中淋巴瘤患者定植率最高，肝病、腹泻和休克是血液病患者肠道定植 CRE 后发生感染的独立危险因素，应对上述患者加强关注，采取合理有效的临床干预措施，减小感染发生的可能。

关键字：耐碳青霉烯类肠杆菌科细菌，CRE，肠道定植，血液病，感染

嗜二氧化碳大肠埃希菌致尿路感染的临床特性和遗传特征分析

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目的 通过对分离自尿液的 2 株嗜二氧化碳大肠埃希菌进行分析，拟研究该菌感染人群的临床特征和遗传特征，为临床诊疗提供帮助

方法 采用全自动细菌鉴定和药敏系统及质谱仪对细菌进行鉴定；采用 K-B 法和全自动细菌鉴定和药敏系统对细菌进行药敏；使用 QIAamp DNA 试剂盒提取细菌 DNA 并用华大基因 DNBSEQ-T10 平台进行测序，测序结果在 Ubantu 系统中进行 blast 比对和耐药基因分析，同时进行 16S rRNA 和多位点序列分型（MLST 分析）

结果 病例 1 和病例 2 为中老年女性患者，患有糖尿病、肾结石和胆囊结石等基础疾病。全自动细菌鉴定和药敏系统 Viteck 2 Compact 可以对该菌

进行鉴定，但是无法完成药敏试验。菌株 A 和菌株 B 被转种至血平板，传代 10 代均仍未恢复到正常表型。在 6%CO2 环境下孵育，菌株 A 对头孢唑林、头孢呋辛、头孢曲松、庆大霉素、复方新诺明、环丙沙星和左氧氟沙星耐药；对哌拉西林/他唑巴坦、头孢他啶、头孢哌酮/舒巴坦、厄他培南、亚胺培南和美罗培南耐药。在 6%CO2 环境下孵育，菌株 B 对头孢唑林、头孢呋辛、头孢曲松、头孢他啶、头孢吡肟、环丙沙星和左氧氟沙星耐药，对庆大霉素、阿米卡星、哌拉西林/他唑巴坦、头孢哌酮/舒巴坦、美罗培南和复方新诺明敏感。菌株 A 和菌株 B 的 MLST 分型为 ST44 和 ST1193，有 bla CTX-M-15 和 bla CTX-M-27 耐药基因。菌株 A 不含有 yadF 基因，菌株 B 有 yadF 基因。

结论 结论 嗜二氧化碳大肠埃希菌可导致有一定基础疾病的人群发生感染。嗜二氧化碳大肠埃希菌可呈现不不同的敏感模式，可出现多重耐药菌。yadF 基因缺失是嗜二氧化碳大肠埃希菌形成的机制之一。

关键字：嗜二氧化碳大肠埃希菌；yadF 基因；K-B 法；

其他

The Development and Validation of A Predictive Model for Voriconazole-Related Liver Injury in Hospitalized Patients in China

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Objective Voriconazole is widely used in the treatment and prevention of invasive fungal diseases. Common drug-induced liver injuries increase the economic burdens and the risks of premature drug withdrawal and disease recurrence. This study explores the risk factors of voriconazole related liver injury in hospitalized patients, and establishes a predictive model of liver injury, so as to reduce voriconazole related liver injuries, improve the compliance of voriconazole medication, enable a higher proportion of patients to complete the course of voriconazole treatment, and then increase the benefits of voriconazole treatment

Methods A single center retrospective study was conducted on the selected inpatients whose blood concentration of voriconazole was measured in West China Hospital of Sichuan University from September 2016 to June 2020. Patient's basic information, diagnosis, medical order sheet, and laboratory tests (liver biochemical indicators, voriconazole blood concentration) were automatically extracted through the hospital information system. After data cleaning, patients with abnormal liver biochemical indicators were manually checked in the electronic medical records to determine whether voriconazole was related, and the disposal cost was analyzed according to the medical order and the cost list. inclusion criteria were that hospitalized patients who received voriconazole and therapeutic drug monitoring (TDM) were eligible. Exclusion criteria were: (1) age ≤ 14 (the pharmacokinetic characteristics and dosage of voriconazole in children under 14 years old are different from those in adults); (2) duration of voriconazole usage < 5 d; (3) not steady-state trough concentration; (4) within 5 days prior to voriconazole use, the liver biochemical indicators were not measured or were higher than the upper limit; (5) during the use of voriconazole, the liver biochemistry was not measured within ±3 days of the TDM time, or the liver biochemical changes were caused by other factors (diseases, other drugs). Those meeting at least one of the above items were excluded. Drug-induced liver injury: There are many diagnostic criteria for drug-induced liver injury, mainly including the diagnostic criteria formulated by the Council for International Organizations of Medical Sciences (CIOMS) in 1990, the diagnostic criteria published by the Drug-Induced Liver Injury Network (DILIN) in 2009 , and the diagnostic criteria

formulated by the International DILI Expert Working Group (DEWG) in 2011. For the early detection and intervention of suspected cases of liver injury, the CIOMS standard with higher sensitivity was selected as the judgment standard of voriconazole-related liver injury in this study. CIOMS standard: (1) ALT > 2 × ULN; (2) DBil >2 × ULN; (3) AST or ALP or TBil > ULN, at least one of which > 2 × ULN. If one of the above three items is met, it will be judged as drug-induced liver injury.Single factor analysis and multiple factor logistic regression were used to analyze the risk factors of voriconazole-related liver injury. The cases that met the inclusion and exclusion criteria were divided into the derivation set and the verification set according to their admission time. The derivation set included cases from 1 September 2016 to 30 June 2019, and the verification set included cases from 1 July 2019 to 30 June 2020. The predictive model was established in the derivation set and independently validated in the validation set

Results The incidence and disposal cost of voriconazole-related liver injuries were calculated. The incidence of voriconazole-related liver injury was 15.82% (217/1372). The disposal cost has been converted to 2023 at a discount rate of 5%. The median (P25, P75) disposal cost of severe liver injury (n = 42), general liver injury (n = 175), and non-liver injury (n = 1155) was 993.59 (361.70, 1451.76) Chinese yuan, 0.00 (0.00, 410.48) yuan, and 0.00 (0.00, 0.00) yuan, respectively, with a statistically significant difference ($p < 0.001$). In the derivation set, the voriconazole-related liver injury group included 152 patients, and the non-voriconazole-related liver injury group included 883 patients. Seven potential predictors with $p < 0.1$ were selected by univariate analysis, including Cmin, hypoproteinemia, transplantation, cryptococcosis, decompensated cirrhosis, heart disease, and anemia. According to multivariable logistic regression, four variables were eliminated, included cryptococcosis, decompensated cirrhosis, heart disease, and anemia ($p > 0.05$). Three factors were found to be independently associated with the voriconazole-related liver injury outcome, including Cmin (OR = 1.099, 95% CI: 1.058–1.140, $p < 0.001$), hypoproteinemia (OR 1.723, 95%CI 1.126–2.636, $p = 0.012$), and transplantation (OR 0.555, 95%CI 0.325–0.948, $p = 0.031$). The prediction model of liver injury was Logit (P)= −2.219 + 0.094 × Cmin + 0.544 × Hydroproteinemia − 0.589 × Transplantation, and the prediction model nomogram was established. The internal and external validation of the nomogram model was carried out. The area under the curve (AUC) of the receiver operating characteristic (ROC) curve of the derivation set was 0.705 (sensitivity 0.789, specificity 0.582), the AUC of the ROC curve of the verification set was 0.733 (sensitivity 0.892, specificity 0.489), and the AUC was greater than 0.7. The nomogram correction curve was made, the consistency index (C-index) generated by the derivation set was 0.706, the C-index generated by the verification set was 0.733, and the calibration curve was close to the standard curve, indicating that the predicted probability was consistent with the actual probability, and the nomogram had a good fitting effect. The Yoden's index of the blood concentration was calculated to provide reference for the prediction of voriconazole-related liver injury. The results showed that the Yodon's index was 0.343, and the corresponding blood concentration was 4.375 mg/L (sensitivity 0.5855, specificity 0.7576), indicating that the liver injury was prone to occur when the blood concentration was greater than 4.375 mg/L after the use of voriconazole

Conclusion The prediction model will be helpful to develop clinical individualized medication of voriconazole and to identify and intervene in the cases of patients at high risk of voriconazole-related liver injury early on, in order to reduce the incidence of voriconazole-related liver injuries and the cost of treatment

关键字：voriconazole，liver injury，disposal cost，risk factor，prediction model，nomogram

1 例伏立康唑药物相互作用致横纹肌溶解的案例报道合并文献分析

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目的 探讨伏立康唑药物相互作用相关性肌损伤的临床特点，为该类不良反应的预防和药学监护提供参考。

方法 分析我院 1 例伏立康唑联合瑞舒伐他汀致横纹肌溶解的病例，同时查阅国内外相关文献并进行综述分析。

结果 我院 1 例肺曲霉菌感染合并颈动脉斑块患者使用伏立康唑联合瑞舒伐他汀治疗 15d 后出现横纹肌溶解早期症状，最终进展为多器官衰竭。文献分析提示伏立康唑与塞来昔布、他克莫司、甲强龙、奥美拉唑、埃索美拉唑、阿托伐他汀、瑞舒伐他汀联用时发生药物相关性肌病风险增加，主要表现为肌痛、肌无力、CK 升高，严重者出现横纹肌溶解，通常于用药后 12~15d 发生；有肝功能损害患者使用伏立康唑与奥美拉唑、埃索美拉唑、阿托伐他汀、瑞舒伐他汀联用时发生横纹肌溶解的风险更大，且大多预后不良。

结论 使用伏立康唑时应充分评估合并用药和患者基础状况，密切监测患者伏立康唑血药浓度、肌酶及临床表现，警惕伏立康唑药物相互作用所致横纹肌溶解的严重罕见不良反应。

关键字：伏立康唑，横纹肌溶解，肌损伤，肌炎，药物相互作用

The Clinical Features and Risk Factors of Coagulopathy Associated with Cefoperazone/sulbactam: A Nomogram Prediction Model

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Objective Cefoperazone/sulbactam (CPZ/SAM) is an important treatment option for infections caused by multidrug-resistant gram-negative bacteria. However, it is associated with an increased risk of coagulation disorders (CD) and causes severe bleeding in some instances. Early identification of risk factors and prediction of CD related to CPZ/SAM are crucial for prevention and treatment. However, limited research has been conducted on the risk factors and there are currently no reliable models available to predict the risk of coagulopathy in patients undergoing CPZ/SAM treatment

This study aimed to explore the risk factors and developed a nomogram model for predicting the risk of coagulopathy in patients undergoing CPZ/SAM treatment.

Methods We retrospectively identified 1719 patients undergoing Cefoperazone/sulbactam (CPZ/SAM) who were hospitalized in the Affiliated Hospital of Southwest Medical University from August 2018, to October 2022. Each patient receiving CPZ/SAM was evaluated for the causal association between drug and coagulopathy adverse drug reactions (ADRs) using the Naranjo algorithm. Based on the occurrence of whether coagulation disorders (CD) after receiving CPZ/SAM treatment, patients were divided into CD and the non-CD groups. The occurrence of CD was designated as the dependent variable. Univariate and multivariate logistic regression analyses were used to identify the risk factors of CD. Then a nomogram model was constructed from the multivariate logistic regression analysis and internally validated for model discrimination and calibration. The performance of the nomogram was estimated using the concordance index (C-index) and area under the receiver operating characteristic curve (AUC)

Results According to the causal association evaluation criteria between drug and coagulopathy adverse drug reactions, 110 of 1719 patients demonstrated CD. Most of the ADRs were mild or moderate, but 47 ADRs were classified as serious. The multivariate logistic regression analysis resulted in the following independent risk factors for CD: baseline INR level (OR: 5.768, 95% CI: 0.484~11.372, p=0.036), nutritional risk (OR:2.711, 95%CI: 1.495~4.125, p＜0.001), comorbidity of digestive system (OR:1.287, 95%CI: 0.434~2.215, p=0.004), poor food intake (OR:1.261, 95%CI: 0.145~2.473, p=0.032), ALB level (OR: -0.132, 95%CI: -0.229~-0.044, p=0.005) and GFR< 30ml/min (OR: 1.925, 95%CI: 0.704~3.337, p=0.004). Then the six factors obtained from multivariate logistical regression analysis were used to establisha nomogram of the risk of CD. And the internal validation confirmed the model's good performance (concordance index [C-index], 0.905 [95% CI: 0.864~0.945]). The calibration plots in the nomogram model were of high quality

Conclusion In conclusion, we constructed and validated a novel prognostic nomogram to predict the risk of CPZ/SAM induced CD. Through this model, clinicians could potentially identify patients at a higher risk of developing CD early on, allowing for timely intervention and management. This could lead to a reduction in the occurrence of CD associated with CPZ/SAM, and consequently improve patients' outcomes

关键字：Cefoperazone/sulbactam, Coagulation disorders, Risk factor, Nomogram, Predictive model

Exploration of A High-performance Liquid Chromatography Method for Antibiotic Drug Monitoring in Melioidosis Patients and Establishment of Its Sampling Procedure

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Objective Melioidosis is an infectious disease caused by the bacteria Burkholderia pseudomallei that poses a significant health issue in endemic regions such as Southeast Asia and the northern and southern parts of Australia. In recent years, the disease has been increasingly detected in known endemic areas, with studies showing that the Hainan Province is also a major endemic area for B. pseudomallei in China. Studies have suggested that insufficient dosage and treatment duration during the intensive and eradication phases is associated with resistance of B. pseudomallei to TMP/SMZ and a relapse of melioidosis. Long-term treatment in the eradication phasecan also lead to an increase in adverse reactions. Therefore, it is very important to monitor the

blood concentration of TMP/SMZ in melioidosis patients receiving this combined therapy and adjust the treatment regimen in a timely manner

Currently, there is a lack of research both in China and internationally on monitoring the blood concentrations and pharmacokinetics of orally administered TMP/SMZ in patients with melioidosis. This study establishes a high-performance liquid chromatography (HPLC) method for determining TMP and SMZ concentrations in human plasma. By monitoring these drug concentrations in the blood of patients with melioidosis, we aim to provide a basis for rational dosing regimens of TMP/SMZ in these patients.

Methods The study established and verified the feasibility of HPLC method using aminopyrine as an internal standardand trichloroacetic acid as precipitant to dilute the supernatant after plasma sample treatment and chromatographic separation by Acutfex YS-C8 column (4.6 × 250 mm, 5 μm) gradient elution. The mobile phase A consisted of 1000 mL of ultrapure water plus 2 mL of triethylamine with the pH adjusted to 6.0 using glacial acetic acid, while the mobile phase B was acetonitrile. The system operated using gradient elution at a flow rate of 1.0 mL·min-1and a wavelength of 240 nm

1.Sample processing

Blank, standard curve (including blank plasma 390 μL and different concentrations of standard working solution 10 μL), quality control (QC) (including blank plasma 390 μL and different concentrations of quality control working solution 10 μL), test plasma sample treatment: A 400 μL aliquot of a blood sample was placed in a pre-added 10 μL of internal standard working solution (blank plasma treatment consisted of 10uL of acetonitrile). Then, 40 μL 0.4 moL·L−1 mol·L trichloroacetic acid precipitant solution was added. The mixture was vortexed for 2 min, allowed to stand, and then centrifuged at 15,000 r·min−1 for 15 min. The supernatant was collected for sample analysis.

2.System adaptability experiment

Blank plasma, standard solutions of SMZ and TMP, and plasma samples of patients with melioidosis were used for the sampling analysis. Using the experimental design described above, we obtain chromatograms for blank plasma, blank plasma with SMZ and TMP control solution, and plasma samples of patients with melioidosis collected after the administration of TMP/SMZ.

3.Linearity

A 390 μL aliquot of blank plasma was added to 10 μL of standard curve working solution of different concentrations and then vortexed until mixed to prepare solutions containing TMP and SMZ at the following concentrations; 0.59, 2.36, 11.80, 29.50, 59.01 and 188.83 μg·mL−1 ; and 0.10, 0.51, 1.03, 2.36, 3.59 and 24.64 μg·mL−1 , respectively. The samples were processed according to the "Sample processing". A regression calculation using the weighted least squares method was then performed, with the concentration of the analyte (SMZ/TMP) as the abscissa (X), and the peak area ratio of the analyte (SMZ/TMP) to the internal standard (aminopyrine) as the ordinate (Y).

4.Precision and recovery rate

A 390 μL aliquot of blank plasma was added to 10 μL of standard curve working solution of different concentrations. The mixture was vortexed to prepare QC samples of SMZ that included a low quality control (LQC, 2.34 μg·mL−1), medium quality control (MQC, 28.13 μg·mL−1), and high quality control (HQC, 98.46 μg·mL−1). The concentration of the corresponding control samples for TMP were LQC (0.57 μg·mL−1), MQC (2.87 μg·mL−1), and HQC (4.78 μg·mL−1). The low, medium, and high concentration quality control samples were then processed with six parallel samples according to the "Sample processing" to determine the recovery rate and intra-day precision. Samples with above concentration were prepared and measured for three consecutive days to determine the daily precision of the method.

5.Stability

We carried out experiments to identify factors that might have affected the stability of SMZ and TMP and needed to be avoided during clinical acquisition and processing of the SMZ and TMP samples. The stability of the plasma quality control samples was investigated after being placed at room temperature for 4.0 h and in ice baths at − 20 ℃ and − 80 ℃ for 14 days, respectively.

6.Establishment of clinical sampling process for SMZ and TMP in patients with melioidosis

The established method was then used to measure the plasma concentrations of SMZ and TMP in 11 melioidosis patients from the Hainan region in China.y. First, the patients took TMP/SMZ tablets orally according to the physician’s prescription, and 2–3 mL blood was collected within 2 h of oral administration to measure peak concentration. The plasma was separated by centrifugation at 15,000 r·min-1 for 15 min and then stored in a − 80 ◦C freezer. After pre-treatment according to the "Sample processing".

Results 1.System suitability experiment

The chromatographic retention times of the internal standard aminopyrine, SMZ and TMP were 12.052 min, 9.615 min and 8.374 min, respectively. Determination of the analytes was highly specific with no interference from endogenous substances in the plasma.

2.Linearity

The linear regression equation for SMZ was Y = 0.0202X-0.0142, r = 0.9997 (n = 6), which showed a good linear relationship in the concentration range of 0.6–190 μg·mL−1 . Similarly, the linear regression equation for TMP was Y = 0.0709X-0.006, r = 0.9999 (n = 6), which showed a good linear relationship in the concentration range of 0.1–25 μg·mL−1.

3.Precision and recovery rate

The recovery rates of the SMZ samples with low,

medium, and high quality control concentrations were 107.12 %, 105.49 %, and 102.33 %, respectively. The relative standard deviation (RSD) for inter-day and intra-day ranged from 1.31 % to 1.68 %, while accuracy ranged between 102.50 % and 107.26 %. The recovery rates of the TMP samples with low, medium, and high quality control concentrations were 93.85 %, 104.81 %, and 105.67 %, respectively, with the inter- and intra-day RSD ranging from 0.39 % to 3.84 %, and accuracy from 89.08 % to 102.46 %. The above results indicate that the recovery rate, precision, and accuracy of this research HPLC method meet the requirements for biological sample analysis and detection.

4.Stability

Low and high concentration quality control samples that had been stored at room temperature for 4 h or at − 80 ℃ or − 20 ℃ for 14 days were tested. Six samples of each concentration were processed to investigate their stability according to the sample treatment method. The results showed that the RSDs of SMZ and TMP were both below 15 %, indicating that the matrix samples can be stored at room temperature for 4 h and at − 80 ℃ and − 20 ℃ for at least 14 days.

5.Clinical monitoring

The blood concentrations of SMZ and TMP in the plasma of 11 patients with melioidosis after oral administration of TMP/SMZ tablets were measured by the HPLC method. The peak concentration range for SMZ was 8.77–102.94 μg · mL−1 and for TMP was 1.89–11.27 μg · mL−1 .

Conclusion Our study developed a simple, cost-effective HPLC method that can be used in hospitals to simultaneously measure SMZ and TMP in plasma samples. The method has excellent linearity, accuracy, and precision, and has been used successfully to measure the blood concentrations of SMZ and TMP in the plasma of patients with melioidosis at Hainan General Hospital after oral administration of TMP/SMZ. The results of the study contribute significantly to clinical pharmacokinetic studies in patients with melioidosis

关键字：Sulfamethoxazole; Trimethoprim; High-performance liquid chromatography; Therapeutic drug monitoring; Melioidosis

小分子化合物CDBN-YGXZ对艰难拟梭菌的体外抗菌作用研究

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目的 通过体外药敏实验、肠道上皮细胞粘附及诱导耐药实验等检测小分子化合物 CDBN-YGXZ 的体外抗菌作用、抗细胞粘附作用及诱导耐药情况。

方法 选取 150 株临床来源艰难拟梭菌，采用琼脂对倍稀释法进行CDBN-YGXZ的药物敏感性检测；选取部分肠道定植菌如金黄色葡萄球菌、阴沟肠杆菌、大肠埃希菌、肺炎克雷伯杆菌、粪肠球菌、屎肠球菌、脆弱拟杆菌、两双歧杆菌、丁酸梭菌等采用琼脂对倍稀释法和微量肉汤稀释法进行药物敏感性检测。选取产二元毒素的标准菌株 ATCC1870（RT027）与肠上皮细胞 Caco-2 共培养，分别对培养后的加药组和未加药组细胞爬片上的菌进行涂平板计数，计算平板上的平均菌落数，定量检测 CDBN-YGXZ 对艰难拟梭菌粘附肠上皮细胞的抑制作用。选取我国流行的几种 ST 型菌株，采用亚抑菌浓度（1/2MIC）肉汤传代法和体外多步诱导实验对该药进行体外诱导耐药检测。

结果 药敏结果显示所有临床来源菌株对 CDBN-YGXZ 都较敏感，MIC 范围为 0.03-0.125mg/L，MIC50 是 0.06 mg/L MIC90 是 0.125mg/L。肠道定植菌中除了两双歧杆菌和丁酸梭菌对该药较为敏感 MIC 值为 0.25mg/L，其他菌对该药不敏感；肠道上皮细胞粘附实验显示，该药能抑制 86.2%的艰难拟梭菌与 Caco-2 细胞粘附；且经过两种方法的诱导，未出现 MIC 值升高 4 倍的菌株。

结论 由以上结果可以看出，CDBN-YGXZ 具有较好的体外抗菌作用，且对肠道菌的影响较小，能够抑制大部分艰难拟梭菌与肠道上皮细胞的粘附，不容易产生耐药等特点。因此该药具有进一步研究的价值。

关键字：艰难拟梭菌，药敏，粘附，诱导耐药，小分子药物

血流感染病原体分布和炎症指标水平变化及其预测价值

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目的 了解血流感染患者的病原菌分布，分析革兰阳性或阴性细菌感染患者血液中降钙素原（PCT）、C反应蛋白（CRP）、中性粒细胞计数（NEUT）及百分比（NEUT%）、淋巴细胞计数（LYMPH）及百分比（LYMPH%）和中性粒细胞淋巴细胞比值（NLR），ROC 曲线分析诊断效能。

方法 本研究选取 2020 年-2023 年本院诊治的患者共 363 例，根据血培养结果分为革兰阳性菌血流感染组（103 例）、革兰阴性菌血流感染组（125 例）和对照组（135 例）。采用胶乳增强免疫比浊法检测 CRP，化学发光法检测血清 PCT，血细胞分析仪检测 NEUT、NEUT%、LYMPH 及 LYMPH%，并计算 NLR。比较三组 CRP、PCT、NEUT、NEUT%、LYMPH、LYMPH%，采用 SPSS 软件绘制受试者工作特征曲

线（ROC）。

结果 三组炎症标志物 CRP、PCT、NEUT、NEUT%、LYMPH、LYMPH%和 NLR 差异均有统计学意义（P<0.05）。CRP、PCT、NEUT、NEUT%、LYMPH、LYMPH%和 NLR 对革兰阳性菌或阴性菌血流感染诊断价值均有统计学意义（P<0.05）。CRP、PCT、NEUT%、LYMPH、LYMPH%和 NLR 在预测革兰阳性菌或阴性菌血流感染中具有诊断价值（P<0.05）。ROC 曲线分析表明，PCT 对革兰阳性菌/阴性菌血流感染诊断效能和细菌感染类型的预测价值最高。

结论 血流感染中革兰阴性菌占 54.82%，略高于革兰阳性菌。不同炎症指标对血流感染诊断效能各有差异，其中 PCT 诊断效能最高。本文研究数据显示：PCT 值高于 1.64 ng/mL，CRP 高于 79.16 mg/L，NLR 大于 11.30 提示革兰阴性菌感染可能性增大。本研究可以为临床上对不同病原菌血流感染辅助检查及治疗提供实验依据。

关键字：血流感染，革兰阳性菌，革兰阴性菌，降钙素原，C 反应蛋白，中性粒细胞淋巴细胞比值

广州市儿童 TORCH 指标筛查结果及常见感染模式分析

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目的 分析广州市 0～18 岁未成年人 TORCH 指标筛查结果和常见感染模式并探讨其可能原因。

方法 选择自 2019 年 1 月 1 日至 2021 年 8 月 11 日共 3 390 例 0～18 岁未成年人的 TORCH 特异性 IgM 结果，分析其阳性率的差异和感染模式。

结果 HSV-1 IgM 抗体阳性率(10.9%)高于 TOX(0.4%)、RUV(0.8%)、CMV(2.9%)、HSV-2(1.7%),差异具有统计学意义(P<0.05)。3～12 岁儿童 HSV-2 IgM 抗体阳性率(5.3%)、TOX IgM 抗体阳性率(1.4%)与 0～3 岁婴幼儿 HSV-2 IgM 抗体阳性率(0.8%)、TOX IgM 抗体阳性率(0.2%)相比，差异有统计学意义(P<0.05);12～18 岁青少年 HSV-2 IgM 抗体阳性率(7.1%)、CMV IgM 抗体阳性率(7.0%)、TOX IgM 抗体阳性率(2.4%)与 0～3 岁婴幼儿 HSV-2 IgM 抗体阳性率(0.8%)、CMV IgM 抗体阳性率(2.4%)、TOX IgM 抗体阳性率(0.2%)相比，差异有统计学意义(P<0.05);TORCH 病原体的阳性率在不同年度、不同性别、不同季节间无统计学差异。单一病原体感染占多数，以单纯疱疹病毒 I 型感染为主，占 6.67%(5/75);混合感染以单纯疱疹病毒I型+单纯疱疹病毒II型感染为主，占 4.0%(3/75)。

结论 广州市儿童 TORCH 感染以 HSV-1 较为普遍，TOX 感染较为少见，存在年龄差异，以单种病原体感染多见。

关键字：TORCH;IgM;儿童;季节;

自上而下法在评定生化测量不确定度中的应用

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目的 探讨自上而下法评估测量不确定度在临床生化检验中的应用。

方法 收集广东省人民医院检验科生化室 2019 年质控批号稳定至少 3 个月的室内质控（IQC）数据和国家卫生健康委临床检验中心 2017-2019 年的室间质评（EQA）回报结果，采用自上而下法评定 15 项临床生化指标的测量不确定度。

结果 采用 Beckman DXI800 化学发光仪检测游离三碘甲状腺原氨酸（FT3）、三碘甲状腺原氨酸（T3）、游离甲状腺素（FT4）、甲状腺素（T4）、促甲状腺激素（TSH）、皮质醇（COR）、叶酸（FA）、维生素 B12（VitB12）、前列腺特异性抗原（PSA）、癌胚抗原（CEA）、甲胎蛋白（AFP）、铁蛋白（FER）、人绒毛膜促性腺激素（β-HCG）、游离前列腺特异性抗原（fPSA）、肌钙蛋白-I（cTnI）15 项生化指标的相对扩展标准不确定度均满足国家卫生健康委临床检验中心室间质量评价标准的要求。其中批间不精密度与相对扩展标准不确定度呈中度相关（r=0.685，P<0.001），偏移呈强相关（r=0.827，P<0.001）。批间不精密度分量占比更大，在大部分生化指标中呈主要分量趋势。

结论 应用自上而下法评定测量不确定度适用于临床生化检验项目，是一种经济可行的评定方法。不同项目不同分量来源的主要占比不同，为实验室质量管理提供了改进方向。

关键字：自上而下法；测量不确定度；室内质控（IQC）；室间质评（EQA）

2017-2022 年中国西南地区基层医疗机构抗生素处方趋势与模式研究

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目的 探讨 2017-2022 年中国欠发达地区基层医疗机构抗生素处方模式及使用趋势，为基层医疗机构抗生素诊疗指南的制定奠定理论基础。

方法 首先，对 2017-2022 年贵州省的 25 家基层医疗机构抗生素处方进行回顾性分析。将抗生素处方分为合理用药和不合理用药，从而分析基层医疗机构抗生素不合理使用的总体情况。合理用药进一步分为首选用药和可以使用或替代用药；不合理用药进一步为不必要使用、抗菌谱不正确和抗生素联合使用。其次，使用广义估计方程分析基层医疗机构抗生素不合理使用的影响因素。最后，比较 Holt-Winters 模型和 SARIMA 模型在抗生素不合理处方量的预测效果，筛选出预测精度更高的模型。

结果 本研究共纳入 941,924 张处方，分析结果显示 2017-2022 年抗生素的处方量和不合理率均呈下降趋势。使用抗生素最多的疾病是呼吸系统疾病，其中多发且部位不明的急性上呼吸道感染占 52.04%。基层医疗机构最常用的抗生素是青霉素类（64.44%）。在所有处方中，不合理的抗生素处方占 66.19%。年龄在 35 岁以上，职称为副主任医师，且工作年限在 11 年以上的医生更容易开出不合理的抗生素，不合理使用抗生素的现象在 5 岁及以下儿童中更为常见。通过模型参数的比较，发现 SARIMA 模型在基层医疗机构不合理抗生素处方量的预测精度优于 Holt-Winters 模型。

结论 2017-2022 年，中国西南地区抗生素处方量和不合理率均呈下降趋势，但不合理抗生素处方仍是基层医疗机构存在的严重问题。因此，今后应着重加强医生专业知识的教育、培训和临床实践。此外，必须加强医生对抗生素不合理使用常见误解的认识，并改变医生以开抗生素来满足患者期望的处方行为。

关键字：抗生素，基层医疗机构，趋势，处方模式，不合理用药

单宁酸联合亚胺培南对耐碳青霉烯鲍曼不动杆菌的体外抑菌和生物膜作用研究

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目的 探究单宁酸与亚胺培南联合用药对耐碳青霉烯鲍曼不动杆菌（CRAB）的体外抑菌活性和抗生物膜作用，为单宁酸联合亚胺培南治疗 CRAB 感染提供理论依据。

方法 收集临床分离的不重复 CRAB 菌株 30 株。利用结晶紫半定量黏附试验观察 CRAB 菌株生物膜形成能力。通过微量肉汤稀释法分别检测单宁酸和亚胺培南对 CRAB 的最低抑菌浓度（MIC），根据联合抑菌浓度指数（FICI）评估药物联合作用效果。观察亚抑菌浓度药物对生物膜形成的影响。通过扫描电子显微镜（SEM）观察在药物作用下成熟生物膜微观形态的变化。

结果 30 株临床分离 CRAB 菌株中，生物膜弱阳性菌株 8 株（26.7%）、生物膜阳性菌株 11 株（36.7%）、生物膜强阳性菌株 10 株（33.3%）。单宁酸和亚胺培南对 30 株 CRAB 菌株的 MIC 范围在 64~256μg/ml 之间，单宁酸与亚胺培南联合用药表现为相加作用。1/4MIC 单宁酸可以有效抑制 CRAB 生物膜形成，光密度值由 0.3462±0.0221 降低至 0.2576±0.0133（P＜0.05），联合用药组光密度值由 0.3462±0.0221 降低至 0.2162±0.0223，抑制效果最好（P＜0.05）。扫描电镜结果显示药物联用组生物膜明显减少，细菌形态有明显变化，细菌菌体皱缩，细菌细胞壁有破洞。

结论 临床分离 CRAB 菌株容易在体外形成稳定的生物膜，单宁酸与亚胺培南联用可以增强对 CRAB 菌株的抑菌效果和抗生物膜作用。

关键字：单宁酸；亚胺培南；碳青霉烯；鲍曼不动杆菌；生物膜；

基于美国 FAERS 的四环素类药物致急性胰腺炎 ADE 信号的挖掘与分析

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目的 挖掘四环素类药物（四环素、多西环素、米诺环素、替加环素及奥马环素）相关急性胰腺炎（AP）的风险信号，分析两者关联性，为临床安全用药提供参考。

方法 收集美国 FAERS 数据库 2004 年 1 月至 2023 年 3 月上报的 4 种四环素类药物相关的 AP 报告。采用报告比值比(ROR)、比例报告比(PRR) 进行数据挖掘。利用《国际医学用语词典》（24.0）版药物不良事件术语集中的首选术语（PT）进行分类统计。

结果 共筛选出 373 例以四环素类药物为可疑药物的 AP 报告，其中替加环素 130 例，多西环素 216 例，米诺环素 27 例，奥马环素及四环素未见与 AP 相关报告。替加环素、多西环素与 AP 均存在统计学相关性，其中以替加环素（ROR 15.62（95%CI：13.08～18.64），PRR14.77）信号最强，米诺环素未检测到与 AP 相关的阳性信号。与 AP 相关报告中，替加环素及多西环素女性患者占比更高。替加环素导致 AP 的发病年龄中位数为 54（5～91）岁，31～55 岁（30/130,23.08%）为其高发病年龄段；多西环素发病中位年龄为 58（16～91）岁，患者中年龄≥70 岁（56/216,25.92%）占比较大。替加环素及多西环素

高发病时间段均为 0～10d，发病时间中位数分别为 7(0～246)d、11（1～484)d，两药中以替加环素（19/130,14.61%）死亡率更高。

结论 替加环素与多西环素均有发生 AP 的风险，与 AP 相关病例中女性均多于男性，31～55 岁为替加环素导致 AP 的高发病年龄段，多西环素中年龄≥70 岁的老年患者占比较高，0～10 d 为替加环素及多西环素高发病时间段。建议临床针对替加环素及多西环素导致 AP 的不同特点进行个体化监护，以提高临床治疗安全性。

关键字：四环素类药物；急性胰腺炎；美国食品和药物管理局不良事件报告系统

GLIM 标准下不同营养风险筛查工具在慢性肝病患者中的应用评估

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目的 探讨营养风险筛查量表 2002（NRS2002）、英国皇家自由医院营养优先工具（RFH-NPT）以及肝病营养不良筛查工具（LDUST）与全球领导人营养不良倡议（GLIM）标准的一致性，以确定慢性肝病患者营养筛查最合适的评估工具。

方法 选取 2020 年 9 月至 2022 年 1 月在四川大学华西医院就诊的 189 例慢性肝病患者。分别使用 NRS2002、RFH-NPT 和 LDUST 进行营养风险筛查，应用 GLIM 标准进行营养不良诊断，确定营养不良患病率，检验筛查工具与 GLIM 标准的一致性。再计算三种筛查工具的受试者工作特征曲线（ROC）下面积（AUC）及敏感度、特异度、阳性预测值、阴性预测值。

结果 GLIM 标准下 42.3%的患者存在营养不良，NRS2002、RFH-NPT、LDUST 分别筛查出 38.1%、51.9%、67.2%的患者存在营养不良。NRS2002 的特异度最高（84.4%），阳性预测值最高（76.4%），LDUST 灵敏度最高（95%）和阴性预测值最高（93.5%）。RFH-NPT 与 GLIM 标准具有最高的一致性（Kappa=0.633，P＜0.001），具有更好的预测价值（AUC=0.82，95%CI: 0.758～0.872）。

结论 GLIM 标准下 CLD 患者营养不良发生率高，RFH-NPT 可以作为 CLD 患者营养筛查最适合的工具。

关键字：慢性肝病，营养不良，营养风险筛查 2002，全球领导人营养不良倡议，营养风险筛查

肠脂肪酸结合蛋白在预测慢加急性肝衰竭发生发展中的应用价值

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目的 探讨肠脂肪酸结合蛋白（intestinal fatty acid binding protein，I-FABP）对慢加急性肝衰竭（acute on chronic liver failure，ACLF）的预测价值。

方法 回顾性分析 2020 年 9 月至 2023 年 3 月我院收治的 168 例成年肝硬化失代偿患者的临床资料，评估器官衰竭评分（Chronic Liver Failure-organ Failure score，CLIF-OF）和终末期肝病模型（model of end-stage liver disease，MELD），观察入院合并 ACLF 和随访六个月新发 ACLF 事件。用 ELISA 法测定患者入院血清 I-FABP 水平。多因素 Cox 回归分析确定随访发生 ACLF 的预测因素。受试者工作特征（ROC）曲线确定最佳截断值，曲线下面积（AUC）比较预测效能。

结果 入组 168 例患者中有 43 例合并 ACLF，125 例无 ACLF 患者中有 19 例在随访期间新发 ACLF。纳入时合并以及随访发展为 ACLF 患者的 I-FABP 水平均高于无 ACLF 者，差异均有统计学意义（Z=4.359，3.414，均 P<0.001）。I-FABP 随 ACLF 分级增加而升高（H=17.385，P<0.001，P 趋势<0.001）。多因素分析显示 I-FABP 与随访期间新发 ACLF 独立相关（HR=2.138，95%CI：1.297～3.525，P=0.003），且 I-FABP 三分位数显示出良好的预测区分能力（Log-rank $\chi2$=12.16，P<0.001）。ROC 曲线显示 I-FABP 对 ACLF 发生和发展具有较高的诊断和预测效能，AUC 分别为 0.854（95%CI：0.791 ～ 0.903）和 0.747（95%CI：0.661～0.820），最佳截断值为 2.07 μg/L 和 1.86 μg/L。

结论 I-FABP 是预测 ACLF 发生和发展的生物标志物，有助于临床识别高危患者，改善临床管理。

关键字：慢加急性肝衰竭，胃肠道功能障碍，肠脂肪酸结合蛋白

Protective Role of The Novel Cytokine Metrnl/ Interleukin-41 in Host Immunity Defense During Sepsis by Promoting Macrophage Recruitment and Modulating Treg/Th17 Immune Cell Balance

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Objective Metrnl play an immunocytokine-like

role in several diseases, which is also known as meteorin-like because it is homologous to the neurotrophic factor meteorin (Metrn). Although the expression and function of Metrnl, including neurotrophic, immunomodulatory, and insulin resistance functions in different tissues have been extensively studied, its role in sepsis has remained largely limited.

Methods The present work analyzed the levels of Metrnl and cytokines in the circulation, such as tumor necrosis factor (TNF-α), interleukin (IL-1)β, IL-6, IL-8, together with IL-10 among septic adult patients. Clinical information was obtained from such patients, including sofa score, procalcitonin(PCT)count, and C-reactive count (CRP) within 24 h when entering the intensive care unit (ICU). We constructed a sepsis model in Metrnl-deficient or normal wild-type mice using cecal ligation and perforation to study its functions in bacterial burden, survival, cytokine/chemokine generation, peritoneal lavage fluid neutrophils, macrophage and lymphocyte recruitment, and Treg/Th17 immune cell balance after CLP-induced sepsis.

Results The expression of Metrnl was remarkably elevated in the early phase of sepsis clinically. Its serum content in patients dying of sepsis slightly decreased relative to that in survivors. Furthermore, the concentration of Metrnl in septic cases when entering the ICU independently predicted the 28-day mortality. For septic patients who had low serum Metrnl content (≤ 274.40 pg/mL), the death risk increased by 2.3 folds relative to those who had a high serum content. It is reported that Metrnl is probably insufficient among patients dying of sepsis. Additionally, the content of Metrnl in the serum of septic patients when entering the ICU is markedly and negatively related to the levels of TNF-α, IL-1β, IL-6, IL-8, IL-17, PCT, and Sofa score. Collectively, Metrnl could be a potential therapeutic target for sepsis. A low-lethality non-severe sepsis (NSS) model was constructed, which suggested that Metrnl insufficiency elevated the death rate and reduced bacterial clearance during sepsis. For Metrnl-deficient mice, impaired sepsis immunity defense might be related to decreased macrophage recruitment and Treg/Th17 lymphocyte imbalance. Recombinant Metrnl administered to Metrnl-deficient mice abolished the immunity defense impairment following NSS while protecting the high-lethality severe sepsis (SS) model in wildtype (WT) mice. In addition, Metrnl-induced sepsis prevention was intricately associated with the increased recruitment of peritoneal macrophages and modulation of the Treg/TH17 immune cell balance. Furthermore, CCL3 exposure in Metrnl-deficient mice reduced peritoneal bacterial loads while improving survival during sepsis partially by promoting the recruitment of peritoneal macrophages. Furthermore, Metrnl regulated the polarization of M1 macrophages through the ROS signaling pathway and promoted macrophage phagocytosis, thereby killing Escherichia coli.

Conclusion The present proof-of-concept work suggests that Metrnl-mediated recruitment of macrophages significantly affects sepsis defense in the host and modulates the Treg/Th17 immune cell balance. Findings in this work shed more light on the development of host-directed treatments that can be used to manipulate host immunity to treat sepsis.

关键字：Sepsis, Metrnl, Treg/Th17 lymphocytes, ROS, P-STAT3, P-STAT5

Predicting COVID-19 Severity and Mortality: Role of Respiratory Microbiota

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目的 明确不同病情，不同临床结局新冠感染患者呼吸道微生物群的特征。

方法 回顾性分析 2022.12.26-2023.02.17 入住我院的 40 名新型冠状肺炎患者临床资料，对住院期间肺泡灌洗液超多重 PCR 靶向高通量测序的结果进行汇总，根据新型冠状病毒感染诊疗方案（试行第十版）进行临床分期，比较不同临床结局、不同转归患者呼吸道菌群多样性，差异物种，分析临床指标的差异。

结果 将患者按照不同病情分为轻（n=3）、中（n=13）、重（n=16）、危重组（n=8），组间呼吸道菌群 α 多样性（Chao, Shannon , Simpson, Richness Index）差异无显著性（P＞0.05），菌群组成结构 β 多样性差异具有显著性，不同病情呼吸道微生物组成不同（P＜0.05），且与其它组相比，危重组患者菌群中铜绿假单胞菌、白色念珠菌丰度高，淋巴细胞计数，血小板计数升高，PCT 降低（P＜0.05），铜绿假单胞菌可以作为病情危重的预测指标（AUC:0.837）。按照转归情况分为死亡组（n=5）和好转组（n=35），组间呼吸道菌群 α 多样性差异无显著性（P＞0.05），菌群组成 β 多样性差异有显著性，不同临床结局呼吸道微生物组成不同（P＜0.05），与好转组相比，死亡组患者铜绿假单胞菌、白色念珠菌、木糖氧化产碱菌、多食伯克霍尔德菌丰度高，淋巴细胞值降低（P＜0.05）。铜绿假单胞菌（AUC:0.84）、淋巴细胞（AUC: 0.842），血小板（AUC: 0.742）可以作为新型冠状病毒肺炎死亡的预测指标。

结论 呼吸道菌群多样性较少，不同组别间差异不大，但是组成差异明显。菌群的组成与病情严重程度及临床预后有明显的相关性。其中铜绿假单胞菌可以作为一个新型冠状病毒肺炎死亡、病情危重的预测指标。

关键字：COVID-19，呼吸道菌群，超多重 PCR 靶向测序，临床预测指标

A Novel Strategy for Therapeutic Drug Monitoring: Application of Biosensors To Quantify Antimicrobials in Biological Matrices

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Over the past few years, therapeutic drug monitoring (TDM) has gained practical significance in antimicrobial precision therapy. Yet two categories of mainstream TDM techniques (chromatographic analysis and immunoassays) that are widely adopted nowadays remain certain inherent limitations. Biosensor, an innovative strategy for rapid evaluation of antimicrobial concentrations in biological samples, enables the implementation of point-of-care testing (POCT) and continuous monitoring, which may circumvent the constraints of conventional TDM and provide strong technological support for individualized antimicrobial treatment. This comprehensive review summarized the investigations that harnessed biosensors to detect antimicrobial drugs in biological matrices, provided insights into the performance and characteristics of each sensing form, and explored the feasibility of translating them into clinical practice. Furthermore, the future trends and obstacles to achieving POCT and continuous monitoring were further discussed. More efforts are necessary to address the four key "appropriateness" challenges to deploy biosensors in clinical practice, paving the way for personalized antimicrobial stewardship.

关键字：Biosensors, Antimicrobial drugs, Therapeutic drug monitoring, Point-of-care testing, Continuous monitoring, Biological matrices

Nephroprotective Potential of Piceatannol-3′-O-β-D-glucopyranoside Against Polymyxin B-induced Kidney Injury by Reducing Ferroptosis and Apoptosis Via Activating NRF2 Signaling Pathway

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Objective Nephrotoxicity remains a key obstruction for clinical applications of polymyxin B (PMB), an effective method to ameliorate injury is desperately needed. As a new drug, piceatannol 3′-O-β-d-glucoside (PG) has been proved to attenuate the pathological changes of nephrotic syndrome rats. In the study, we aim to explore the molecular mechanism of PMB-induced nephrotoxicity and PG's reno-protective effect in vivo and in vitro

Methods Proteomics technique was applied to screen the differentially expressed proteins in HK2 cells exposed to PMB, providing data for further mechanism research. Furtherly, PMB-induced kidney injury cell model and mice model were established and verified. In vitro, CCK8 assay was used to determine PMB's toxicity in HK2 cells. In vivo, kidney injury model was constructed with ICR mice treated with PMB. Mice were randomly divided into three groups: control, PMB (15 mg/kg), PG intervention (PG 8 mg/kg + 15 mg/kg PMB). HE staining, biochemical markers (BUN, Cre) and kidney index were used to analyze the degrees of kidney injury. Then, the influence of PMB and PG+PMB on oxidation stress, mitochondria, apoptosis and ferroptosis was evaluated. Especially, antioxidant substances (SOD, CAT, GSH), lipid peroxidation substance malondialdehyde (MDA) in kidney tissue was assessed using ELISA experiment, ROS level in HK2 cells was assessed using flow cytometry. Mitochondria morphology and mitochondrial membrane potential ($\Delta\psi$ m) were analyzed by electron microscope and laser scanning confocal microscopy. Apoptosis level and lipid peroxidation level was determined by flow cytometry, Ferrous iron was analyzed by ELISA experiment, western blot experiment was applied to analyzed the expression of apoptosis-related proteins (caspase-9, caspase-3) and ferroptosis-related proteins (SLC7A11, GPX4, ACSL4). Finally, western blot experiment was applied to explore the mechanism of PG's reno-protective effect in PMB-induced nephrotoxicity

Results From proteomic analysis, PMB induced differentially expressed proteins were mainly enriched in signal transduction pathways including oxidative stress, fatty acid oxidation, NRF2 pathway signaling pathways. CCK8 experiment showed PMB possess cytotoxic effect on HK-2 cells. HE staining showed PMB induced an obvious kidney injury. Furtherly, we found that PMB increased ROS level in HK2 cells, which was consistence with decreased level of antioxidant substances (SOD, CAT, GSH) and increased level of MDA in mice treated with PMB. PMB reduced the value of $\Delta\psi$ m and mitochondrial crest, induced mitochondrial damage. Flow cytometry also showed that PMB increased apoptosis level, up-regulated the level of lipid peroxidation, ferrous iron was also increased in HK2 cells after PMB treatment. Finally, western bolt experiments showed that PMB increased the expression of apoptosis proteins (caspase-9, caspase-3) and ferroptosis protein (ACSL4), decreased the expression of ferroptosis-suppressor proteins (SLC7A11, GPX4). After PG intervention, as an antioxidant, PG reduced ROS level and alleviated mitochondrial damage through activating NRF2 pathway, mitigate PMB-induced ferroptosis and apoptosis, finally improved kidney injury. Adding Brusatol (NRF2 inhibitor), PG's reno-protective

effect was reduced

Conclusion In the study, we found NRF2 inhibition induced oxidation stress and mitochondrial damage, promoted the occurrence of ferroptosis and apoptosis, contributed to PMB-induced nephrotoxicity. PG as a NRF2 activator, mitigated PMB-induced ferroptosis and apoptosis, finally improved kidney injury

关键字：Nephrotoxicity, NRF2 pathway, Oxidative stress, Apoptosis, Ferroptosis

艾滋病患者结核病相关免疫重建炎症综合征临床特征与预测指标研究

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目的 艾滋病合并结核病患者启动抗逆转录病毒治疗（ART）后，可能发生免疫重建炎症综合征（IRIS）使病情恶化，目前对其临床预测指标仍不清楚。

方法 回顾性纳入 2020 年 6 月至 2023 年 6 月广州医科大学附属市八医院艾滋病合并结核病（临床和/或病原学诊断）患者，根据 ART 后是否发生 IRIS 分成 IRIS 组和 Non-IRIS。收集患者基线、发生 IRIS 时的人口学与临床特征、常规实验室指标、HIV RNA 载量、淋巴细胞精细分群，比较两组差异，并采用多因素 Logistic 回归分析与 IRIS 发生可能相关的基线指标。

结果 共 217 例患者纳入研究，54 例（24.9%）ART 后发生 IRIS，IRIS 发生中位时间为 17 天（IQR: 11～31），33 例（61.1%）发生于 ART 启动后 3 周内；症状主要包括：再次发热（83.3%）、呼吸道症状加重（18.5%）及淋巴结肿大加重（14.8%）。比较两组基线，IRIS 组白细胞介素-2（IL-2）和干扰素-γ（IFN-γ）显著高于 Non-IRIS 组（1.93 vs 1.39 pg/ml，P=0.036；7.69 vs 4.94 pg/ml，P=0.045），B 淋巴细胞数量显著低于 Non-IRIS 组（20 vs 43 个/μl，P=0.049）。IRIS 组抗结核治疗到 ART 启动间隔短于 Non-IRIS 组（9 vs 15 天，P=0.008）。发生 IRIS 时 IRIS 组和 Non-IRIS 组比较，前者的 C 反应蛋白（37.14 vs 0mg/L，P<0.001）、降钙素原（0.357 vs 0.075ng/mL，P=0.001）、IFN-γ（6.38 vs 4.88pg/mL，P=0.05）、白细胞计数（6.3 vs 3.47 109/L，P<0.001）、中性粒细胞计数（4.53 vs 3.54 109/L，P=0.033）、总 T 活化%（57.12 vs 39.52%，P=0.007）、杀伤性 T 活化%（58.03 vs 43.07%，P=0.035）及 CD4/CD8 增长值（0.045 vs 0.007，P=0.023）明显更高，HIV RNA 明显更低（316 vs 535 拷贝/ml，P=0.005）。多因素分析显示，更高的基线 IL-2 水平和总 T 细胞活化%，可能与 IRIS 发生相关（OR=1.76，P=0.048；OR=1.03，P=0.048）。

结论 艾滋病合并结核病患者主要于 ART 后 3 周内发生 IRIS，主要表现为多个炎症指标及 CD4+ 计数明显升高，HIV RNA 明显更低，较高的基线 IL-2 水平和总 T 细胞活化比例可能是 IRIS 发生的预测因子。

关键字：免疫重建炎症综合征，结核病，艾滋病，白细胞介素-2（IL-2）

AECOPD 患者气道微生物群落组成及其与宿主营养、炎症的关联研究

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背景 COPD 患者的气道处于一种微生态紊乱的状态，然而其细菌群落和真菌群落结构与机体营养状态的关联分析较少。

方法 我们通过对 63 名 AECOPD 患者痰液进行收集，对痰液 DNA 的 ITS1 和 16S rRNA V4 区段测序，探索气道中酵母菌的多样性及气道细菌真菌互作网络模式。通过菌群与宿主营养、炎症相关指标的关联分析探索 AECOPD 患者与宿主营养状态相关的特征菌 。

结果 微生物组学测序发现人群气道中酵母菌属检出数量与气道细菌的 α-多样性呈反比，此外，念珠菌属与气道中的常驻细菌普氏菌属等相对丰度呈负相关，细菌与真菌互作的相关性网络图显示梭杆菌细菌与赤霉菌属真菌是与其他微生物关联最为密切的。菌群的 beta 多样性与临床炎症、营养指标分析，发现在细菌层面 AECOPD 患者 NAR、TP、ALB、IL-17A、IL-6 群落 beta 多样性之间有不同程度差异（P<0.05）。真菌层面 IL-8 与群落 beta 多样性有显著的差异（P<0.05）。营养指标 BMI、Hb、TP、ALB 、PNI，炎症指标 PCT、WBC、NEU、LY、NAR、PLR、NLR 分别与细菌、真菌群落有不同程度的相关关系（P<0.05）。营养指标显示白蛋白与萨特氏菌呈正相关关系，而与普雷沃菌、慢生根瘤菌属呈负相关关系（P<0.05）。

结论 AECOPD 气道细菌和真菌相互作用，细菌与营养相关指标关联更为密切。

关键字：AECOPD，营养水平，16S rRNA，ITS1

AECOPD 患者气道来源的 8 种酵母菌促进小鼠宿主炎症反应比较研究

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背景 COPD 患者的气道处于一种微生态紊乱的状态，真菌的气道内定植在 COPD 的免疫炎症中发挥着重要作用。课题组前期研究报道了 COPD 患者气道中定植了多种念珠菌属，然而其功能尚不明确。

方法 我们通过对 63 名 AECOPD 患者痰液进行真菌培养，分离其中主要的酵母菌；进一步将气道中分离得到的 8 种主要的酵母菌定植到小鼠气道中，对小鼠肺组织的 HE 染色、qPCR、16S rRNA V4 区段测序等方法以探索不同酵母菌促进宿主炎症反应的差异。

结果 在入组 63 例 AECOPD 志愿者中，50（80.95%）人痰液中检出酵母样真菌，检出率排名前 5 的酵母样真菌为白色念珠菌、光滑念珠菌、近平滑念珠菌、拟平滑念珠菌、都柏林念珠菌。酵母菌定植到小鼠气道后会不同程度诱发小鼠气道炎症反应，肺组织 HE 染色评分 2-7 分不等。小鼠的体重显示白色念珠菌、克柔念珠菌、近平滑念珠菌、热带念珠菌在第 11 和 13 天均有不同程度的下降（$P<0.05$）。白色念珠菌干预后小鼠气道中 CCL20、TNF-α、CCL16、IL-1β 显著上升；都柏林念珠菌干预后气道中 TNF-α 显著上升；光滑念珠菌、克柔念珠菌、热带念珠菌和季也蒙念珠菌干预后小鼠气道中 IL-8 水平显著上升。

结论 COPD 气道中酵母菌属多样性高，不同酵母菌属促进宿主炎症反应水平不一致，白色念珠菌促进宿主气道炎症反应最显著。

关键字：AECOPD，气道酵母菌属，16S rRNA，ITS1

糖尿病足患者足溃疡不同位置菌群结构差异比较研究

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背景 研究表明糖尿病足患者及健康人之间的皮肤菌群在组成及多样性上存在差异，此外糖尿病足患者菌群有希望可以预测疾病的预后。然而糖尿病足患者足溃疡面积大，形态多样性高，不同溃疡位置菌群结构差异尚未可知。

方法 为了探索糖尿病足溃疡患者溃疡表面由浅入深不同部位皮肤菌群的变化情况，我们于厦门大学附属第一医院糖尿病足门诊纳入了 56 个糖尿病足患者及其家属对照人员，每组家庭采集 5 个标本（溃疡、溃疡表面、溃疡周边、对侧足，对照 1 个），共纳入 265 个标本进行分析。对所有标本进行 DNA 提取和 16S rRNA V4 区段测序。比较分析 5 个采样点皮肤菌群结构差异组成。

结果 组间 alpha 差异比较分析发现，溃疡面细菌 alpha 多样性显著降低。对照组和健康创面最为接近。PCoA 图展示菌群 beta 多样性构成情况，每个组之间的样本有所重叠，其中溃疡组与其他组重叠面积最小，表明其差异较为突出，此外菌群 beta 多样性组间差异和组内差异情况分析表明，不用采样位置的组间差异显著高于人群组内差异。以下菌属的相对丰度在溃疡面增加：普氏菌属、链球菌属、厌氧球菌属、假单胞菌属、Finegoldia、Peptoniphilus。以下菌属相对丰度在溃疡面显著下降：鞘脂单胞菌属、葡萄球菌属。

结论 溃疡患者溃疡内部菌群最为特殊，溃疡内部菌群与溃疡表面菌群一致。溃疡周边菌群和健康足对照以及健康家属对照菌群一致。可以使用溃疡表面标本代替溃疡里面标本进行疾病菌群的描述。

关键字：糖尿病足，皮肤菌群，16S rRNA

铜绿假单胞菌适应性进化与致病机制

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目的 铜绿假单胞菌（Pseudomonas aeruginosa, PA）较大且高度多样性的基因组和复杂的细胞内转录网络赋予其参与多种协同相互作用的能力，生理代谢可塑性很高，具有易定植、难清除的特点。铜绿假单胞菌作为一种临床常见病原细菌，可引起呼吸道感染的反复发作，耐药性 PA 感染的治疗更困难、病死率更高，位列世卫组织“最为重要”新型抗生素研发重点病原体清单。PA 通过基因突变的方式获取有利于慢性感染相关性状的方式可能是多样的，对这种演进特征的解析有可能为慢性感染的诊治提供新的思路，然而其长期定植和适应性进化机制仍不清楚。

方法 使用从慢性阻塞性肺病（COPD）患者纵向收集的分离株来研究多态性铜绿假单胞菌种群的进化动态。

结果 我们发现铜绿假单胞菌在肺部感染微环境中的进化经常导致具有不同能力的分离株共存，PA 在呼吸道的演化主要集中在改变 lasR 突变菌株的适应性，缺乏产生不同可共享细胞外产物的分离株被依次选择，由此提出了由不同演化程度的 lasR

突变菌株介导的多级公共物品博弈理论。包括 lasR 突变菌株在内的多态性细菌群体在动物感染模型中表现出生存优势并调节宿主免疫反应。

结论 具有不同进化程度的 lasR 突变菌株与野生型菌株在级联公共产品游戏框架下相互作用，多态铜绿假单胞菌种群可以显著降低宿主对病原细菌持续定植的免疫反应，从而实现细菌持久性定植。

关键字：铜绿假单胞菌；适应性进化；致病因子；病原宿主互作；

综合干预对降低血管导管相关感染发病率的效果评估

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目的 探讨综合干预提高核心防控措施执行率对降低血管导管相关血流感染发病率（VCAI）的效果。

方法 采用双向性队列研究方法，以某三甲医院 2021 年 1 月-12 月在院并留置血管内导管的患者为对照组，经综合干预提高核心防控措施执行率后，以 2022 年 1 月-12 月在院并留置血管内导管的患者为试验组,对比两个时期的医务人员核心防控措施考核合格率，比较两组患者 VCAI 发病率、平均置管天数、置管率的前后差异。

结果 VCAI 核心防控措施执行率从干预前 69.21%提升至 91.24%，医务人员核心防控措施考核合格率从 53.33%提高至 91.67%，差异均有统计学意义（P＜0.001），血管导管置管率从 39.03%提高至 39.91%，差异有统计学意义（P＜0.001），VCAI 发病率从 0.58‰降至 0.23‰，差异有统计学意义（P=0.006）。

结论 通过综合干预提高 VCAI 核心防控措施执行率可提高医务人员核心防控措施考核合格率，有助于降低 VCAI 发病率，保障患者医疗安全，为 VCAI 防控提供循证依据。

关键字：血管导管相关感染；血管内导管；综合干预措施；VCAI 发病率

Design of A Multi-epitope MRNA Vaccine Targeting Outer Membrane Proteins of Clostridioides Difficile Using Reverse Vaccinology and Immunoinformatics Approaches

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Objective To provide a theoretical basis and new insights for the clinical development of a broad-spectrum multi-epitope mRNA vaccine against Clostridioides difficile (C. difficile)

Method 118 complete proteome sequences of the C. difficile strain were used to screen target proteins which were further employed to identify immunodominant epitopes. These epitopes were then fused with adjuvants and pan HLA DR-binding epitope (PADRE) sequences using diverse linkers, culminating in the development of vaccine candidates. Afterward, vaccine candidates were docked with toll-like receptors (TLRs) and the molecular dynamics simulation (MD) was conducted for the docking complexes. Additionally, the analyses of population coverage and immune simulation were also performed using different computational tools

Result Two vaccine constructs, namely WLcd1 and WLcd2, were constructed by integrating ideal T-cell epitopes, B-cell epitopes, adjuvants, and pan HLA DR-binding epitope (PADRE) sequences. Biophysical and chemical analysis of the vaccine candidates revealed their appropriateness for immunogenic application. The molecular docking suggested that the WLcd1 exhibited higher affinity to Toll-like receptors (TLRs) compared to WLcd2. MD simulation performed utilizing Gmx_MMPBSA v1.56 validated the binding stability of WLcd1 to TLR2 and TLR4. The immune simulation showed that WLcdx1 can elicit significant immune responses against C. difficile. Finally, the mRNA vaccine was formulated through the integration of WLcd1 and multiple essential components

Conclusion The predicted results indicated that the WLcd1 could be severe as a promising candidate for protecting against CDI; however, experimental validation is required to substantiate the study's results.

关键字： Clotridioides difficile (C. difficile), mRNA vaccine, Immunoinformatics, Reverse Vaccinology (RV), Molecular docking, Molecular dynamics (MD) simulation

Clinical Characteristics and Associated Factors for Mortality in Pneumonia Patients Infected with Carbapenem-Resistant Klebsiella Pneumoniae

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Objective The purpose of this study was to analyze the clinical features and risk factors associated with mortality of the pneumonia patients infected with carbapenem-resistant Klebsiella pneumoniae（CRKP）

Methods This retrospective, single-center study

included pneumonia patients infected with CRKP from January 2020 to December 2022.The clinical characteristics and predictors of mortality were analyzed.Independent risk factors for morality were identified by Cox regression analysis

Results A total of 93 patients were enrolled in this study.The median age was 73[65,83] years,and 72(77.4%) patients were male.26(28.0%) patients have a history of hospitalization three months prior to admission.The most common underlying diseases were cerebrovascular disease(47.3%), hemiplegia(39.8%) and diabetes(31.2%).80(86.0%) patients were admitted to intensive care unit(ICU) during hospitalization.The top three invasive operation performed during hospitalization were urinary catheters(91.4%), mechanical ventilation(72.0%), and central venous catheters(69.9%).Overall duration of hospitalization was 34[21,63] days.The duration from admission to CRKP detection was 10[5,21.5] days.The most common co-infection of carbapenem-resistant pathogens were carbapenem-resistant Pseudomonas aeruginosa(25.8%), followed by Stenotrophomonas maltoophilia(19.4%) and carbapenem-resistant Acinetobacter baumannii (17.2%).The commom prior empirical antibiotic therapy before CRKP isolated was carbapenem(67.7%).The mean APACHE II scores when CRKP isolated was 23.2±6.6.The targeted treatment strategy were primarily based on tigecycline, polymyxin B, and aminoglycosides.The bacterial susceptibility results showed that Klebsiella pneumoniae had a high level of resistance to carbapenem.The mortality was 45.2%.Multivariate COX regression analysis showed that metastatic solid tumor(HR, 4.515;95% CI,1.107-18.414;p=0.036),co-infection with carbapenem-resistant Acinetobacter baumannii(HR,2.666;95% CI,1.229-5.785;p=0.013) and APACHE II scores when CRKP isolated(HR, 1.062;95%CI,1.003-1.124;p=0.040)were independent risk factors for mortality.Kaplan-Meier analyses confirmed that mortality was higher in patients with metastatic solid tumor,co-infection with carbapenem-resistant Acinetobacter baumannii and APACHE II scores of ≥26 when CRKP isolated

Conclusion Most pneumonia patients with CRKP were admitted to ICU and underwent invasive procedures during hospitalization.The target treatment for CRKP was uncertain, and the mortality was high.Clinicians should identify and pay more attention to patients at high risk of death

关键字：carbapenem-resistant Klebsilla pneumoniae，Pneumonia，Clinical Characteristics，Risk factors，Mortality

心脏大血管手术术后持续性发热发生率及其危险因素列线图预测模型的构建

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目的 本研究旨在通过回顾性分析了解心脏大血管手术患者术后发热率，并建立术后持续性发热的列线图预测模型，为临床诊疗提供指导。

方法 回顾性收集 2023 年在南京医科大学第一附属医院心脏大血管外科接受手术并在术后入住 ICU 患者的病历信息。根据术后体温是否持续 3 天超过 38℃将患者分为两组，采用单因素及多因素 Logistic 回归模型来确定独立危险因素，基于心脏大血管术后持续性发热独立危险因素构建列线图风险预测模型并验证。

结果 共纳入 343 名接受心脏大血管手术的患者，术后总体发热率为 70.55%，持续发热（≥3 天）率为 38.78%，术后第 1 天，第 2 天发热率最高。多因素 Logistic 回归分析显示：入院年龄(OR=1.302，95%CI：1.004~1.060)、吸烟史(OR=3.015，95%CI：1.672~5.434) 、 Controlling Nutritional Status Score(CONUT)分值(OR=1.305，95%CI：1.087~1.567)、Monocyte-to-LymphocyteRatio(MLR)分值(OR=7.090，95%CI：1.252~40.152)、手术时长(OR=1.417，95%CI：1.189~1.690) 、 体 外 循 环 (OR=3.687 ， 95%CI ：1.799~7.555)、术中输注机洗红细胞(OR=2.068，95%CI：1.213-3.525)是心脏大血管术后持续性发热的独立危险因素，基于以上独立危险因素构建列线图预测模型并验证，ROC 曲线下面积(AUC)为 0.821(95%CI：0.775~0.866)，提示该模型具有良好的区分度和判别能力。

结论 该研究建立的列线图,可为临床早期评估心脏大血管术后持续性发热的发生概率提供定量、直观的参考，并及时管理，指导临床个体化治疗。

关键字：心脏大血管手术；术后持续性发热；危险因素；列线图预测模型

美罗培南首次监测稳态血药谷浓度不达标的影响因素分析

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目的 分析美罗培南首次监测稳态血药谷浓度不达标的影响因素。

方法 选择西安交通大学第一附属医院 2021 年 7 月至 2023 年 6 月使用美罗培南治疗并监测稳态血药谷浓度的 324 例患者为研究对象，记录患者的年龄、性别等病史资料。测定美罗培南稳态血药谷浓度，并确定靶标。根据监测结果分为达标组

（2.0~16.0 mg·L-1）和未达标组（低浓度组 < 2.0 mg·L-1 或高浓度组 > 16.0 mg·L-1）。对低浓度组、高浓度组分别与达标组进行相关变量的单因素及多因素 Logistic 回归分析，筛选美罗培南稳态血药谷浓度不达标的危险因素。

结果 共纳入 324 例患者，其中血药谷浓度达标者 189 例，达标率 58.33%，未达标者 135 例（低浓度组 86 例，高浓度组 49 例），未达标率 42.67%。通过多因素 Logistic 回归分析结果显示，低浓度组与达标组相比，肾小球滤过率（CI 0.967-0.996，P＜0.05）、白蛋白（CI 0.852-0.973，P＜0.05）及颅脑疾病（CI 0.055-0.313，P＜0.05）是美罗培南浓度偏低的危险因素，并发现颅脑损伤患者的肾小球滤过率显著高于无颅脑损伤者；而胱抑素-C（CI 1.010-4.153，P＜0.05）是这两组患者中美罗培南浓度达标的保护因素。高浓度组与达标组相比，美罗培南日剂量（CI 0.431-0.862，P＜0.05）及降钙素原（CI 0.955-0.977，P＜0.05）是美罗培南血药浓度偏高的危险因素，而肾小球滤过率（CI 1.054-1.132，P＜0.05）是这两组患者中美罗培南浓度达标的保护因素。

结论 肾小球滤过率、白蛋白、颅脑疾病是美罗培南稳态血药谷浓度偏低的危险因素，而美罗培南日剂量、降钙素原是美罗培南稳态血药谷浓度偏高的危险因素。

关键字：美罗培南， 浓度不达标， 颅脑损伤， 肾小球滤过率， 影响因素

基于微生物组和多组学分析的弥漫性大 B 细胞淋巴瘤内部异质性、预后指标及免疫治疗反应性研究

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目的 本研究致力于探讨弥漫性大 B 细胞淋巴瘤（DLBC）患者微生物组对预后、肿瘤微环境及免疫治疗反应性的影响。通过深入分析 DLBC 患者微生物组，旨在揭示其与患者预后的关系，探索微生物组如何调节肿瘤微环境和免疫响应，并基于相关微生物建立肿瘤内微生物亚型及特征标签，为 DLBC 治疗策略和患者个性化治疗提供新见解。

方法 本研究利用了来自 TCGA 的微生物组、转录组和临床数据集，评估微生物组与 DLBC 患者生存之间的关联性。首先通过单因素 Cox 回归分析筛选与预后相关的微生物属，进而通过 Kaplan-Meier 生存曲线验证筛选微生物的预后价值。取两种分析交集部分作为与 DLBC 的关键预后微生物属。基于关键预后微生物属，应用共识聚类方法对 DLBC 患者进行亚组划分，探究患者群体内部的生物学异质性。差异基因分析用于识别不同亚组间的生物标志物，利用基因集富集分析（GSEA）对这些基因在相关生物学途径中的作用进行了注释。此外，免疫浸润分析评估了肿瘤微环境中免疫细胞组成的亚组间差异，进一步探索微生物属在免疫微环境中的贡献。

结果 本研究获取来自癌症基因组图谱（TCGA）数据库的 47 例 DLBC 患者的转录组、微生物组及临床数据。通过单因素 Cox 回归分析，从 1406 个微生物属种筛选出 185 个显著影响预后的微生物属。风险因素 167 个，其中包括 162 个菌属和 5 个病毒属，菌属占比 97.01%；保护因素 18 个，其中包括 12 个菌属和 6 个病毒属，菌属占比 66.7%。Kaplan-Meier 生存分析结果表明，Fictibacillus、Acidithiobacillus、Elizabethkingia、Mamastrovirus、Flammeovirga 等 59 个微生物属与生存显著相关。将两种方法的结果取交集，共得到了 41 种关键预后微生物属。以 41 种微生物属为生物标签，通过共识聚类方法，将 47 例患者分为两个亚组，Kaplan-Meier 生存曲线表明两个亚组在生存上存在明显差异。进一步的差异基因分析揭示了两个亚组间存在 658 个显著差异表达的基因，其中 106 个基因上调，552 个基因下调。基因集富集分析（GSEA）结果表明，这些差异基因主要富集在与免疫系统相关的路径、肽配体结合受体以及小分子的运输等生物学过程中，暗示了微生物组对 DLBC 肿瘤微环境和患者免疫响应的潜在影响。

结论 本研究首次在弥漫性大 B 细胞淋巴瘤（DLBC）中建立基于肿瘤内微生物的亚型，揭示微生物组与 DLBC 患者预后的显著关联，强调其在肿瘤微环境调控及免疫反应中的作用。这一发现不仅深化了对 DLBC 病理机制的理解，也为预后评估和免疫治疗选择提供了新视角。

关键字：微生物组；弥漫性大 B 细胞淋巴瘤（DLBC）；肿瘤微环境；免疫治疗反应性；免疫浸润；生物标志物

脓毒症相关的严重血小板减少患者的多因素预后分析

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目的 脓毒症相关的血小板减少患者通常预后较差，其中血小板严重减少的患者死亡率更高。目前缺乏一个系统的预后模型对这些患者进行预后分析。早期建立预后模型对于及时发现、早期干预并

最终改善脓毒症相关的严重血小板减少患者的预后至关重要。本研究拟构建一个脓毒症相关的严重血小板减少的临床预后模型。

方法 利用重症医学公共大型数据库(Medical Information Mart for Intensive Care, MIMIC)-IV 2.2 中的患者作为训练集，eICU 数据库中的患者作为验证集。纳入入 ICU 24 小时内诊断为脓毒症，且在入 ICU48 小时内血小板计数最低值≤50×109/L 的患者，排除年龄＜18 岁的患者，入 ICU 48 小时内死亡或转出的患者，主诊断为血液系统疾病、创伤失血性休克及妊娠患者。收集患者基本人口学数据，生命体征，疾病严重程度评分，实验室指标，慢性基础疾病情况、感染部位、治疗措施，结局变量为 28 天的生存结局，住院时间及住 ICU 时间等。利用单因素 Cox 回归，Lasso 回归，贝叶斯信息准则（BIC）方法筛选纳入预后模型中的变量，简化模型。而后拟合多因素预后模型，并用 Nomogram 将模型可视化。对预后模型的区分度及校准度及临床有效性进行评价，最后用 eICU 数据库对模型进行外部验证。

结果 我们纳入 1489 名患者作为训练集，通过单因素 Cox 分析、lasso 回归及贝叶斯信息准则，筛选出用于构建模型的变量有 8 个，分别是：年龄、AKI 分期、尿量、尿素氮最小值、心率最大值、INR 最大值、部分凝血活酶时间最小值、是否有肝脏疾病。训练集和验证集的 C 指数分别为 0.71 和 0.64。训练集中 7 天、14 天和 28 天生存概率的 AUC 分别为 0.723、0.733 和 0.736。内部校准曲线表现出较好的一致性。临床决策曲线表示模型临床适用性良好。对预后模型用 eICU 数据外部验证，校准曲线一致性表现仍良好。

结论 通过对 MIMIC-IV 2.2 数据的分析，构建了包含 8 个变量的多因素预后模型，通过内部验证及 eICU 数据库的外部验证，证明了该模型对于脓毒症相关的严重血小板减少患者的预后具有预测价值。

关键字：脓毒症，严重血小板减少，预后分析，重症医学

结核分枝杆菌 PhoY2 基因原核表达及其应用价值评价

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目的 构建表达结核分枝杆菌(Mycobacterium tuberculosis, M.tb) 持续感染相关抗原 PhoY2，通过人群实验评价其作为结核病疫苗靶抗原及用于结核病免疫学诊断的价值。

方法 构建重组质粒 pET30b（+）-PhoY2，诱导表达并纯化重组蛋白质，经 Western blot 鉴定后，用全血干扰素释放试验和血清特异性抗体检测评价重组蛋白 rPhoY2 在结核分枝杆菌感染人群中的免疫原性，进一步通过 ROC 曲线分析 rPhoY2-WBIA 和抗 rPhoY2 特异性抗体诊断 M.tb 不同感染人群的诊断值及灵敏度和特异度。

结果 rPhoY2 刺激活动性结核病患者（active TB, ATB）和潜伏结核病患者（latent TB infections, LTBI）产生的特异性 IFN-γ 水平显著高于健康对照者（Healthy control,HC），LTBIs 抗 rPhoY2 特异性 IgG 水平显著高于 ATBs 和 HCs 。rPhoY2-WBIA 诊断 M.tb 感染的 cutoff 值为 309.2pg/ml ，灵敏度为 72.2%，特异度为 93.7%；抗 rPhoY2 特异性 IgG 诊断 LTBIs 的 cutoff 值为 0.1765, 灵敏度为 61.5%，特异度为 75%。rPhoY2-WBIA 联合特异性抗体诊断三种人群与临床诊断的一致率为 69.9%。

结论 rPhoY2 具有良好的免疫原性，是有潜力的结核病亚单位疫苗候选靶抗原；rPhoY2-WBIA 联合特异性抗体检测在区分 M.tb 不同感染人群方面有一定的价值，尤其在排除 M.tb 感染时特异度较高，但在区分 ATBs 和 LTBIs 方面，其灵敏度仍需进一步提高。

关键字：结核分枝杆菌；PhoY2；原核表达；免疫原性

Low-density Neutrophils and Myeloid-derived Suppressor Cell Subsets As Immune Indicators of Early Diagnosis and Prognosis in Patients with Sepsis

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Objective Immunosuppression is a leading cause of septic death. Therefore, it is necessary to search for biomarkers that can evaluate the immune status of patients with sepsis. We assessed the diagnostic and prognostic value of low-density neutrophils (LDNs) and myeloid-derived suppressor cells (MDSCs) subsets in the peripheral blood mononuclear cells (PBMCs) of patients with sepsis

Methods LDNs and MDSC subsets were compared among 54 inpatients with sepsis, 31 inpatients with infection, and 32 healthy controls to investigate their potential as immune indicators of sepsis. The percentages of LDNs, monocytic MDSCs (M-MDSCs), and polymorphonuclear MDSCs (PMN-MDSCs) in PBMCs were analyzed. Sequential organ failure assessment (SOFA) scores, C-reactive protein (CRP), and procalcitonin (PCT) levels were measured concurrently

Results The percentages of LDNs and MDSC subsets were significantly increased in the healthy controls, infection, and sepsis groups. MDSCs performed

similarly to CRP and PCT in diagnosing infection or sepsis. LDNs and MDSC subsets significantly correlated with PCT and CRP levels and showed an upward trend with the number of dysfunctional organs and SOFA score. Non-survivors had elevated M-MDSCs compared with that of patients who survived sepsis within 28 days after enrollment

Conclusion LDNs and MDSC subsets were promising diagnostic biomarkers in infection and sepsis, even in distinguishing sepsis from infection. M-MDSC is a potential prognostic biomarker of sepsis and can be used to predict 28-day hospital mortality in patients with sepsis

关键字：Low-density neutrophils (LDNs), Monocytic myeloid-derived suppressor cells (M-MDSCs), Polymorphonuclear myeloid-derived suppressor cells (PMN-MDSCs), Sepsis, Infection, Prognosis

Machine Learning Models for Prediction of Invasion Klebsiella Pneumoniae Liver Abscess Syndrome in Diabetes Mellitus: A Singled Centered Retrospective Study

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Objective This study aimed to develop and validate a machine learning algorithm-based model for predicting invasive Klebsiella pneumoniae liver abscess syndrome(IKPLAS) in diabetes mellitus and compare the performance of different models

Methods The clinical signs and data on the admission of 213 diabetic patients with Klebsiella pneumoniae liver abscesses were collected as variables. The optimal feature variables were screened out, and then Artificial Neural Network, Support Vector Machine, Logistic Regression, Random Forest, K-Nearest Neighbor, Decision Tree, and XGBoost models were established. Finally, the model's prediction performance was evaluated by the ROC curve, sensitivity (recall), specificity, accuracy, precision, F1-score, Average Precision, calibration curve, and DCA curve

Results Four features of hemoglobin, platelet, D-dimer, and SOFA score were screened by the recursive elimination method, and seven prediction models were established based on these variables. The AUC (0.969), F1-Score(0.737), Sensitivity(0.875) and AP(0.890) of the SVM model were the highest among the seven models. The KNN model showed the highest specificity (1.000). Except that the XGB and DT models over-estimates the occurrence of IKPLAS risk, the other models' calibration curves are a good fit with the actual observed results. Decision Curve Analysis showed that when the risk threshold was between 0.4 and 0.8, the net rate of intervention of the SVM model was significantly higher than that of other models. In the feature importance ranking, the SOFA score impacted the model significantly

Conclusion An effective prediction model of invasion Klebsiella pneumoniae liver abscess syndrome in diabetes mellitus could be established by a machine learning algorithm, which had potential application value

关键字：Diabetes mellitus，Klebsiella pneumoniae，Machine learning，Prediction model，Pyogenic liver abscess.

糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征预测模型的建立与验证

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目的 分析糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征的危险因素，构建在线列线图预测模型并进行验证。

方法 病例对照研究。回顾性分析 2015 年 1 月 1 日至 2021 年 12 月 31 日在苏州大学附属第三医院治疗的 213 例糖尿病合并肺炎克雷伯菌肝脓肿患者的临床资料。运用分层随机抽样法按 7∶3 将患者分为训练集（149 例）和测试集（64 例）。使用人工少数类过采样法（SMOTE）过采样处理不平衡数据，再运用 Lasso 回归在训练集中筛选出最优特征变量并利用 logistic 多因素回归分析构建糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征的预测模型，并在训练集及测试集中进行验证，采用受试者工作特征（ROC）曲线、校准曲线及决策曲线分析（DCA）评估模型的预测效能，并构建简易列线图及在线交互动态网页列线图。

结果 入选的 213 例患者中，男 60 例，女 153 例，年龄（61.4±12.0）岁。共有 25 例糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征（11.74%），分入 IKLAS 组，其他 188 例为 NIKLAS 组。在过采样后的训练集中基于 Lasso 回归筛选出 5 个主要危险因素，分别为空腹血糖(λ=0.063)、血红蛋白（λ=-0.042）、血尿素氮（λ=-0.050）、脓肿大小（λ=-0.025）和序贯性器官功能衰竭评分（SOFA）（λ=0.450）。logistic 多因素回归分析结果显示，空腹血糖（OR=1.20，95%CI：0.98～1.48，P=0.006）；血红蛋白（OR=0.90，95%CI：0.86～0.47，P=0.001）；血尿素氮（OR=1.22，95%CI：1.03～1.43，P=0.017）；脓肿直径（OR=0.76，95%CI：0.61～0.94，P=0.010）；SOFA 评分（OR=3.08，95%CI：2.18～4.36，P=0.001）。训练集中 ROC 的曲线下面积为 0.966（95%CI：0.943～0.989），灵敏度为 90.5%，特异度为 91.3%。

验证集 ROC 的曲线下面积为 0.946（95%CI：0.902～0.991），灵敏度 79.6%，特异度 88.9%。分别在训练集和测试集绘制的校准曲线与理想曲线拟合较好。DCA 显示列线图预测模型在预测糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征风险为 0.10～0.40。

结论 空腹血糖、血红蛋白、尿素氮、脓肿大小、SOFA 评分是糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征的危险因素，构建的列线图可有效预测糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征的风险，具有潜在的临床应用价值。

关键字：糖尿病,肺炎克雷伯菌,肝脓肿,列线图,预测模型

Type I BREX System Defends Against Antibiotic-resistant Plasmids in Escherichia Coli

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The Bacteriophage Exclusion (BREX) system is a novel antiphage defense system identified in Bacillus cereus in 2015. The purpose of this study was to investigate the presence of the BREX system defenses against antibiotic-resistant plasmids such as blaKPC and blaNDM invasion in Escherichia coli. The BREX system was present in 5.4% (23/424) of E. coli clinical isolates and 6.5% (84/1283) of E. coli strains with completely sequenced genomes in the GenBank database. All 23 BREX-positive E. coli clinical isolates were susceptible to carbapenems, while all five isolates carrying blaKPC and 11 carrying blaNDM were BREX-negative. For E. coli strains in the GenBank database, 37 of 38 strains carrying blaKPC and 109 of 111 strains carrying blaNDM were BREX negative. The recognition site sequence of methyltransferase PglX in a clinical E. coli 3756 was 5′-CANCATC-3′ using PacBio single-molecular real-time sequencing. The transformation efficiency of plasmid psgRNA-ColAori-target with the PglX recognition site was reduced by 100% compared with the plasmid without the recognition site in E. coli DH5α-pHSG398-BREX. The BREX showed lower defense efficacy against plasmid psgRNA-15Aori-target which had the same plasmid backbone but different surrounding sequences of recognition sites with psgRNA-ColAori-target. The conjugation frequency of the KPC-2 plasmid and NDM-5 plasmid in E. coli 3756-ΔBREX was higher than that in E. coli 3756 clinical isolate (1.0 × 10−6 vs 1.3 × 10−7 and 5.5 × 10−7 vs 1.7 × 10−8, respectively). This study demonstrated that the type I BREX system defends against antibiotic-resistant plasmids in E. coli.

关键字：BREX system, carbapenem resistance, plasmids, Escherichia coli

Overactivated MX1+NK Cells Promote The Progression of Sepsis-induced Acute Respiratory Distress Syndrome

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Objective Natural Killer (NK) cells play crucial roles in the regulation of immune defense during acute respiratory distress syndrome (ARDS) caused by sepsis. However, the characteristics of NK cell clusters and their intercellular communication during ARDS have not been well illustrated

Methods A prospective and observational study enrolled septic patients with ARDS or not was conducted to determine the NK cell percentage via flow cytometry. The transcriptomes of peripheral blood mononuclear cells (PBMCs) from healthy controls, patients with sepsis-induced ARDS, and septic patients without ARDS were profiled. In vitro experiment was performed to confirm the major mechanism mediating MX1+NK cell infiltration

Results A total of 115 septic patients were analyzed, among of whom 63 patients developed ARDS and 52 patients did not. Decreased NK percentage was found in sepsis with ARDS patients [%, 7.46 ± 4.40 vs. 11.65 ± 6.88, P=0.0001] compared with sepsis only patients. And lower percentage of NK cells showed significant increase of 28-day mortality. According to single-cell sequencing analysis, NK cells exhibited multiple distinctive characteristics in sepsis-induced ARDS, especially a distinguishing cluster defined as MX1+NK cells. Flow cytometry analysis showed an elevated percentage of MX1+NK cells specifically in individuals with sepsis-induced ARDS, comparing with patients with sepsis only. Pseudo-time analysis showed that MX1+NK cells were characterized by upregulation of type I interferon-induced genes and other pro-inflammatory genes. MX1+NK cells can respond to type I interferons and secrete type I interferons themselves. Ligand-receptor interaction analysis also revealed extensive interaction between MX1+NK cells and T, B cells

in ARDS, leading to an uncontrolled inflammatory response in ARDS

Conclusion This study provides novel insight about the association between NK cells and ARDS development caused by sepsis, as well as the cellular and molecular effects of a specific MX1+NK cluster on ARDS

关键字：ARDS; Inflammation; Natural Killer (NK) cells; Sepsis

中枢神经系统布鲁菌病临床特征分析

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目的 中枢神经受累是布鲁菌病罕见而致命的合并症。分析中枢神经系统布病患者临床特点、诊疗及预后，为早期识别疾病，指导诊疗供临床依据。

方法 收集 2012 年 8 月至 2023 年 7 月山东大学齐鲁医院收治的 561 名布鲁菌病患者中的 20 名中枢神经系统布鲁菌病患者的临床资料并随访治疗后半年以上，进行流行病学、临床症状体征、实验室检查、影像学检查、治疗和预后的总结和相关分析。

结果 20 例患者中男性 14 例，女性 6 例，年龄 17～73 岁，平均 50.5 岁。发病到确诊时间 7 天至 16 个月，平均 154 天。12 例(60%，12/20)患者有明确牛、羊、奶制品等接触的流行病学史。合并症：2 例睾丸炎、1 例附睾炎，2 例垂体炎、1 例股骨头坏死、1 例滑膜炎、1 例脊柱炎、1 例心肌炎。4 例(20%，4/20)病人有基础疾病，分别是糖尿病、系统性红斑狼疮、高同型半胱氨酸血症和冠心病。症状：头痛(45%，9/20)，下肢乏力、走路不稳(25%，5/20)，发热(80%，16/20)，意识障碍(79%，14/20)，听力下降（15%,3/20），视物模糊（10%，2/20）；常见的体征包括病理征阳性(40%，8/20)及肌力减退(25%，5/20)。20 例患者布菌血清凝集试验均为阳性；脑脊液试管凝集试验阳性或 ELISA IgG 阳性 5 例(50%，5/10)，血培养阳性 1 例(10%，1/10)，脑脊液培养阳性 4 例(50%，4/8)，脑脊液宏基因组测序阳性(40%，2/5)。脑脊液蛋白含量升高（90%，18/20，16 例＞1.0g/l），脑脊液淋巴细胞数升高（100%，20/20，14~1130 个/ml），脑脊液免疫球蛋白升高（100%，12/12），血白细胞减少(10%，2/20)，CRP 升高(15%，3/20)，贫血（10%，2/20），肝功异常（25%，5/20），血钠降低（5%，1/20）。脑电图异常（80%，8/10），颅脑磁共振影像异常（70%，14/20）。20 例患者均给予抗菌药物联合治疗方案，多西环素或米诺环素联合利福平、头孢曲松治疗，总有效率 100%(20/20)；3 例听力下降患者（诊为感音神经性耳聋，其中两位为青壮年）经治疗仍遗留后遗症，两例听力丧失，1 例听力严重受损。3 名精神障碍病人仍未完全恢复。

结论 中枢神经系统布鲁菌病临床表现多样，易误诊，遗留后遗症。来自布鲁菌病流行区患者出现不明原因神经系统症状、多系统症状时，需警惕中枢神经系统布鲁菌病，并应进行必要的血液和脑脊液检查。脑脊液病原体宏基因组测序有助于诊断。联合方案治疗可以取得较好的治疗效果。

关键字：布鲁菌病，中枢神经系统，临床医学

ICU 耐碳青霉烯类肺炎克雷伯菌感染菌与肠道定植菌耐药基因及同源性关系

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目的 探索重症监护室(ICU)患者耐碳青霉烯类肺炎克雷伯菌(CRKP)感染菌和肠道定植菌耐药基因及同源性关系。

方法 收集 2020 年 6 月 1 日-2022 年 11 月 30 日川北医学院附属医院神经外科 ICU、中心 ICU 及急诊 ICU 患者中从 CRKP 感染到肠道定植、CRKP 肠道定植到感染各 20 例患者分离的 CRKP 菌株，对其 CRKP 菌株进行耐药基因检测，采用肠杆菌科基因间重复序列聚合酶链反应(ERIC-PCR)技术进行同源性分析。

结果 40 例患者共收集 CRKP 菌株 98 株。同一患者 CRKP 定植菌和感染菌株均携带 KPC 基因。遗传聚类分析显示，98 株 CRKP 可分为 A～G 型 7 种不同菌型。同一菌型在同一时间段内不同 ICU 检出，同一时段不同患者菌株间同源性较高，同一 ICU 同时段有同一菌型聚集现象。两组各有 18 例患者定植菌和感染菌间相似系数>0.85,其亲缘关系较近；虽两组各有 2 例患者定植菌与感染菌之间亲缘关系较远，但其定植菌或感染菌与同科室或不同科室其他患者定植菌或感染菌之间具有较高同源性。

结论 同一患者 CRKP 肠道定植菌和感染菌株之间所携带的耐药基因一致，均为 KPC 型。两组患者自身肠道定植菌和感染菌株之间同源性均较高。存在同一时段的一个 CRKP 克隆菌株在不同患者间传播流行现象，也存在不同科室间的流行现象。

关键字：重症监护室;耐碳青霉烯类肺炎克雷伯菌;肠道定植;感染;耐药基因;同源性;

ABO 血型不相容肾移植术后肺部感染发生临床特征和死亡危险因素分析

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目的 分析 ABO 血型不相容肾移植术后肺部感染的临床特征和预后，探索 ABO 血型不相容肾移植术后肺部感染发生和死亡的危险因素，为降低肾移植术后肺部感染并发症的发生率及死亡率提供指导意见。

方法 研究对象为 2019 年 1 月至 2022 年 12 月在中国科学技术大学附属第一医院进行的 184 例 ABO 血型不相容肾移植患者，随访至 2023 年 12 月 31 日。根据随访期间有无发生肺部感染分为感染组和非感染组，收集患者的年龄、性别、BMI、血型、供体年龄、性别、免疫抑制剂使用、随访期间实验室指标、病原学和预后等相关指标，采用 Logistic 回归分析患者发生肺部感染的影响因素，COX 回归分析患者死亡的危险因素。

结果 本研究共纳入 ABO 血型不相容肾移植术后肺部感染患者 42 例，移植术后非肺部感染患者 142 例，两组患者在供受体性别、BMI、基础疾病、移植血型、HLA 错配、群体反应性抗体(Panel reactive antibody, PRA)、诱导免疫方案、维持免疫方案、移植肾失功等方面无显著差异(P>0.05)，肺部感染组供体及受体年龄显著高于非感染组，感染组通常合并泌尿系感染及血流感染，且入住 ICU 及死亡概率显著高于非感染组（P<0.05）。两组随访期间白细胞、中心粒细胞、淋巴细胞、IgG 抗体、IgM 抗体、他克莫司及环孢素血药浓度无显著差异(P>0.05)，而感染组胱抑素明显高于非感染组，非感染组肾小球滤过率显著高于感染组（P<0.05）。进一步分析发生肺部感染患者相关资料，发现首次发生肺部感染高峰为移植术后 6 至 12 个月，病原学方面，呼吸道感染主要为新型冠状病毒（Corona Virus Disease 2019, COVID-19）、疱疹病毒、肺孢子菌（Pneumocystis jiroveci, PJP）、曲霉等，血液主要检测出巨细胞病毒（Cytomegalovirus, CMV）、微小病毒、PJP 等，泌尿道主要检测出 BK 多瘤病毒（BK polyomavirus, BKV）、细菌等。最后进行 Logistic 回归多因素分析发现随访期间合并血流感染和术后肾小球滤过率低于 60ml/min/1.73m2 是肺部感染的独立危险因素。进行 COX 回归分析发现重症肺炎是患者死亡的独立危险因素。

结论 ABO 血型不相容肾移植术后肺部感染的病原体主要为真菌和病毒，尤其是 PJP、COVID-19 和 CMV；对于随访期间合并血流感染及术后肾小球滤过率低于 60ml/min/1.73m2 与肺部感染的发生相关，一旦发展为重症肺炎，死亡率极高，临床可据此予以早期防治。

关键字：ABO 血型不相容，肾移植，肺部感染

抗真菌肽 MAF-1A 设计改造及对近平滑念珠菌抗菌活性及溶血活性研究

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目的 以抗真菌肽 MAF-1A 为模板优化设计改造，探讨衍生肽抗近平滑念珠菌的活性及对人红细胞的溶血活性。

方法 采用氨基酸替换法、引入 ATCUN 基序等对抗真菌肽 MAF-1A 进行分子设计；使用生物信息学网站和软件分析模板肽 MAF-1A 和衍生肽 12GGH5 的理化性质、结构特征；通过将抗真菌肽 MAF-1A 及其衍生肽 12GGH5 与铜离子共同孵育获得相应的铜-肽孵育物；采用微量液体稀释法及及菌落记数法测定模板肽 MAF-1A、衍生肽 12GGH5 及其铜-肽孵育物对近平滑念珠菌的最低抑菌浓度（MIC）和最低杀菌浓度（MFC）；利用分光光度法检测模板肽 MAF-1A、衍生肽 12GGH5 及其铜-肽孵育物对人红细胞的溶血活性。

结果 衍生肽 12GGH5 的正电荷增加至 5 个，疏水残基含量为 12 个（46.15%），疏水值提高为 0.423。与 MAF-1A 比较,衍生肽 12GGH5 抑制近平滑念珠菌生长的活性提高了 30 倍，MIC 为 0.02mg/mL，MFC 为 0.08mg/mL；对人红细胞的溶血活性升高。与模板肽 MAF-1A、衍生肽 12GGH5 比较，其相应的铜-肽孵育物对抑制近平滑念珠菌的生长的活性分别提高了 3 倍及 1.3 倍，MIC 分别为 0.2mg/mL、0.015mg/mL；MFC 分别为 0.3mg/mL、0.08mg/mL；对人红细胞的溶血活性显著降低。

结论 通过氨基酸替换法、引入 ATCUN 基序设计改造抗真菌肽 MAF-1A，衍生肽 12GGH5 能较好地抑制近平滑念珠菌生长；通过与铜离子共同孵育，可降低衍生肽对人红细胞溶血活性，实验为进一步优化设计抗真菌药物提供了方向。

关键字：抗真菌肽；改造设计；抗菌活性；溶血活性；近平滑念珠菌

基于转录组学分析抗真菌肽 MAF-1A 对血源性近平滑念珠菌的抗菌机理

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目的 探讨抗真菌肽 MAF-1A 对不同毒力血源性近平滑念珠菌临床分离株的抗菌机理。

方法 1.取真菌感染患者的血液标本，经分离培养、生化鉴定及基因鉴定等方法获得 2 株近平滑念珠菌临床株，分别命名为 F2109、F1047，并以近平滑念珠菌 ATCC22019 作为参照菌株。进一步采用酶标仪和光学显微镜观察法检测 F2109、F1047 的生物膜形成能力及情况，同时通过卵黄琼脂平板法、三丁酸平板法、牛血清蛋白平板法、血琼脂平板法分别检测近平滑念珠菌的胞外磷脂酶、脂肪酶、天冬氨酸蛋白酶以及溶血素等毒力因子的分泌活性。2. 通过 RNA-seq 分析 MAF-1A 作用下不同毒力血源性近平滑念珠菌基因表达情况，拟从分子水平上初步探究 MAF-1A 对血源性近平滑念珠菌的作用机制。

结果 结果显示近平滑念珠菌临床分离株 F2109 生物膜形成强，胞外水解酶中磷脂酶、天冬氨酸蛋白酶为高表达，磷脂酶呈低表达，为强毒力菌株；溶血素分泌活性强，较 F2019，F1047 生物膜、胞外水解酶及溶血素分泌活性均弱，为弱毒力菌株。经过 MAF-1A 处理后，强毒力菌株 F2109 共有 798 个差异基因（DEGs），其中 368 个基因上调，430 个基因下调；这些基因主要与细胞壁合成、细胞膜组成、细胞膜金属离子稳态、氨基酸代谢、能量代谢、线粒体及转录翻译等途径相关；弱毒力菌株 F1047 仅有 44 个 DEGs，其中 28 个基因上调，16 个基因下调，这些基因主要与细胞膜组成、能量代谢、氨基酸代谢等过程相关。

结论 1.近平滑念珠菌临床分离株间生物膜形成、胞外水解酶分泌活性和溶血素产生活等毒力因子存在差异，具体的机制有待进一步研究 ，2.转录组学数据分析从分子水平揭示了 MAF-1A 对近平滑念珠菌的作用机制 提供了新的见解。

关键字：抗真菌肽 MAF-1A；近平滑念珠菌；毒力因子；RNA-Seq，转录反应

书面交流

细菌真菌感染的流行病学

Acinetobacter Spp. Bloodstream Infection in Hematological Patients: A 10-year Single-center Study

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Objective This study investigated the clinical and antimicrobial characteristics of Acinetobacter spp. bloodstream infection (BSI) in hematological patients. Risk factors for 30-day mortality and carbapenem-resistant Acinetobacter spp. (CRA) BSI acquisition were also identified

Methods We reviewed forty hematological patients with Acinetobacter spp. BSI in a large Chinese blood disease hospital between 2013 and 2022. The remaining CRA isolates were subjected to whole-genome sequencing

Results The 30-day mortality rate was high at 35%. Hematological patients with Acinetobacter spp. BSI often presented with severe conditions and co-infections at multiple sites. All strains were colistin-susceptible and 40.0% were CR. Multivariate analysis identified several risk factors associated with CRA BSI acquisition, including previous exposure to carbapenems within 30 days and CRA colonization. Very severe aplastic anaemia, tetracycline-resistant Acinetobacter spp. BSI, and unresolved neutropenia after infection were closely associated with 30-day mortality. Non-survivors often presented with higher median PCT and CRP levels and severe complications, such as intracranial infection, cardiac dysfunction, respiratory failure, and severe sepsis or septic shock. Our study also identified inappropriate empirical antibiotic therapy as an independent predictor of 30-day mortality (OR: 11.234, 95% CI: 1.261–20.086, P=0.030). This study was the first to report A. oleivorans as a human pathogen, and to identify its unique oxacillinase, OXA-325

Conclusion An environment-originated non-pathogenic species can become pathogenic when the body's immunity is compromised. Our results also highlighted the importance of improving neutropenia after infection, treating severe organ dysfunction, and administering appropriate empirical antibiotic therapy to reduce mortality in this patient population

关键字：Acinetobacter, bloodstream infection, risk factors, treatment, outcome

念珠菌医院感染流行病学分布特征

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目的 研究念珠菌分离及医院感染的流行病学特征，为控制侵袭性念珠菌医院感染提供依据。

方法 回顾性收集江苏省人民医院 7 665 株念珠菌的微生物及临床资料，分析念珠菌分离来源及医院感染分布情况。

结果 白假丝酵母整体分离率最高（58.49％），其次为近平滑假丝酵母(22.58%)、热带假丝酵母(15.53％)、光滑假丝酵母(2.13％)、克柔假丝酵母(1.02%)，标本类型中来自于痰标本的菌株数量 4 548 株，占 59.33％，其次为泌尿道(1 183 株，15.43％)及粪便(682 株，8.90％)。分离科室最多是内科(2 879 株，37.55%)，其次为外科(2 366 株，30.86%)、ICU(2 232 株，29.11%)及急诊(190 株，2.48%)。共有 688 例患者发生侵袭性念珠菌医院感染，占全年医院感染的 23.93%，年龄＞60 岁的侵袭性念珠菌医院感染患者占 66.72%(459/688)，基础疾病以高血压和心血管疾病为主，感染科室主要在 ICU(41.13%，283/688)，住院时间主要集中在 15~30 d(49.42%，340/688)，抗菌药物使用时间≥3 周的比例占 65.12%(448/688)。

结论 侵袭性念珠菌医院感染的患者逐渐增多，侵袭性念珠菌医院感染与年龄、基础疾病、科室、住院时间、抗菌药物使用时间等因素有关，亟需加强医院防控。

关键字：医院感染； 侵袭性； 真菌； 假丝酵母； 流行病学分布； 感染防控；

Clinical Characteristics of Corynebacterium Striatum Isolated From Sterile Fluid Specimens

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Objective Corynebacterium striatum is an aerobic, non-spore forming and gram-positive bacterium that mainly colonizes on human skin and nasopharynx, so it is difficult to determine whether the C. striatum cultured in the laboratory for the first time is a polluting bacterium or a pathogenic one. Our study focuses on exploring the clinical characteristics and risk factors for

Corynebacterium striatum(C. striatum) infection in sterile fluid, to provide theoretical basis for early clinical prevention, nosocomial transmission control and the significance of identification, and improve the awareness of infection prevention and control, and minimize the infection rate of C. striatum

Methods A retrospective study was conducted from Jan 2018 to Jun 2023 in the Affiliated Hospital of North Sichuan Medical College of the People's Republic of China. 74 cases from blood, cerebrospinal fluid (CSF), abdominal effusion (AE) and pleural effusion (PE) were collected, and 27 samples with C. striatum infected were named as C. striatum group, and the rest 47 cases with non- C. striatum (such as Klebsiella pneumoniae, Staphylococcus aureus, Candida albicans and others) isolated from the same type, department and period as the experimental group were classified into non-C. striatum group. The clinical characteristics and predisposing factors were statistically evaluated to comprehensively judg the pathogenicity of C. striatum from both clinical and laboratory results

Results TThe patients of C. striatum group were mainly distributed in intensive care unit (ICU), neurosurgery, and nephrology department. The underlying diseases of these patients involve multiple systems, the most common being the nervous, kidney, respiratory and digestive systems. From 2018 to 2023, the highest detection rate of C. striatum was in 2018, up to 15.98%, and the lowest was only 2 C. striatum infection cases in 2019. C. striatum was detected in 2 out of 17 pleural effusion specimens in 2022, which was the highest detection rate among the single specimens. There was no difference in age, sex and length of hospital stay between the two groups, but the time and duration from invasive operation to detection of pathogenic bacteria in the C. striatum infection group were longer than those in the control group. In addition, the proportion of patients with ≥2 invasive operations and ≥2 antibiotic types in C. striatum infection group were more than that in non- C. striatum infection group, which was statistically significant (P<0.05). Compared with the non-C. striatum infection group, the duration and times of invasive operations and the number of antibiotics used in the C. striatum infection group were increased (P<0.05), which were independent risk factors for C. striatum infection in the sterile site by logistic regression analysis

Conclusion C. striatum isolates cause severe infection in the sterile site of body. For patients with serious underlying diseases and low immunity, the invasive operations and antibiotic treatment will highly raise the possibility of C. striatum infection. Clinical staff need to raise the awareness on such patients, further reducing the infection of C. striatum in patients. Our data provide new insights into evaluating the clinical significance when patients were cultured with C. striatum in the sterile site. A prospectively designed study is needed to further confirm the results

关键字：Corynebacterium striatum; Sterile body fluids; Clinical manifestation; Risk factors

耐碳青霉烯类肺炎克雷伯菌肺部感染的危险因素及预后分析

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目的 分析耐碳青霉烯类肺炎克雷伯菌（CRKP）肺部感染患者的危险因素及预后，为 CRKP 感染防控及临床抗菌药物选择提供参考。

方法 以 2021 年 1 月至 2023 年 6 月四川大学华西医院收治的 CRKP 肺部感染患者为研究对象，并针对患者年龄及性别使用倾向评分匹配按 1∶1 匹配碳青霉烯类敏感肺炎克雷伯菌（CSKP）肺部感染患者作为对照组。收集纳入患者的病历资料，进行 CRKP 肺部感染的危险因素及预后分析。采用 logistic 回归模型和 Cox 回归模型进行多因素分析。

结果 CRKP 组和 CSKP 组各纳入 190 例患者。CRKP 组来源于综合重症监护病房（ICU）最多，占 24.2%（46/190）。logistic 回归模型分析显示，采样前住院时长[比值比（OR）=1.050，95%可信区间（95%CI） 1.030~1.071]、ICU 入住史（OR=4.239，95%CI 1.970~9.122)、≥3 d 碳青霉烯类抗菌药物用药史（OR=9.821，95%CI 5.486~17.581）为 CRKP 肺部感染的独立危险因素（均 P<0.001）。CRKP 分离株对替加环素、多黏菌素、头孢他啶阿维巴坦均有较高的敏感率（≥94.9%）。序贯器官衰竭（Sequential Organ Failure Assessment ，SOFA）评分是 CRKP 肺部感染疗效不佳的独立危险因素（OR=1.238，95%CI 1.057~1.450，P=0.008）。CRKP 肺部感染患者感染后 28 d 的全因死亡率为 39.5%（75/190）。Cox 回归模型分析显示，年龄大[风险比（HR）=1.021，95%CI 1.002~1.040，P=0.033]、高 SOFA 评分（HR=1.265，95%CI 1.158~1.382，P<0.001）是患者发生 CRKP 肺部感染后 28 d 死亡的独立危险因素。

结论 采样前住院时长、ICU 入住史和≥3 d 碳青霉烯类抗菌药物用药史是 CRKP 肺部感染的独立危险因素。CRKP 感染预后差，尤其是在年龄较大和高 SOFA 评分的患者中。

关键字：耐碳青霉烯类肺炎克雷伯菌；危险因素；预后分析

2012 2021 年成都地区淋病奈瑟菌耐药变迁

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目的 分析成都地区性病监测点淋病奈瑟菌临床分离株对常用抗菌药物的耐药变迁，为淋病的社会防治提供科学依据。

方法 收集 2012-2021 年成都地区性病监测点临床分离培养的淋球菌菌株，采用纸片酸度法测定产青霉素酶淋球菌,琼脂稀释法测定四环素、青霉素、环丙沙星、阿奇霉素、头孢曲松、大观霉素的最小抑菌浓度（MIC）。

结果 1002 株淋球菌中，产青霉素酶淋球菌(PPNG)564 株（56.29%）、高水平四环素耐药淋球菌（TRNG）421 株（42.02%）。各年间 PPNG 和 TRNG 阳性率分别是 51.04%～68.63%、26.13%～59.09%,前者总体变化趋势较平稳，而后者总体呈下降趋势且变化明显（$\chi 2$ =69.809，P＜0.01)。青霉素耐药率 66.67%～94.87%，总体呈下降趋势且变化明显（$\chi 2$ =44.730，P＜0.01）。环丙沙星各年间耐药率变化不大，高达 93.75%～100%。阿奇霉素平均非敏感率 10.33%，其 MIC50 、MIC90 分别从 2013 年的 0.50mg/L、1mg/L 下降到 2021 年的 0.25mg/L 和 0.50mg/L，均下降了 1 个稀释度。10 年间头孢曲松非敏感率 1.90%，其 MIC90 从 2012 年的 0.06mg/L 上升到 2021 的 0.25mg/L，上升了 2 个稀释度；大观霉素中敏率和耐药率分别为 0.90%、0.20%。

结论 头孢曲松和大观霉素可以继续作为成都地区治疗淋病的一线药物，未来阿奇霉素或许也可加入该行列。

关键字：淋病奈瑟菌；抗菌药物；耐药监测；最小抑菌浓度

Extraintestinal Pathogenic Escherichia Coli (ExPEC) O-serotype Distribution and Antibiotic Resistance Profiles Among Aging Population in China: A Longitudinal, Multi-center Study

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Objective Extraintestinal pathogenic Escherichia coli (ExPEC) comprises a pathogenic group of Escherichia coli (E. coli) strains, which can colonize normally sterile body sites and cause severe invasive E. coli disease (IED) at nonintestinal sites. The risk of developing ExPEC bacteremia and sepsis increases considerably with age, which contributes to the substantial burden of E. coli bacteremia in older adults. This study aimed to estimate the O-serotype distribution of ExPEC in China among aging populations and its correlation with the resistant phenotype and genotype

Methods A total of 499 non-duplicated clinical isolates of ExPEC from sterile body fluids of patients aged ≥ 60 years from 55 medical institutions in China from 2016 to 2022 were collected. The minimum inhibitory concentration of drugs against 499 ExPEC isolates was determined by broth microdilution. Whole-genome sequencing was performed for all ExPEC isolates collected to obtain a genetic overview of the O genotype, resistance profiles, and other features. Standardized agglutination assay was performed to validate the 9 common O-serotypes (O1, O2, O4, O6, O15, O16, O18, O25, and O75) after O-genotyping

Results About 82.2% of ExPEC isolates were tested as MDR isolates. Imipenem and meropenem showed resistance levels of 9.8% and 10%, respectively. Polymyxin B and tigecycline showed good antibacterial activity against tested ExPEC strains with 98.6% and 100% susceptibility. Genomic analysis revealed that there were 7.2%(36/499) of tested ExPEC isolates harboring blaNDM-5, 0.4%(2/499) harboring blaNDM-1, 0.2%(2/499) harboring blaNDM-13, and 0.6%(3/499) harboring blaKPC-2. The sequencing types were widely distributed among ExPEC isolates, mainly including ST131(14.2%), ST69(7.4%), and ST1193(7.0%). Based on genotyping and O serotyping, the most prevalent O serotypes in this study were O25 (13.6%), O75(5.8%), O1(5.4%), O6(4.6%), and O15(3.8%). The O2;O50(3.0%), O16(2.4%), O4(1.0%) and O18(0.6%) were not common serotypes in this study. O25 was the dominant O serotype among MDR isolates(14.1%) and bloodstream isolates(16.5%)

Conclusion In conclusion, O25 was the dominant O serotype, and the ExPEC serotype prevalence is generally consistent across MDR, and different genders, except in different types of cities, geographical regions, and years of isolations, where some differences were observed

关键字：O serotype; ExPEC, MDR

ICU 碳青霉烯耐药肺炎克雷伯菌毒力基因分布及分子流行研究

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目的 探讨重症监护室（ICU）碳青霉烯耐药肺

炎克雷伯菌（CRKP）的毒力基因分布、荚膜血清型及分子流行情况，了解 ICU CRKP 感染特点，为 ICU 有效监测防控 CRKP 感染提供科学依据。

方法 收集 2021 年 1 月～2022 年 12 月医院 ICU 所分离的并已确定为 CRKP 的非重复菌株共 40 株，采用全基因组测序方法，分析待测菌株耐药基因、毒力基因、荚膜血清型的分布，同时将 CRKP 基因组 7 个管家基因序列上传至肺炎克雷伯菌（KPN）多位点序列分型（MLST）数据库，明确菌株的序列型（ST）。

结果 40 例 ICU CRKP 感染患者年龄为 69.03±17.82 岁，且伴有多种基础疾病，病死率较高，所分离菌株主要来源于中段尿、肺泡灌洗液等标本。全基因组测序结果显示，其主要携带 blaKPC-1（29 株，72.5%）、blaNDM-1（6 株，15.0%），以及有 5 株同时携带 blaKPC-1+ blaNDM-1。所携带的毒力基因有多种，其中 entA、entB、entE、entS、fepA、fepC、fepG、yag/ecp、ompA 等基因的携带率达到 100%，entD、fimB、iroB、iroD、fes、pla 等基因携带率较低。ICU 所分离的 CRKP 以 ST11 型（27 例，67.5%）为主，荚膜血清型以 KL64 型（29 例，72.5%）为主。ST11-KL64 型 CRKP 检出 23 例，占 57.5%。

结论 ICU CRKP 主要为 ST11-KL64 型，并携带有多种毒力基因，以铁吸收类毒力基因为主，且 blaKPC 已由 blaKPC-2 转为 blaKPC-1，因此需密切监测 CRKP 的分子流行变化，同时制定出严格的防控措施，有效遏制 CRKP 感染的发生。

关键字：重症监护室；碳青霉烯耐药肺炎克雷伯菌；全基因组测序；毒力基因；荚膜血清型；多位点序列分型；分子流行病学

Factors Associated with Prevalence of Cryptococcal Capsular Antigen Among People Living with HIV: A Retrospective Observational Cohort Study

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Objective Cryptococcosis, caused by Cryptococcus, is an invasive fungal disease that poses a significant health risk, particularly to people living with HIV (PLHIV), who are considered one of the most vulnerable groups. In 2016, the World Health Organization recommended cryptococcal capsular antigen (CrAg) screening for AIDS patients with CD4+ T cell count below 100 cells/μl before initiating antiretroviral therapy (ART). This strategy has been implemented successfully in numerous countries and regions, yielding significant results. However, research related to this strategy has only recently commenced in China, and there is limited reporting on this matter. The primary objective of this study is to identify the factors associated with the prevalence of CrAg among PLHIV in southern China

Methods PLHIV were recruited from a designated HIV/AIDS clinic in southern China during the period from March 1, 2018, to December 31, 2019. Serum CrAg was qualitatively detected using colloidal gold immunochromatography (LFA). Additionally, fungal culture and pathological examinations of cerebrospinal fluid (CSF) were performed. Statistical analyses were conducted using the Chi-squared test and Wilcoxon rank-sum test to assess factors associated with the prevalence of CrAg

Results The study cohort included a total of 1478 PLHIV, among whom 297 (20.1%) were classified as ART-naive, while 1181 (79.9%) were ART-experienced. The median of CD4+ T cell count was 43 cells/μl [interquartile range (IQR):13-117]. The overall CrAg positive rate was determined to be 5.1% (75/1478). Notably, the majority of CrAg positive patients (71/75, 94.7%) had a baseline CD4+ T cell count ≤ 200 cells/μl. When stratified by ART status, the CrAg positive rates were 6.4% (19/297) among ART-naive patients and 4.7% (56/1181) among ART-experienced patients. There was no significant correlation between the CrAg positive rate and ART status (P=0.245). However, within the ART-experienced group, CrAg-positive individuals displayed lower baseline and latest CD4+ T cell counts (P ＞0.05). Among the 75 CrAg positive patients, 63 patients underwent fungal culture or pathological tests. 51 patients (51/63, 81.0%) were diagnosed with cryptococcosis, including 34 previously diagnosed patients and 17 newly diagnosed patients (14 untreated patients and 3 treated patients). Significantly, none of the patients with newly diagnosed cryptococcosis had a CD4+ T cell count exceeding 200 cells/μl

Conclusion The CrAg positive rate in ART-naïve PLHIV was similar with that in ART-experienced. Lower CD4+ T cell count was the primary factors associated with prevalence of CrAg among HLHIV. Serum CrAg screening should be recommended for both ART-naive and ART-experienced PLHIV with CD4+ T cell counts ≤200 cells/μl

关键字：PLHIV, ART, prevalence, CrAg

恶性血液病患者洋葱伯克霍尔德菌感染的临床特征和死亡危险因素

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目的 近年来免疫力低下患者合并洋葱伯克霍尔德菌复合体（Burkholderia cepacia complex，Bcc）感染日渐增多，而恶性血液病患者感染 Bcc 的临床特征和预后的相关研究较少。因此，本研究旨在探讨恶性血液病患者感染 Bcc 的风险，并为该类患者的感染及预后制定相应策略。

方法 收集 2019 年 11 月 1 日至 2022 年 11 月 31 日在苏州大学附属第一医院就诊的 197 例恶性血液病合并 Bcc 感染患者的临床信息，分析其临床特征及预后。

结果 单因素分析显示 Bcc 感染突破、合并其他病原学感染、呼吸衰竭、血管活性药物、肝功能不全、肾功能不全与恶性血液病合并 Bcc 感染患者的预后不良相关（P＜0.05）。多因素分析显示 Bcc 感染突破是血液病患者预后不良的独立危险因素（P=0.0121，HR=3.07，95%CI 1.254-7.409）。亚组分析显示 Bcc 感染突破对预后的影响受到患者粒缺状态、有侵入性操作和肝功能不全的影响（P＜0.05）。

结论 Bcc 感染突破是恶性血液病患者短期死亡的重要危险因素。因此，预防 Bcc 感染突破、缩短患者粒缺时间以及减少侵入性操作可能是改善患者预后的重要治疗手段。

关键字：洋葱伯克霍尔德菌复合体，恶性血液病，临床特征，预后

幽门螺杆菌抗体分型检验结果分析

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目的 探究幽门螺杆菌阳性结果及四种毒力因子 UreA、UreB、VacA 和 CagA 的检验结果分析。

方法 回顾性分析 2023 年 7 月 -2023 年 12 月在本实验室所做的幽门螺杆菌分型共 13089 例，采用免疫印迹法检测血清中的四种幽门螺杆菌毒力因子。从男女性别差异、各年龄段感染率及四种毒力因子分布的情况对其检验结果进行统计学分析。

结果 13089 例幽门螺杆菌总阳性率为 36.08％（4723/13089）。其中男性的阳性率为:38.10%(2895/7598) 、女性的阳性率为：33.29%(1828/5491) 。男性和女性幽门螺杆菌阳性率比较，差异有统计学意义(P ＜ 0． 05)。男性感染率高于女性; 再将 13089 例分为 ＜ 20 岁、21 ～ 40 岁、41 ～60 岁和 .>60 岁 4 个组，幽门螺杆菌阳性率在 4 个年龄组分别为 24.65% (706 2864) 、36.59% (1020/2788) 、44.16% (2004 /4538) 和 34.25% (993/2899) ，组间幽门螺杆菌阳性率差异具有统计学意义(P ＜ 0． 05) 。幽门螺杆菌感染率与年龄有明显的相关性，婴幼儿及青少年幽门螺杆菌感染率较低，20 岁以后感染阳性率逐渐升高，41-60 岁年龄段达到高峰。UreA、UreB、VacA 和 CagA 四种毒力因子的表达阳性率 分别是 19.54%（2558/13089）、36.08%（4723/13089）、15.96%（2089/13089） 和 25.88%（3388/13089），四种毒力因子共阳性的表达率是 15.64% （2047/13089），其中 UreB 的阳性表达率最高。CagA 抗体阳性率（25.88%）高于 VacA 抗体阳性率（15.96%）,UreB 抗体阳性率（36.08%）高于 UreA(19.54%)，差异均有统计学意义(P ＜ 0． 05)。

结论 幽门螺杆菌阳性率分布与性别和年龄有关。幽门螺杆菌感染及其 CagA 、VacA 抗体阳性在胃癌的发生发展中起到重要作用。免疫印迹法可以同时检测四种毒力因子尿素酶 A（UreA）、尿素酶 B（UreB）、细胞空泡毒素（VacA）和细胞毒相关蛋白（CagA），能够为幽门螺杆菌感染进行分型。为临床制定幽门螺杆菌诊疗方案提供重要参考依据。

关键字：幽门螺杆菌，抗体分型，阳性率

2016-2023 年常州恙虫病的临床特征和实验室诊断

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目的 探讨恙虫病患者的诊断方法和临床特点。

方法 选择常州市某医院 2016 年至 2023 年 50 例恙虫病患者，回顾性分析患者的数据，采用受试者工作特征（ROC）曲线分析恙虫病的感染生物标志物。

结果 56.00%的病例为男性,以中、老年患者为主。患者有明确的流行病学接触史占 80%。临床上恙虫病呈季节性发病，病例主要集中在 10 月-12 月份。以发热伴畏寒、皮肤焦痂伴皮疹、头痛、纳差乏力和淋巴结肿大为主要临床特征。主要并发症是肝功能障碍，占 46.00%。AST、LDH-H、ALT、CRP、SAA、FER、ESR、D-二聚体升高和 β2-MG 升高均升高；ALB、PA 降低和 Fe 降低。胸部影像学异常占 60.00%；腹部 B 超检查异常 27 例。ROC 分析表明当 FER 的临界值为 167.14 ng/mL 时，约登指数最大值为 0.950，敏感度和特异度分别为 95.00%和 95.00%；当 CRP 的临界值为 18.22 mg/L 时，约登指数最大值为 0.726，敏感度和特异度分别为 81.30%和 91.30%，治疗以多西环素联合复方冬草口服液治疗最常见，药物治疗方案的平均治疗时间为 10 天。50 例患者治愈、好转。

结论 恙虫病临床表现多样，患者有流行病学史。实验室检测无特异性。临床应开拓诊疗思路。

关键字：恙虫病；斑疹伤寒； 临床特点； 感染生物标志物

老年患者侵袭性念珠菌血流感染临床特点及死亡危险因素分析：基于 9 年纵向监测数据

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目的 了解某三甲医院老年患者医院获得性侵袭性念珠菌血流感染的临床特点与死亡相关危险因素，为开展防控提供理论依据。

方法 回顾性收集江苏省连云港市第一人民医院 2016 年 1 月-2023 年 12 月检出念珠菌并确诊为医院获得性侵袭性念珠菌血流感染且年龄≥60 岁的老年患者人口学信息及临床诊疗信息，对其临床特征及死亡危险因素开展分析。

结果 共收集相关病例 53 例，其中男女比例为 34:19，年龄中位数 73（60~89）岁，主要集中在综合 ICU、急诊 ICU 和胃肠外科，分别占 30.19%、26.42%和 11.32%。排名前三位的念珠菌为白色念珠菌、热带念珠菌和近平滑念珠菌，分别占 45.28%、18.87%和 18.87%。主要血流感染部位为导管相关血流感染和菌血症，占比为 49.06%和 47.17%。患者死亡率为 43.40%（23/53），主要分布于综合 ICU（21.74%）、急诊 ICU（21.74%）、胃肠外科（17.39%），死亡患者中检出前三位病原体为白色念珠菌（34.75%）、热带念珠菌（34.75%）和光滑念珠菌（21.74%），高龄老年患者（≥75 岁）IC 血流感染病原体与普通老年患者（60~74 岁）有一定区别，其中白色念珠菌占比明显偏高（54.17%vs37.93%），近平滑念珠菌则明显下降；药敏结果显示，白色念珠菌整体耐药率较低，仅对伊曲康唑超过 10%，热带念珠菌除对两性霉素 B 敏感外，其余耐药性均超 50%，近平滑念珠菌耐药性最低，光滑念珠菌主要对伊曲康唑耐药性最高，达 88.89%；单因素及 logistic 二元回归分析结果提示肺部基础病、侵入性操作≥3 种以及碳青霉烯类抗菌药物使用为老年患者侵袭性念珠菌血流感染死亡的独立危险因素。

结论 老年患者发生侵袭性念珠菌血流感染病死率较高，主要集中于 ICU，机械通气等是独立危险因素，应强化针对性防控。

关键字：袭性念珠菌；血流感染；临床特点；死亡危险因素

Global Distribution of CMY-42-Producing Escherichia Coli Related To Reduced Aztreonam/avibactam Sensitivity: A Genome-based Study

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Escherichia coli, the most frequently isolated pathogen in clinics, poses a major public health challenge due to the diverse infections it causes. Aztreonam/avibactam, a last-resort defense against these resistant strains, has seen a worrying trend of increasing resistance. The β-lactamase CMY-42 is one of the known mechanisms contributing to this resistance. Nevertheless, the global distribution of this β-lactamase is not fully mapped. Our study aims to analyze the molecular epidemiological characteristics of the CMY-42 in E. coli, providing new perspectives for the monitoring and management of resistance to aztreonam/avibactam.

We retrieved 167,518 E. coli genomes from EnteroBase with an N50 value of no less than 100kb up until November 4, 2023. Quality assessment using CheckM2 v1.0.1 led to the exclusion of 8,048 genomes that failed to meet the criteria of ≥100% completeness_specific and ≤1.25% contamination. Analysis using AMRFinderPlus v3.11.26 identified 729 genomes containing the blaCMY-42 gene, which is approximately 0.46% of the analyzed genomes. These strains were collected from 2007 to 2023 and showed a marked increase from 2014 onwards . They are spread across 41 countries on six continents, with Asia reporting the highest number (212 strains across 18 countries, almost half of them from Israel, China, Pakistan and Cambodia), followed by North America (145 strains across two countries, mainly concentrated in US). More than half of strains collected from the following 10 countries, including US (n=130,17.83%), Australia (n=63, 8.64%), Israel (n=47, 6.45%), Canada (n=30, 4.12%), UK (n=28, 3.84%), Netherlands (n=24, 3.29%), Pakistan (n=20, 2.74%), China (n=20, 2.74%), Germany (n=20, 2.74%), and Cambodia (n=17, 2.33%) . Human hosts accounted for most strains (72.84%, 531/729), followed by environmental (3.70%,27/729) and animal sources (1.92%, 14/729). This distribution pattern underscores the extensive global dissemination of CMY-42. The presence of CMY-42 in different hosts highlight the complexity and severity of the resistance issue.

Further investigation into Clermont phylogroups revealed that the CMY-42 carrying strains predominantly belong to groups C (n=198), A (n=185), and B1(n=145), followed by groups D, F, B2, and G with counts being 93, 93, 14, and 1, respectively. A detailed breakdown of sequence types showed a total of 54 STs, with ST410 (n=168, group C; concentrated in Israel, the US, and China), ST167 (n=85, group A, common in the US, Australia, and the Netherlands), ST405 (n=43,

group D, mainly found in the US, Japan, and Canada), ST648 (n=43, group F, a higher detection rate in Australia, the UK, and the US), and ST448 (n=37, group B1, primarily located in Saudi Arabia, the US, and Australia) being the most prevalent (Fig 1, Fig S2). The data showed CMY-42 was combined with high-risk multidrug-resistant clones such as ST410, ST167, and ST405, may lead to an accelerated worldwide spread.

Within these CMY-42 positive genomes, 65.71% (479/729) also carry at least one type of carbapenemase, such as NDM, KPC and OXA, with the NDM being the most prevalent (73.70%,353/479). These data indicates that CMY-42 are more concentrated in carbapenem-resistant E. coli (CREC). Although aztreonam/avibactam is a preferred treatment for CREC infections, especially those producing NDM enzymes, CMY-42's presence compromises treatment efficacy. In order to know the prevalence of CMY-42 in all CREC in our dataset, carbapenemase genes of the 159,470 E. coli genomes were predicted using software mentioned above, and found that 6,107 (3.83%) strains carry at least one carbapenemase gene, including NDM, KPC, OXA, VIM, GES, IMP, and IMI. Of these carbapenemase-producing strains, 7.84%, (479/6107) also produce CMY-42, with ST410 (n=124), ST167 (n=71) and ST448 (n=31) being the most common . Among the 479 strains, 353 (73.70%) produce NDM, with the majority being NDM-5 (85.27%, 301/353). This finding underscores the severe resistance challenges faced by current CREC treatment strategies when using aztreonam/avibactam and emphasizes the importance of monitoring CMY-42, as well as the urgent need to develop new antibiotics or treatment strategies to combat antibiotic resistance.

In summary, the global spread of CMY-42-positive E. coli remains limited but poses a significant risk due to potential rapid dissemination among high-risk multidrug-resistant clones, such as ST410, ST167, and ST405. Notably, these bacteria are more prevalent in CREC and, together with PBP3 insertion mutations, may contribute to aztreonam/avibactam resistance—a serious public health concern. Therefore, an integrated surveillance strategy employing whole-genome sequencing within a one health framework is essential for effective resistance monitoring and control.

关键字：Escherichia coli ; CMY-42; antimicrobial resistance; genome analysis.

Epidemiology and Antifungal Susceptibility of Fungal Infections From 2018 To 2021 in Shandong, Eastern China

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Purpose To provide the basis for empiric antifungal therapy, we analyzed the pathogenic fungal epidemiology and antifungal susceptibility from 2018 to 2021 in Shandong Province, China

Methods Fungal isolates were collected from 54 hospitals in Shandong province during 2018 to 2021 though the Shandong Province Pediatric bacterial & fungal Antimicrobial Resistance Surveillance System (SPARSS), WHONET v5.6 and SPSS software v20.0 were used for statistical analysis

Results We collected a total of 15348 fungi, with Candida accounting for 78.25%, followed by Aspergillus 15.45%, and other species 6.27%. The most predominant Candida species was C. albicans, over half of the isolates (58.17%) were non-albicans species, with C. tropicalis being the most dominant (22.74%), followed by C. glabrata (17.50%) and C. parapsilosis (11.02%). The proportion of C. albicans was higher in children (47.30%) compared with non-child population (32.06%). Among the Aspergillus species, A. fumigatus was the most prevalent at 66.24%, followed by A. flavus at 18.87% and A. niger at 8.91%. The study found that the wild-type rate of Candida for Amphotericin B was less than 3%, while Cryptococcus neoformans was 10.61%. In addition, less than 6% of C. albicans and C. parapsilosis were resistant to fluconazole and voriconazole, and 96.3% of C. glabrata were SDD to fluconazole. We also found that 80.56% of C. glabrata and 83.70% of C. krusei were voriconazole WT/susceptibility phenotype. However, the susceptibility rates of C. tropicalis to fluconazole/voriconazole decrease from 70.4%/46.4% in 2018 to 62.3%/35.2% in 2021 separately. The comprehensive susceptibility rates to fluconazole of C. albicans, C. tropicalis, C. parapsilosis and C. glabrata isolated from blood have decreased from 69.36% to 56.62%

Conclusions The study reveals that the composition and antifungal susceptibility of pathogenic fungi in Shandong region differ from other regions. Moreover, the resistance to azoles is more severe in Shandong especially in C. tropicalis. These findings indicate the need for region-specific antifungal treatment strategies to combat fungal infections effectively

Fungal infection, Antifungal susceptibility, Epidemiology, Azoles, antifungal therapy

关键字：Fungal infection, Antifungal susceptibility, Epidemiology, Azoles, antifungal therapy

Bacterial Epidemiology and Antimicrobial Resistance Reported by The China Paediatric Intensive Care Unit Pathogen Surveillance Network From 2016 To 2022

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Background The China Paediatric Intensive Care Unit (PICU) Pathogen Surveillance Network was established in 2021 to monitor and to analyse trends in bacterial epidemiology and antimicrobial resistance (AMR) in PICUs

Methods Clinical bacterial isolates were collected from 17 tertiary paediatric hospitals in China between 2016 and 2022. Antimicrobial susceptibility testing was conducted using the Kirby-Bauer method or an automated system. The interpretation of the results was based on the 2022 Clinical and Laboratory Standards Institute breakpoints

Results A total of 26638 isolates were collected, and the top 10 predominant bacteria were Acinetobacter baumannii (12%), Staphylococcus aureus (12%), Klebsiella pneumoniae (10%), Pseudomonas aeruginosa (8%), Escherichia coli (8%), Streptococcus pneumoniae (6%), Haemophilus influenzae (6%), Staphylococcus epidermidis (5%), Stenotrophomonas maltophilia (5%), and Enterococcus faecium (4%). The proportion of carbapenem-resistant A. baumannii increased from 68.8% in 2016 to 77.4% in 2018 and slightly decreased to 66.5% by 2022. Similarly, the proportion of carbapenem-resistant Enterobacteriaceae and carbapenem-resistant K. pneumoniae initially decreased after 2020 but increased again by 2022

Conclusion Multidrug-resistant organisms exhibit significantly high levels of AMR in PICUs, indicating the need for antibiotic management strategies and monitoring

关键字：antimicrobial resistance, bacteria, children, China Paediatric Intensive Care Unit Pathogen Surveillance Network, multidrug-resistant organisms

2021-2023 年某院烟曲霉临床分离株的分布及流行病学特征

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目的 分析烟曲霉临床分离株感染分布特点，为针对性防控烟曲霉感染提供依据。

方法 回顾性收集 2021 年 1 月-2023 年 12 月南京医科大学第一附属医院(江苏省人民医院、江苏省妇幼保健院)住院患者的烟曲霉临床分离株作为研究对象，剔除同一患者相同部位重复菌株，将其分为社区获得性感染、医院获得性感染和定植三种感染类型。

结果 共检出烟曲霉临床分离株 561 株，其中男性患者 402 株(82.35%)，女性患者 159 株(17.65%)。年龄分布在 51-90 岁之间的人群构成比为 78.97%(443/561)。检出科室主要集中在监护病房和内科(占 81.11%)，除了外科以定植居多，其他科室均以 CAI 居多主(P=0.002)。CAI 组和定植组住院天数均以<15 天为主，HAI 组住院天数以 15-30 天为主(P<0.001)。三组感染部位均是下呼吸道感染为主(占 95.37%)，呼吸机相关肺炎在 HAI 组中占比最高(P<0.001)。2021-2023 年烟曲霉检出率分别为 3.89‰、7.15‰、12.50‰，烟曲霉菌检出率均呈逐年升高趋势(P<0.001)。三组烟曲霉菌临床分离株的主要来源都是痰标本，分别为 61 株(89.71%)、277 株(78.69%)、122 株(86.52%)，其次为肺泡灌洗液标本。

结论 烟曲霉菌检出率近 3 年呈逐年上升趋势，不同感染类型之间的流行病学特点不一，医疗机构应根据烟曲霉感染特点，针对性制定烟曲霉医院感染防控措施。

关键字：社区获得性感染；医院获得性感染；烟曲霉；流行病学分布

T6SS 阳性 CRKP 临床感染特征及毒力基因分析

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目的 分析 T6SS 阳性 CRKP 临床感染特征，及其耐药、毒力基因携带率和生物膜形成能力，为临床防控 CRKP 感染提供参考数据。

方法 收集 2019 年 1 月至 2022 年 12 月本地某三甲医院临床分离的 CRKP 菌株及患者资料；PCR 法检测 T6SS 基因、毒力基因、耐药基因和分子分型；96 孔板结晶紫染色法检测生物膜形成能力。

结果 共纳入 160 株 CRKP。标本来源以痰液（46.9%）和血液（26.3%）为主，呈现多重耐药表型，CRKP 菌株以携带 blaKPC（80.6%）为主，其次为 blaNDM（18.1%）。根据是否携带 T6SS 将 CRKP 分为 T6SS 阳性组（129 株，80.6%）和 T6SS 阴性组（31 株，19.4%）。在患慢性肺部疾病和心脏疾病方面，T6SS 阳性组患者比例高于 T6SS 阴性组（P<0.05），且 T6SS 阳性组患者预后较阴性组差（P<0.05）。T6SS 阳性组中 iucA、rmpA2、peg344、wabG、fimH、mrkD 阳性率均高于 T6SS 阴性组（P<0.05）。CRKP 中以 ST11 型（69.3%）为主，其中 K64-ST11 型占比 69.6%，K47-ST11 型占比 25.2%，T6SS 阳性组 ST11 型和 K64-ST11 型阳性率均高于 T6SS 阴性组（P<0.05）。T6SS 阳性组 CRKP 生物膜形成能力强于 T6SS 阴性组。两组在耐药基因和抗生素耐药率方面无明显差异。

结论 该地区 CRKP 呈现多重耐药，T6SS 在 CRKP 中的携带率高，T6SS 阳性 CRKP 毒力基因携带率更高且生物膜形成能力更强。

关键字：肺炎克雷伯菌，T6SS，毒力基因，耐碳青霉烯类耐药，碳青霉烯酶

成人慢性呼吸系统疾病继发肺部感染病原菌分布特点、耐药性分析及感染预测模型

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目的 以往研究慢性呼吸系系统疾病合并病原菌感染多侧重于某种特定疾病如慢性阻塞性肺病或支气管哮喘合并病原菌感染，少有研究常见慢性呼吸系统疾病背景下继发下呼吸道感染的一般病原菌特点、临床特征以及预测感染临床指标。

方法 这是一项回顾性病例对照研究，选取2019 年-2022 年来自中国江苏省苏州大学附属第一医院收治的确诊为慢性呼吸系统疾病的 154 例成年住院患者，根据患者住院初次痰液细菌培养或支气管肺泡灌洗液细菌培养结果分为观察组（合并病原菌感染）和对照组（未合并病原菌感染），观察组所占比例 35%（54/154）。

结果 154 例慢性呼吸系统疾病中以慢性阻塞性肺病（44.2%，68/154），间质性肺炎（35.7%，55/154）较为多见，其次为肺纤维化（9.7%，15/154）、支气管哮喘（4.5%，7/154），观察组中患者年龄大于对照组，性别并无差异，病原菌感染以革兰阴性菌多见，其中以铜绿假单胞菌为主，占比 37%（20/54），主要见于慢性阻塞性肺病，其次为肺炎克雷伯杆菌，真菌感染以丝状真菌烟曲霉菌为主，多见于间质性肺炎，占比 14.8%（8/54），铜绿假单胞菌对亚胺培南和美罗培南，及喹诺酮类环丙沙星和左氧氟沙星相对耐药，对头孢他啶、头孢吡肟、阿米卡星和妥布霉素高度敏感，慢性呼吸系统疾病合并病原菌感染患者其咳嗽、咳痰与胸闷气喘等症状与单纯慢性呼吸系统疾病差异无明显统计学意义（P＜0.05），且前者发热症状并不突出，经典病原菌感染指标白细胞计数、中性粒细胞计数并不能发挥良好提示作用，C 反应蛋白升高、中性粒细胞百分比升高、淋巴细胞计数降低、三尖瓣反流压力阶差增大、体重过低一定程度提示合并慢性呼吸系统疾病患者继发病原菌感染，但是三尖瓣反流压力阶差增大，体重过低、淋巴细胞计数减少三者联合（（AUC 0.788，P=0.000，95CI 0.689～0.887）更加良好预测慢性呼吸系统疾病继发细菌感染。

结论 在慢性呼吸系统疾病背景下，患者继发细菌感染以革兰阴性菌多见，其中以铜绿假单胞菌为主，真菌感染以烟曲霉菌为主，临床表现以咳嗽、咳痰、胸闷气喘多见，与单纯肺部感染相比发热及部分病原菌感染指标变化并不典型，三尖瓣反流压力阶差增大，体重过低、淋巴细胞计数减少三者联合对预测合并慢性呼吸系统疾病患者继发细菌、真菌感染有较高价值。

关键字：慢性呼吸系统疾病，病原菌特点，临床特征，预测模型

Characteristics of Mucormycosis in Hematological Patients and A Death Prediction Model

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Objective The aim of our study was to explore the high-risk factors and predict the death of hematological disease complicated with mucormycosis

Methods We retrospectively analyzed clinical data of 31 patients with hematological disease complicated with mucormycosis, adopted random forest to establish the death prediction model, and validated the model in another 15 patients. The median age of the 31 cases was 46 (28–51) years, male to female ratio 1.38:1, and 90-day mortality rate 54.8%. The most common underlying disease was acute myeloid leukemia (58.1%). The main clinical symptoms were fever (100%), cough (87.1%), sputum (80.6%), chest pain (61.3%), and hemoptysis (19.4%). Reversed halo sign (83.9%) was the most common computed tomography sign. A total of 48.4% of patients also had aspergillus or bacterial infections. Discriminative models were constructed by random forest with 17 non-survivors and 14 survivors

Results Procalcitonin, the duration of intravenous administration of amphotericin B or amphotericin B liposomes, and neutropenia at death or 90 days of survival were the leading risk factors for poor prognosis, with area under the curve of 0.975 (95% CI 0.934–1). We chose 0.6775 as death prediction threshold (with 82.3% sensitivity and 100% specificity) and validated the model successfully in another 15 patients

Conclusion Chest pain and reversed halo sign are specific clinical and image signs of hematological disease complicated with mucormycosis. Neutropenia, elevated procalcitonin, and insufficient use time of amphotericin B or amphotericin B liposomes are risk factors for death

关键字：mucormycosis, hematological diseases, death prediction model, high-risk factors, random forest

Genomic Analysis and Characterization of Emerging OXA-232-Producing ST231 Multidrug Resistant Klebsiella Pneumoniae in China

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Objective OXA-232 carbapenemase, being a vital resistance mechanism against carbapenems, has been increasingly reported recently. In China, the identified OXA-232-producing K. pneumoniae isolates almost belonged to ST15 and were not hypervirulent despite harboring a virulence plasmid. ST231, an epidemic multidrug resistant (MDR) K. pneumoniae clone in South Asia, has never been found in East Asia

Methods Four OXA-232-producing K. pneumoniae isolates of ST231 were first isolated from a tertiary hospital in Yunnan, China. Antimicrobial susceptibility test, genomic sequencing approaches, phylogenetic analysis and mice infection models were implemented to study the resistance profiles, genomic features, clonal origin and virulence potential

Results All isolates displayed an MDR phenotype, only susceptible to polymyxin B and colistin, and the blaOXA-232 gene was located on a ColKP3-type nonconjugative plasmid of 6.1 kb. Phylogenetic analysis of global ST231 isolates (n=231) suggested that the four ST231 isolates gathered with strains from South Asia (especially India), indicating the emerging Chinese ST231 clone was more closely related to South Asia isolates and might have spread from South Asia. Virulence assays suggested that the ST231 strains were not highly virulent, although three ST231 strains harbored a plasmid-borne aerobactin gene cluster

Conclusion This is the first report of ST231 K. pneumoniae clinical strains bearing blaOXA-232 in China, highlighting the emergence of the ST231 clone in a healthcare setting and representing a critical and worrying step toward the rise of another epidemic clone as a public threat

关键字：Multidrug Resistance; Klebsiella Pneumoniae; OXA-232 Carbapenemase; ST231; Dissemination

2013-2022 年孕产妇血流感染的临床特点及病原菌分布

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目的 通过探讨孕产妇血流感染的临床特征、病原菌分布和药敏试验情况，为临床诊断和治疗提供参考依据。

方法 回顾性分析 2013 年 1 月至 2022 年 12 月期间广东省人民医院产科病区血流感染病例的临床病历资料、送检血培养阳性病原菌分布和药敏试验情况。

结果 共收集 50 例血流感染孕产妇，其中妊娠期 3 例（6%），剖宫产 31 例（62%），自然分娩 9 例（18%），引产 2 例（4%），刮宫钳 5 例（10%）。44 例（88%）患者并发妇产科相关疾病和并发症，46 例（92%）患者在病程中出现发热，2 例（4%）患者出现感染性休克。50 例血流感染患者的炎症指标在病程中均有升高。50 例患者经积极治疗好转痊愈出院，但有 6 例（12%）出现感染性流产。50 例血流感染患者中，共分离出 57 株病原菌，最常见的病原菌分别为大肠埃希菌 22 株（38.60%）、无乳链球菌 10 株（17.5%）和粪肠球菌 7 株（14.0%）。大肠埃希菌 ESBL（超广谱 β-内酰胺酶）阳性率为 50%（11/22），对阿米卡星、亚胺培南、厄他培南的敏感率为 100%，对氨苄西林的耐药率最高。无乳链球菌对氨苄西林、青霉素 G、万古霉素、奎奴普丁/达福普汀、利奈唑胺的敏感率为 100%，对四环素的耐药率最高。

结论 孕产妇血流感染主要发生在分娩后，会导致感染性休克和感染性流产，对母婴健康造成严重危害。孕产妇血流感染分离病原菌主要以大肠埃希菌、无乳链球菌、粪肠球菌为主，临床应根据相应的病原菌结合药敏结果合理规范选用抗菌药物。

关键字：血流感染；孕产妇；病原菌分布；药敏试验

广东地区妇产科患者尿路感染的病原菌分布及耐药性变迁

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目的 了解某地区妇产科患者尿路感染的病原菌分布状况及耐药特点，分析其耐药性变迁，合理规范化使用抗菌药物。

方法 收集广东省人民医院妇产科病区 2018 年 1 月-2022 年 12 月 634 例尿路感染患者送检的中段尿培养的结果，比较分析不同年份病原菌分布状况及耐药性变化趋势。

结果 共检出病原菌 706 株，其中革兰阴性杆菌 581 株，革兰阳性球菌 94 株，念珠菌 31 株，分别占 82.30%、13.31%和 4.39%。排名前 3 位病原菌依次为大肠埃希菌、肺炎克雷伯菌和粪肠球菌，分别占 66.29%、8.22%和 6.23%。尿路感染随着年龄增长呈显著上升趋势（$\chi2=133.46$，$P<0.001$），≥61 岁的人群具有最高的感染率（34.97%，135/386）。大肠埃希菌和肺炎克雷伯菌对头孢唑林的耐药率较高，对碳青霉烯类、β-内酰胺酶抑制剂合剂、阿米卡星等抗菌药物的耐药率较低。大肠埃希菌和肺炎克雷伯菌

产 ESBLs（超广谱 β-内酰胺酶）菌株的检出率较高，检出率分别为 61.11%和 46.55%，大肠埃希菌产 ESBLs 菌株呈上升趋势（$\chi2=10.03$，$P<0.05$）。粪肠球菌对四环素的耐药率较高且稳定，未发现对青霉素 G、氨苄西林、万古霉素、呋喃妥因的耐药株。

结论 大肠埃希菌是妇产科尿路感染的主要病原菌，产 ESBLs 菌株检出率较高，且呈上升趋势。临床需密切关注病原菌分布状况及耐药性变化趋势，合理规范化使用抗菌药物。

关键字：妇产科；尿路感染；病原菌；分布；耐药性

妊娠期糖尿病孕妇尿路感染的临床特征与危险因素分析

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目的 探讨妊娠期糖尿病（Gestational diabetes mellitus，GDM）孕妇尿路感染的临床特征与可能相关危险因素，为降低尿路感染和临床治疗提供参考依据。

方法 收集 2018 年 1 月至 2022 年 12 月确诊为 GDM289 例患者，对 GDM 孕妇尿路感染的发病率、病原菌分布以及耐药性进行回顾性分析，并采用 Logistic 回归模型分析 GDM 孕妇尿路感染的可能相关危险因素。

结果 289 例 GDM 孕妇中有 32 例发生尿路感染，发病率为 11.07%。洁净中段尿培养共检出 32 株病原菌，其中以大肠埃希菌（53.13%，17/32）为主，其次是无乳链球菌（15.63%，5/32）。大肠埃希菌对氨苄西林耐药率较高，对阿米卡星、β-内酰胺酶抑制剂合剂、碳青霉烯类等抗菌药物耐药率较低。多因素 Logistic 回归分析显示，甘油三酯（OR=1.276、95%CI：1.066-1.526、P<0.05）是 GDM 孕妇尿路感染的独立危险因素。

结论 甘油三酯与 GDM 孕妇尿路感染的发生有关，临床上可采取相应措施，降低尿路感染的发病率，并根据患者病情合理选择抗菌药物。

关键字：妊娠期糖尿病；尿路感染；病原菌；危险因素

危重症监护室血流感染预后危险因素分析

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目的 分析危重症监护室血流感染患者的临床特点及影响预后的危险因素，以期改善患者的生存情况，助力临床精准诊疗。

方法 采用病例对照研究的形式，回顾性分析广东省人民医院 2022 年 1 月至 12 月危重症监护病房的 160 名血流感染病患的临床资料，包括其基础疾病、临床表现、危险因素、病原菌耐药情况、治疗用药及其预后情况等相关信息。根据 28 天的患者预后情况，将 160 例血流感染患者分为存活组 93 例与死亡组 67 例，比较两组之间的各项指标，用 logistic 回归分析危重症监护室血流感染预后危险因素。

结果 共纳入 160 例危重症监护室血流感染患者，检出病原菌 177 株，其中革兰阳性（G+）菌 94 株，占 53.11%；革兰阴性（G-）菌 60 株，占 33.90%；真菌 23 株，占 12.99%；前 5 位分离的病原菌分别为表皮葡萄球菌（占 17.51%）、肺炎克雷伯菌（占 8.47%）、鲍曼不动杆菌（占 7.34%）、头状葡萄球菌（占 7.34%）、屎肠球菌（占 6.78%）。通过对多因素 Logistic 回归模型的深度分析，发现感染性休克（OR=5.144、95%CI：2.034-13.01、P<0.05）、碳青霉烯类药物使用（OR=3.064、95%CI：1.089-8.626、P<0.05）是影响危重症监护室血流感染患者 28 天死亡的独立危险因素。

结论 危重症监护室血流感染的病原菌主要以 G+菌为主，其中感染性休克、碳青霉烯类药物使用是危重症监护室患者血流感染 28 天死亡的独立危险因素。对于此类患者，应加强对相关危险因素的评估，采取针对性的防控干预措施，以改善血流感染患者的预后。

关键字：危重症监护室；血流感染预后；病原菌；危险因素

新冠疫情前后儿科病区病原菌分布及耐药性分析

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目的 分析新型冠状病毒肺炎疫情（简称新冠疫情）前后儿科病区病原菌分布及耐药性情况。

方法 回顾性比较广东省人民医院儿科病区在新冠疫情发生前的 2018 年 1 月至 2019 年 12 月与新冠疫情期间的 2020 年 1 月至 2021 年 12 月的标本送检和病原菌检出情况，并对主要病原菌药敏结果进行分析。

结果 新冠疫情发生前（2018-2019 年）儿科病区检出的病原菌中革兰阴性菌占 59.5%，革兰阳性菌占 34.4%，真菌占 6.1%，肺炎克雷伯菌、大肠埃希菌和表皮葡萄球菌是最常见的病原菌。新冠疫情

期间（2020-2021 年）儿科病区检出的病原菌中革兰阴性菌占61.2%，革兰阳性菌占33.1%，真菌占5.7%，大肠埃希菌、肺炎克雷伯菌和金黄色葡萄球菌是最常见的病原菌。疫情前后，上呼吸道、血液和洁净中段尿均是检出病原菌较多的标本类型，其中肺炎克雷伯菌、表皮葡萄球菌和大肠埃希菌分别在以上标本类型中检出最多。疫情前后革兰氏阴性杆菌的耐药率普遍有所下降，特别是鲍曼不动杆菌，而革兰氏阳性球菌的耐药率变化不大。疫情前后多重耐药菌的检出率，CRE 分别为 10.8%和 5.8%，CRAB 分别为32.4%和 12.5%，差异均有统计学意义；而 CRPA 分别为 14.0%和 7.3%，MASA 分别为 47.4%和 5.8%，差异均无统计学意义。

结论 疫情前后儿科病区病原菌检出率、各类标本送检比例、检出菌药敏情况、多重耐药菌检出情况均有所改善，这说明新冠肺炎疫情暴发后，全国采取的做好个人防护等疫情防控措施，可有效降低儿科病区病原体，特别是呼吸道病原菌的感染率，可为今后临床诊断及用药和医院感染防控提供参考。同时，加强儿科病区，特别是儿科重症监护病房的环境卫生学监测，落实医感防控措施至关重要。

关键字：新型冠状病毒肺炎，儿科，病原菌，耐药性

2019—2022 年甘肃省阴沟肠杆菌的临床分布特征及耐药性分析

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目的 分析 2019—2022 年甘肃地区阴沟肠杆菌的分布及其耐药性，为该地区阴沟肠杆菌抗感染治疗提供参考。

方法 收集甘肃省细菌耐药监测网成员单位 2019—2022 年各医院阴沟肠杆菌的分布及耐药监测资料，使用药敏纸片扩散法、最低抑菌浓度（MIC）法和全自动化仪器法对阴沟肠杆菌进行体外药敏试验，按 2021 年美国临床实验室标准化协会（CLSI）标准判读结果，采用 WHONET 5.6 和 SPSS 26.0 软件进行数据分析。

结果 2019—2022 年甘肃地区共分离细菌 307550 株，其中阴沟肠杆菌 13219 株，检出率为 4.3%；阴沟肠杆菌主要分离自痰液标本，其次为尿液、伤口脓液标本，检出率分别为 61.2%、7.8%、6.5%；2019—2021 年科室分布以呼吸内科、儿科、重症医学科为主，检出率分别为 16.7%、10.8、8.5%；患者年龄分布以成人组（15—65 岁）最多，检出率为 46.2%；药敏结果显示阴沟肠杆菌对替加环素（0.7%）、阿米卡星（1.7%）、美罗培南（2.6%）、头孢哌酮/舒巴坦（7.0%）、左氧氟沙星（7.1%）的耐药率稍低外，对其他常用的抗菌药物存在较高的耐药率。耐碳青霉烯类阴沟肠杆菌的检出率呈现上升趋势，由 2019 年的 1.3%上升到 2022 年的 3.4%。

结论 阴沟肠杆菌的检出率变化趋势不明显，但仍居高位。对部分药物的耐药率呈逐年上升趋势，临床医师应根据药敏试验结果选择合适的抗菌药物进行治疗，以减少耐药菌株的产生。

关键字：阴沟肠杆菌，抗菌药物，耐药性，合理用药

The Draft Genome Sequence of BlaCTX-M-270-carrying Kluyvera Ascorbata Isolated From Human Sputum

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Objective The primary aim of this study was to elucidate the genomic characteristics and antibiotic resistance profile of an Kluyvera ascorbata strain 141611, which was isolated from the sputum of a patient with pulmonary infection at our hospital in 2023 as part of standard care. kluyvera ascorbata can cause a variety of infections, including bacteremia, cholangitis, and urinary tract infections, some of which are life-threatening. However, compared to many other Enterobacteriaceae species, Kluyvera remains less studied.Specifically,The resistance to penicillin and the first- and second-generation cephalosporins may be explained by the presence of blaCTX-M-270, and determining the comprehensive antibiotic resistance gene profile of the strain

Methods The Kluyvera ascorbata strain 141611 was isolated from the sputum of a patient with pulmonary infection. The sputum was inoculated onto blood and chocolate plates for 24-h incubation at 37°C. The strain was preliminarily identified as K. ascorbata using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (Bruker, Billerica, MA, USA). Subsequently, the strain was cultured on Luria-Bertani agar at 37°C for 24 h, and a single colony was subcultured overnight in broth using the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany) for genomic DNA extraction following the instruction without modifications. Sequencing library was constructed using the NEBNext Ultra II kit (NEB, Ipswich, MA, USA). Genome sequencing with a 150-bp paired-end protocol was performed on HiSeq X10 (Illumina, San Diego, CA, USA). Generated reads were processed with Cutadapt v4.0 for trimming 10 bp from both ends and removing adapters and quality filtering (minimum quality, Q15; minimum length, 50 bp) using BBMap v39.01.The sequencing data were assembled and annotated using bio-

informatic tools. The genome was screened for the presence of antibiotic resistance genes. Susceptibility testing was performed using Vitek II (bioMérieux, Marcy-l'Étoile, France) using Escherichia coli ATCC25922 as the reference, and results were interpreted according to CLSI 2022 guidelines

Results The genome of Kluyvera ascorbata strain 141611 was found to be approximately 5.18 megabases (Mb) in size, encoding a wide array of genes associated with antibiotic resistance.Three antimicrobial resistances, blaCTX-M-270, fosA, and tet(34), were identified using ResFinder. Strain 141611 was resistant to piperacillin, cefuroxime, cephalothin, and cefazolin but was susceptible to amoxicillin/clavulanate, ticarcillin/clavulanate, ampicillin/sulbactam, piperacillin/tazobactam, ceftriaxone, cefepime, cefotaxime, ceftazidime, cefpodoxime, ertapenem, imipenem, meropenem, doripenem, amikacin, tobramycin, gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, doxycycline, minocycline, tigecycline, tetracycline, and trimethoprim-sulfamethoxazole. The resistance to penicillin and the first- and second-generation cephalosporins may be explained by the presence of blaCTX-M-270

Conclusion The genomic analysis of the Kluyvera ascorbata strain 141611 isolated from human sputum reveals a complex antibiotic resistance profile underscored by the presence of the blaCTX-M-270, fosA, and tet(34) gene. Genome sequencing for more Kluyvera strains is required to understand the genus of clinical relevance

关键字：pathogen, CTX-M, Kluyvera, Kluyvera ascorbata

耳道分离的耐甲氧西林金黄色葡萄球菌的基因组特征

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目的 对某医院耳道分离的耐甲氧西林金黄色葡萄球菌（MRSA)菌株进行分子流行病学分析，从而了解此类来源 MRSA 的基因组特征。

方法 收集 105 株耳道分离的耐甲氧西林金黄色葡萄球菌，采用药物敏感性试验（微量肉汤稀释法）、多位点测序分析(multilocus sequence typing,MLST)、全基因组测序等方法对菌株的基因组特征进行分析。

结果 金黄色葡萄球菌是导致耳部感染的主要菌种之一。在本研究中我们分析了 105 株耳道分离的 MRSA 的基因组特征。其中最流行的序列型（ST）是 ST59（27.62%；29/105），ST398（15.24%；16/105），ST764(12.38%；13/105)，ST1(7.62%；8/105)和 ST22（7.62%；8/105）。使用核心基因多位点序列型(cgMLST)分析（≤11 个核心基因多态性位点），识别到了 12 个传播簇，每个传播簇包含 2 至 4 个分离株。药敏结果表明，没有对替考拉宁，利奈唑胺以及万古霉素耐药的菌株。对大环内酯类抗生素的耐药率为 69.52%（73/105）；对氨基糖苷类抗生素的耐药率为 9.52%（10/105）；对氟喹诺酮类抗生素的耐药率为 45.71%（49/105）。我们发现传播链中的分离株多为氟喹诺酮耐药株，通过卡方检验表明 MRSA 的氟喹诺酮耐药与克隆传播显著相关（p=3.84×10-6）。在不同 ST 型中我们发现，ST764 和 ST22 中的克隆传播的菌株占比最高，分别为 84.62%（11/13）和 75.00%（6/8）。这两种 ST 型中氟喹诺酮耐药株占比分别为 100%（13/13）和 87.50%（7/8）。

结论 氟喹诺酮类抗生素耐药是 MRSA 在耳道感染患者之间传播的危险因素。ST764 和 ST22 可能是 MRSA 在耳道感染患者之间传播的高危克隆群。

关键字：耐甲氧西林金黄色葡萄球菌，耳道感染，基因组，流行病学

导管相关血流感染中真菌性感染的病原菌分布及耐药性分析——一项单中心回顾性研究

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目的 通过对单中心近三年导管相关血流感染（CRBSI）中真菌性感染的病原菌分布及耐药性分析，为控制真菌性 CRBSI 及合理用药提供参考依据。

方法 对西安交通大学第一附属医院 2021 年 1 月-2023 年 12 月期间，患者血培养结果及导管培养结果提示的有病原学证据的导管相关血流感染确诊患者的临床资料进行回顾性分析。

结果 共收集到 CRBSI 确诊患者 125 例，共检出病原菌 130 株，其中真菌性 CRBSI 确诊患者 28 例，共检出病原菌 28 株，占同期全部 CRBSI 患者检出病原菌的 21.54%（28/130 株）。28 例患者来自 8 个不同科室，以各类 ICU 为主，占 75%（21/28 例），包括心血管外科 ICU9 例、肝胆外科 ICU7 例、中心 ICU4 例、神经外科 ICU1 例。28 株病原菌均为假丝酵母菌，其中以非白色假丝酵母菌为主，占 60.71%（17/28 株），其中又以近平滑假丝酵母菌为主（76.47%，13/17 株），而白色假丝酵母菌占 39.29%（11/28 株）。本研究共检出耐药真菌 5 株，占 17.86%，其中近平滑假丝酵母菌对氟康唑、伏立康唑的耐药率分别为 23.08%、15.38%，热带假丝酵母菌对氟康唑、伏立康唑的耐药率分别为 66.67%、33.33%，未发现对氟康唑、伏立康唑、伊曲康唑和两性霉素 B

耐药的白色假丝酵母菌。

结论 本院CRBSI患者中真菌性感染占到两成以上。病原菌分布以非白色假丝酵母菌为主，其中又以近平滑假丝酵母菌最多。本研究所检出的近平滑假丝酵母菌和热带假丝酵母菌对氟康唑和伏立康唑均存在不同程度的耐药，临床在治疗时应注意根据药敏报告及时调整用药。

关键字：导管相关性血流感染，真菌，耐药性

难治性耐药肺炎克雷伯菌血流感染的危险因素及预后评价

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目的 探讨医院内难治性耐药肺炎克雷伯菌（Difficult-to-treat resistance Klebsiella pneumoniae，DTR-KP）血流感染患者的临床危险因素及预后情况，为临床及时遏制其流行，改善患者预后提供依据。

方法 收集广东省人民医院 2018 年 1 月~2023 年 6 月临床已确诊为 DTR-KP 血流感染患者病历资料 50 例，采用病例-对照 1：2 研究方法，随机选取同期被诊断为非 DTR-KP 所致血流感染的患者资料 100 例，运用单因素及多因素 logistics 回归分析 DTR-KP 血流感染患者的临床危险因素，采用 χ^2检验分析患者临床预后情况。

结果 DTR-KP 血流感染患者年龄中位数为 64 岁，主要分布于重症监护室、老年医学科、新生儿科。两组患者在伴有血液系统疾病（χ^2=5.081，P=0.024）、合并 3 种及以上基础疾病（χ^2=9.949，P=0.002）、入住 ICU＞7d（χ^2=8.824，P=0.003）、中心静脉插管（χ^2=8.036，P=0.005）、机械通气（χ^2=4.216，P=0.040）、使用 β-内酰胺酶抑制剂（χ^2=8.517，P=0.004）和糖皮质激素（χ^2=3.898，P=0.048）等方面的比较存在统计学差异。经 logistics 回归分析结果显示，患者伴有血液系统疾病（OR=3.935，P=0.017）、合并 3 种及以上基础疾病（OR=3.389，P=0.004）、入住 ICU＞7d（OR=3.970，P=0.003）和中心静脉插管（OR=6.809，P=0.026）可能是导致 DTR-KP 血流感染发生的重要危险因素。DTR-KP 血流感染患者死亡率高于对照组（χ^2=25.729，P<0.001）。

结论 DTR-KP 血流感染患者预后较差，临床需提高对其的认知能力与防控意识，通过采取主动筛查等措施，进而有效减少 DTR-KP 血流感染的发生。

关键字：难治性耐药肺炎克雷伯菌；血流感染；危险因素；临床预后

ST11-KL64 型碳青霉烯类耐药肺炎克雷伯菌的耐药特点和分子流行病学特征

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目的 明确本院呼吸科病房 ST11-KL64 型碳青霉烯类耐药肺炎克雷伯菌(CRKP)的耐药特点和分子流行病学特征，为临床抗感染治疗提供依据

方法 收集解放军总医院呼吸与危重症医学部呼吸道感染患者痰液样本，经微生物培养后使用 BD Phoenix 全自动细菌鉴定及药敏分析系统进行 CRKP 菌株鉴定与药敏试验。提取细菌 DNA 进行全基因组测序（Whole-genome Sequencing, WGS），通过 Sourmash 分析细菌基因组序列相似性；Pathogenwatch 确定菌株多位点序列分型（Multilocus sequence typing，MLST）、荚膜血清型与耐药基因、质粒复制子、毒力因子。

结果 在 26 份痰液样本中共鉴定到 24 株 CRKP，其中 9 株为 ST11-KL64 型 CRKP。药敏结果显示，这些分离株对哌拉西林-他唑巴坦钠、氨苄西林-舒巴坦钠等青霉素类抗生素均耐药；对厄他培南、亚胺培南、美罗培南均耐药；对左氧氟沙星、诺氟沙星、莫西沙星、环丙沙星等喹诺酮类抗生素均耐药；对头孢西丁、头孢呋辛、头孢他啶、头孢曲松和头孢哌酮钠-舒巴坦、头孢吡肟等头孢菌素类抗生素均耐药；氨基糖苷类抗生素率也较高，55%分离株（5/9）对庆大霉素、妥布霉素、阿米卡星耐药率；77%分离株（7/9）对替加环素处于中间敏感性；未见对多粘菌素耐药分离株。全基因组分析结果显示，这些 ST11-KL64 型 CRKP 均同时携带 3 种质粒复制子 ColRNAI、IncR 和 IncFII 与多种抗生素耐药基因，其中碳青霉烯类耐药基因均为 blaKPC-2；毒力基因分析结果显示，1 株 ST11-KL64 型 CRKP 携带 ybt、iuc 与 rmpA2 三种毒力基因，8 株 ST11-KL64 型 CRKP 携带 ybt、iuc、rmpA 与 rmpA2 四种毒力基因。

结论 分研究分离的 ST11-KL64 型 CRKP 均为 MDR 同时携带多种毒力因子。这些拥有高毒力及高耐药双重表型的 KP，不仅能在抗生素压力环境中轻松存活，而且可以作为毒力质粒的传播者传播更多的 CRKP 菌株。

关键字：碳青霉烯耐药肺炎克雷伯菌，细菌基因组学，细菌耐药

Effect of Climate on Enterobacteria for

Bloodstream Infection

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Objective There is a growing awareness of the impact of various climate factors on pathogenic bacteria, and numerous studies have underscored the seasonality of Enterobacteriaceae. Our study is to explore the correlation between climatic factors and bloodstream infection of Enterobacteriaceae bacteria and identify key prevention and treatment strategies for Enterobacteriaceae infection in the context of a subtropical monsoon climate in China

Methods Conducted as a single-center ecological study, we collected clinical data on patients with Enterobacteriaceae bloodstream infection from January 2016 to December 2022, alongside meteorological data from Hangzhou City. The clinical data, categorized by department (ICU, non-ICU) and bacteria type (CRE, CSE), were analyzed for correlation with climatic factors. The study aimed to elucidate the impact of climatic factors on Enterobacteriaceae bloodstream infection and carbapenem resistance, identifying relevant climatic factors.

Results Involving 1,740 cases of Enterobacteriaceae bloodstream infections, the study revealed the following: (1) Positive correlation between the number of CSE, CSE-non-ICU bloodstream infections, and monthly maximum wind speed. (2) Positive correlation between ICU temperature and CSE bloodstream infection, peaking with a one-month lag. Seasonal correlation of CSE bloodstream infection, with higher incidence in summer and positive correlation with average temperature. (3) CRE bloodstream infection negatively correlated with cryogenic group temperature, and overall drug resistance of Enterobacteriaceae showed a negative correlation with temperature

Conclusion Wind speed, air temperature, and air pressure exhibit associations with Enterobacteriaceae bloodstream infection. Variances in the effects of climatic factors on CRE and CSR bloodstream infections, coupled with the particularity of intensive care rooms, underscore the necessity of nuanced prevention and control strategies for drug-resistant bacteria, considering environmental and climatic nuances

关键字：climate;Enterobacteria;Bloodstream Infection;Carbapenem-Resistant Enterobacteriaceae

Characterization of Staphylococcus Aureus Strains with Novel Incomplete Hemolytic Phenotype

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Objective To explore the microbiological characteristics of S. aureus with novel incomplete hemolytic phenotype (novel SIHP)

Methods Hemolytic phenotypes were detected and categorized by using the three-point inoculation method. A total of 11 novel SIHP and 33 randomly matched S. aureus with complete hemolytic phenotype (SCHP) were included. Antibiotic susceptibility test was performed using broth microdilution method. Coagulase test was performed with freeze-dried rabbit plasma. Catalase activity was detected by slide catalase test. Expression of hemolysin genes was detected by qRT-PCR. Toxicity to human red blood cells was assessed by microplate method. Microplate biofilm formation was measured using crystal violet staining method. Growth kinetic determination was performed through microcultivation assay

Results Compared with SCHP, the expression profiles of the four hemolysin genes (hla, hlb, hlc, and hld) in the novel SIHP are different. The novel SIHP has higher resistance rates to penicillin, oxacillin, gentamicin, quinolones, clindamycin, and trimethoprim-sulfamethoxazole. Furthermore, the novel SIHP has stronger hemolytic toxicity, plasma coagulase activity, and biofilm formation ability. Additionally, the novel SIHP grows faster in the logarithmic phase

Conclusion Taken together, the microbiological characteristics of the novel SIHP are different from those of SCHP, including stronger antibiotic resistance and pathogenicity, which should be paid more attention by clinicians

关键字：Staphylococcus aureus, hemolysin, hemolytic phenotype, microbiological characteristics

慢加急性肝衰竭合并侵袭性肺曲霉病的危险因素分析及预测模型建立

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目的 慢加急性肝衰竭（Acute-on-chronic liver failure, ACLF）合并真菌感染常常预后不良，ACLF 合并侵袭性肺曲霉病(Invasive pulmonary aspergillosis, IPA)是 ACLF 较为常见的肺部真菌感染类型。本研究旨在描述性分析 ACLF 发生 IPA 的危险因素，为 ACLF 合并 IPA 风险人群的早期识别提供依据。

方法 回顾性收集 2014 年 1 月至 2023 年 8 月在西安交通大学第一附属医院感染科住院的 ACLF

患者的临床资料，根据 IPA 诊断标准严格筛选出符合 IPA 临床诊断的患者。选取同期住院可排除肺部真菌感染的 ACLF 合并肺部感染的患者为对照组，采用多因素 logistics 分析 ACLF 合并 IPA 的独立危险因素。

结果 1. 835 例 ACLF 患者中 IPA 的发生率为 6.6%(55/835)，IPA 在 ACLF 合并肺部感染人群的发生率为 19.9%(55/276)。

2.55 例 ACLF 合并 IPA 的年龄为 50.64±12.22，69.1%为男性(38/55)，65.5%的病因为 HBV 感染(36/55)，94.5%合并肝硬化(52/55)，18.2%合并糖尿病(10/55)。IPA 组的中位住院时间为 25 天，90 天无移植生存率为 28.3%(17/55)。55 例患者从起病到发生 IPA 的中位时间为 31 天，34 例 ACLF 患者发生 IPA 的中位时间为 13 天。

3. 肝硬化(OR=7.97, P=0.013)、糖尿病(OR=3.35, P=0.044)、糖皮质激素应用(OR=4.15, P=0.006)、年龄(OR=1.06, P=0.008)是 ACLF 合并 IPA 的独立危险因素。

4.根据以上四项危险因素建立预测模型 CDGA-IPA，CDGA-IPA=1.773×[合并肝硬化(有：1,无：0)]+1.621×[合并糖尿病(有：1,无：0)]+1.173×[糖皮质激素应用(有：1,无：0)] +0.037×年龄-5.941。训练集 ROC 曲线下面积 AUC 为 0.779(95%CI=0.689-0.869)，测试集 ROC 曲线下面积 AUC 为 0.824(95% CI=0.691-0.956)。

结论 ACLF 合并 IPA 发生率约为 6.6%，常发生于病程的 1 个月左右，在入院的 2 周左右需警惕 IPA 发生。肝硬化、合并糖尿病、使用糖皮质激素、年龄是 ACLF 合并 IPA 的独立危险因素。根据这四项因素建立的预测模型可对于 ACLF 发生 IPA 的发生风险进行评估。

关键字：侵袭性肺曲霉病；慢加急性肝衰竭；危险因素；

Epidemiological Characteristics of Pulmonary Tuberculosis Among Inpatients in A Grade-A Tertiary Hospital in Jiangxi Province Based on GeoDa Software

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Objective To understand the epidemiological changes of tuberculosis among inpatients in general hospitals during the post-epidemic period, and provide reference for exploring a new model of tuberculosis prevention and control

Methods From 2020 to 2022, the information of tuberculosis patients in a Grade-A tertiary hospital hospital in Jiangxi Province was collected. R3.0 software was used to calculate the distribution and visualize the results，while GeoDa1.22 software was used for spatial autocorrelation analysis

Results A total of 2327 cases of pulmonary tuberculosis were collected and reported, with a ratio of male to female of 2.3:1, with an average age of 57 (46,69) years. Farmers were the main occupation, and the proportion of students and workers increased. The average reported incidence rate was 81.7/10,000. The incidence rate of pathogen positive reports is increasing year by year (=8.76，P<0.001）). The reported incidence of pulmonary tuberculosis was different among male among different ages.(=22.56，P=0.012). The three-year global Moran's I index values are -0.046, -0.024 and -0.033, respectively (P values all exceed 0.05). Hot spots in HH cluster were Nanchang, Fuzhou and Yichun. In addition to the above three places, Jiujiang has been added to the hot spots in LH gathering area. The reported peak incidence was mainly in winter (2020 and 2021), while the reported peak incidence was in autumn in 2022

Conclusion In the future, it will be a challenge for the hospital infection control in Jiangxi Province to explore a new mode of tuberculosis prevention and control that consider the situation in Jiangxi Province, from the perspectives of continuing to pay attention to high-risk groups, early warning of spatial geographical risks, improving the screening rate of admission and exploring the treatment habits of patients in general hospitals

关键字：Tuberculosis; Epidemic characteristics; Spatial autocorrelation; Post-epidemic period

腹膜透析液培养阳性腹膜炎临床特征

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目的 探讨腹膜透析中由不同病原菌引起的腹膜炎的临床特点。

方法 回顾性分析 2018 年 1 月至 2022 年 12 月在四川大学华西医院肾病护理单元收治的腹膜透析相关性腹膜炎(peritoneal dialysis-associated peritonitis, PDAP)病人的临床资料。根据检出病原菌的不同，分为革兰阳性(G+)菌组、革兰阴性(G-)菌组和真菌组，比较三组间病原学分布特点和临床特征。根据患者是否拔管分为两组，分析两组间白介素 6(interleukin-6，IL-6)、降钙素原(procalcitonin, PCT)、白细胞、血小板(platelet,PLT）、血红蛋白、白蛋白、C 反应蛋白(C-reactive protein，CRP)等指标，二元 Logistic 回归

分析拔管的影响因素。

结果 2018 年 1 月至 2022 年 12 月送检 1066 例腹透液样本，其中 332 例检出病原菌，阳性检出率为 31.1%(332/1066)，病原菌检出 337 株。G+菌组 244 株，占比 72.4%(244/337)；以凝固酶阴性葡萄球菌(57.4%)、链球菌(19.7%)为主。G-菌组 64 株，占比 19.0%(64/337)；以大肠埃希菌(26.6%)和铜绿假单胞菌(17.2%)为主。真菌组 29 株，占比 8.6%(29/337)；以近平滑念珠菌(41.4%)为主。拔管组与非拔管组在年龄、IL-6、CRP、PLT 和病原菌感染类型比较差异有统计学意义，二元回归分析显示真菌感染是腹膜炎拔管的独立危险因素。

结论 PDAP 的主要致病菌以 G+菌为主，G-菌感染患者具有更高水平的 PCT 和 IL-6，真菌感染者具更高水平的 PLT 数量；感染性腹膜炎尤其是真菌性腹膜炎是患者终止腹膜透析改为血液透析的主要危险因素。

关键字：腹膜透析，腹膜炎，临床特点

Extended-Spectrum B-Lactamase-Producing Escherichia Coli and Klebsiella Pneumoniae: Risk Factors and Economic Burden Among Patients with Bloodstream Infections

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Objective Extended-spectrum β-lactamase-producing Escherichia coli and Klebsiella pneumoniae (ESBL-EK) are important sources of bloodstream infection (BSI),Most existing studies show that bacteremia caused by ESBL generally has a higher disease burden compared with bacteremia caused by non-ESBL-producing bacteria. WHO has included extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae in the WHO list of priority pathogens for new antibiotic research and development and classified them as priority category 1: extremely important part. However, in recent bacteremia prevalence data, there are large gaps in estimates of the additional burden caused by ESBL bacteria in different regions and countries. These data gaps mean that large-scale epidemiological surveys globally or across China may not reflect local conditions. Regional epidemiological survey data are crucial for local hospitals' decision-making on antibiotic selection and nosocomial infection management

Methods We performed a retrospective analysis of inpatients diagnosed with Escherichia coli or Klebsiella pneumoniae bacteremia in a tertiary hospital from January 2020 to December 2022 in Guangzhou, China. We employed the chi-square test to examine ESBL risk factors and utilized propensity score matching (PSM) to negate baseline confounding factors, assessing economic burden through disability-adjusted life years (DALYs), hospital costs and productivity losses. We employed mediation analysis to eliminate confounding factors and better identify ESBL sources of burden related

Results A total of 318 patients meeting study specifications were identified, including 152 non-ESBL-EC/KP BSI patients (47.8%) and 166 (52.2%) ESBL-EC/KP BSI patients. Before matching, there were statistically significant differences in hospitalization time before infection, organ transplantation rate, ICU admission rate, Age-adjusted Charlson Comorbidity Index (ACCI), and SOFA score between the two groups (all $p<0.05$). The ESBL group has lower empiric antimicrobial therapy effective rate than that in the non-ESBL group (non-ESBL=80.3% vs ESBL=58.4%, $p<0.001$), and a higher total mortality rate (non-ESBL=17.8% vs ESBL=27.1%, $p=0.047$). After using PSM-adjusted estimates, the ESBL group still had a lower rate of effective empirical antimicrobial therapy than the non-ESBL group (non-ESBL=79.3% vs ESBL=59.5% $p=0.001$). The median total hospitalization cost was $5638 for non-ESBL patients and $7685 for ESBL patients ($p=0.014$), but there was no significant difference in total mortality (non-ESBL=19.0% vs ESBL=20.7%, $p=0.747$) and mean DALYs (non-ESBL=1.84 DALYs vs ESBL=2.12 DALYs, $p=0.098$) between two groups. Using Baron and Kenny's steps for mediation analysis, we identified that the relationship between ESBL and hospitalization costs is largely or fully mediated by inappropriate empirical antibiotic therapy and hospital stay

Conclusion Patients with BSI due to ESBL-producing ESBL-EK incur higher costs compared to those with non-ESBL-EK BSI. This cost disparity is rooted in varying rates of effective empirical antimicrobial therapy and differences in hospital stay durations. A nuanced approach, incorporating a thorough understanding of regional epidemiological trends and judicious antibiotic use, is crucial for mitigating the financial impact on patients

关键字：Escherichia coli, Klebsiella pneumoniae, bacteremia, ESBL, risk factors, medical costs

衢州市单中心儿童分离肺炎链球菌临床特征及血清型分布研究

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目的 探讨衢州市儿童感染肺炎链球菌流行情况及其血清型的分布特征，为指导该地区的疫苗应用和研发提供依据。

方法 收集 2020 年 1 月至 2022 年 6 月衢州市人民医院 16 岁以下儿童患者的不同来源标本中分离的肺炎链球菌，进行系列菌株鉴定实验，并通过乳胶凝集试验、荚膜肿胀试验对所有菌株进行血清型鉴定，并分析血清型分布和相关感染性疾病的流行特点。

结果 共收集到 107 株肺炎链球菌，除 2 株不能明确分型外共鉴定出 21 种血清型，排名前 5 位的血清型为 19F、6B、14、19A 和 3。肺炎链球菌多糖结合疫苗 7（Polysaccharide Conjugate Vaccine 7，PCV7）、PCV13 和 PCV20 的血清型覆盖率分别为 56.1%（60/107）、71.0%（76/107）、78.5%（84/107）。本研究中肺炎链球菌引起儿童支气管肺炎是主要感染类型，不同 PCV 覆盖血清型肺炎链球菌引起支气管肺炎病例数的方差比较分析表明，PCV7 覆盖血清型与非 PCV7 血清型无明显差异；但 PCV13（P=0.0083）和 PCV20（P=0.0016）覆盖血清型显著高于非该类疫苗覆盖血清型引起肺炎病例数。

结论 引起衢州市儿童肺炎链球菌疾病的主要流行血清型为 19F、6B、14、19A 和 3，其中支气管肺炎为最主要感染类型。肺炎链球菌多糖结合疫苗 PCV13 和 PCV20 对该地区儿童感染肺炎链球菌支气管肺炎有显著保护力。建立肺炎球菌疾病发病状况的监测系统，针对肺炎链球菌血清型分布和感染性疾病进行长期流行病学监测是非常必要的。

关键字：肺炎链球菌；血清型；多糖结合疫苗；儿童

脑脊液检测指标对早期预测中枢神经系统感染病原菌种类的临床价值

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目的 分析神经外科不同病原菌所致中枢神经系统感染的脑脊液常规及生化检测指标，早期预测感染病原菌种类，为临床药师参与临床会诊提供参考依据。

方法 回顾性纳入 2019 年 10 月至 2022 年 12 月 南昌大学第一附属医院神经外科收治的 311 例中枢神经系统感染患者。根据脑脊液培养结果分为革兰阳性 菌组、革兰阴性菌组。比较两组的脑脊液生化及常规指标差异。

结果 共纳入中枢神经系统感染患者 311 例，其中革兰阳性感染 151 例，革兰阴性菌感染 139 例，真菌感染 21 例。剔除真菌感染 21 例及脑脊液常规数 据缺失 48 例后，采用 spss26.0 软件进行分析发现，除脑脊液凝块及氯离子含量指标外，革兰阳性菌组（121 例）与革兰阴性组患者（121 例）的脑脊液各项常规及生化检测指标差异均具有统计学意义（P＜0.05）。 其中革兰阴性菌组患者的脑脊液白细胞总数、蛋白含量均高于革兰阳性菌组（P＜0.001），而脑脊液葡萄 糖含量低于革兰阳性菌组（P＜0.001）。ROC 曲线分析结果显示：脑脊液白细胞总数＞200/UL、脑脊液蛋 白质＞100mg/dL、脑脊液葡萄糖＜2.2mmoL/L 及三者联合预测的曲线下面积（AUC）分别为 0.619（95%CI： 0.547-0.691）、0.642（95%CI：0.571-0.713）、0.653（95%CI：0.583-0.723）、0.704（95%CI：0.637-0.771）。

结论 脑脊液白细胞总数、脑脊液蛋白质及脑脊液葡萄糖检测指标对中枢神经系统感染革兰阴性菌有一定的 预测价值，三者联合的预测价值更高，为临床药师会诊提供精准经验性治疗，减少细菌耐药发生率。

关键字：中枢神经系统感染，脑脊液检测指标，早期预测，病原菌种类，临床价值，临床药师会诊

2018 年-2023 年某三甲中医院临床分离的真菌临床分布及耐药性分析

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目的 分析 2018 年-2023 年某三甲中医院临床分离的真菌患者资料，研究该院真菌流行特征、分布特点及耐药性，为真菌感染合理用药和真菌感染的危险因素分析提供数据。

方法 收集某大型三甲医院 2018 年 1 月-2023 年 12 月期间临床分离的真菌 195 株，使用利用全自动微生物质谱仪 Autof ms1000（郑州安图生物工程有限公司）和全自动微生物鉴定药敏分析仪 AutoMic-i600 进行菌种鉴定和药敏试验。

结果 2018 年 1 月-2023 年 12 月日期间共检出真菌 195 株。主要以白假丝酵母菌和热带假丝酵母菌为主，尿和痰中检出最高，而科室分布中 ICU 的检出最高。白假丝酵母菌菌株 104 株，对两性霉素 B 和伊曲康唑之外的抗真菌药物均有较好的体外抗真菌活性，而热带假丝酵母菌 34 株是对除伊曲康唑和泊沙康唑之外的抗真菌药物均有较好哦的体外抗真菌活性，不同的假丝酵母菌呈现出不一样的耐药性。

结论 本研究中该院在历年，ICU（重症监护室）在科室分布中占比最高,因此对真菌感染特别是重症患者应合理使用抗生素，加强尿液和痰液的病原学检测，同时加强隔离消毒清洁等防控管理，并研究结合中医医药特长，调节患者免疫力，多方面防控真菌的发生和传播。

关键字：真菌，感染，流行病学，耐药性

Clinical Characteristics and Drug Resistance of 170 Children with Invasive Streptococcus Pneumoniae Infection

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Objective Invasive pneumococcal diseases (IPD) is an important and common infectious disease in children, with high morbidity and mortality, which affects the healthy growth and development of children.By analyzing the clinical characteristics and drug resistance of IPD in children in our hospital, we hope to provide evidence for the diagnosis, treatment and reduction of infection rate and mortality of IPD in children

Methods A total of 170 children diagnosed with invasive Streptococcus pneumoniae infection admitted to the Children's Hospital of Zhengzhou University from January 2016 to December 2022 were selected as the study object. Sterile body fluid samples of infected children were isolated and cultured, and antimicrobial susceptibility tests (AST) were carried out on the strains cultured. The resistance of Streptococcus pneumoniae to common antibiotics was analyzed statistically. We consulted the clinical information of infected children through the hospital information system, and made statistical analysis of their general conditions, clinical conditions, laboratory tests and other clinical characteristics

Results 170 cases of IPD were mainly under 3 years old, which mainly caused infection of circulatory system, central nervous system and other infections. The main clinical manifestations of infected children were fever, cough and poor mental performance. Leukocyte, C-reactive protein (CRP), procalcitionin (PCT) and other infection indexes were increased in most infected children. In this study, 18 children died, with a mortality rate of 10.6%. Age less than 1 year old, serious complications, low white blood cells, CRP, PCT significantly increased were the main risk factors for death. In this study, the resistance rate of Streptococcus pneumoniae to penicillin reached 16.8%, and the resistance rate of other β-lacamides was low. No strains resistant to vancomycin and linezolid were detected. The resistance of PNSP (penicillin-nonsusceptible Streptococcus pneumonia) strains to other antibiotics was higher than that of PSSP (penicillin-susceptible Streptococcus pneumonia) strains. The rate of drug resistance of the strain isolated from central nervous system was higher in the age group under 1 year

Conclusion IPD mainly affects children under 3 years old. The main sites of invasion include circulatory system and central nervous system. The drug resistance of pathogens isolated from children under 1 year old and central nervous system was high. The clinical treatment of IPD children should be rationally selected antibiotics according to the results of drug sensitivity

关键字：Children, Streptococcus pneumoniae, Drug resistance, Clinical, Invasive

Genome Editing in Klebsiella Pneumoniae

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Genome editing has been on the crest in the field of reforming gene structure in microorganisms in recent years. Zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and cluster regulatory interspaced short palindromic repeat/CRISPR associated proteins (CRISPR/Cas) are three of the mainstream technologies utilized in genome editing. With the burgeoning of the CRISPR-Cas system, it is now available to knock in or knock out a specific gene to detect gene functions or even reverse the drug resistance in pathogenic bacteria. Considering Klebsiella pneumoniae (K. pneumoniae) is becoming the leading cause of nosocomial infections throughout the world with its extensive drug resistance spreading widely, the stakes for controlling the infections and resistance caused by K. pneumoniae could hardly be higher, where genome editing methods could show great potential. Although K. pneumoniae has put a great threat to global public health, measures to tackle this problem are limited. This review will present brief descriptions about modern genome editing technologies, summarize their current applications in K. pneumoniae along with the advantages and limitations of each technology, to provide more ideas for the further use of genome editing technology in K. pneumoniae.

关键字：genome editing, Klebsiella pneumoniae, CRISPR-Cas, ZFNs, TALENs.

肺炎克雷伯菌高毒力情况及与临床关系的调查研究

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目的 了解我院高毒力肺炎克雷伯菌（Hypervirulent Klebsiella pneumoniae,hvkp）流行情况，比较分析 hvkp 与经典型肺炎克雷伯菌株（Classic Klebsiella pneumoniae,ckp）的毒力基因、荚膜血清型、拉丝实验、临床特征、预后以及药物敏感性等方面的差异，旨在为临床诊疗和院感防控提供参考依据。

方法 收集我院临床分离的肺炎克雷伯菌株（Klebsiella pneumoniae,kp），收集患者的临床资料，并进行药敏试验、拉丝实验，同时通过聚合酶链反应（Polymerase Chain Reaction, PCR）进行毒力基因检测、荚膜血清型检测。并单独分析其中社区感染病例。

结果 分离 kp 菌株 207 株，总体病例中 hvkp 检出 164 株（79.23%），ckp 检出 43 株（20.77%）。总体 hvkp 和 ckp 相比较，在临床特点方面差异无统计学意义（p>0.05）。总体 hvkp 拉丝实验阳性率（78.66%），明显高于 ckp（16.28%），差异有统计学意义（p<0.05）。总体 hvkp 主要以三个毒力基因均为阳性为主（70.12%），主要血清型为 K1（22.56%）、K2（19.51%）、K57（15.24%）。总体 hvkp 耐药率均低于 ckp，检出 7 株耐碳青霉烯高毒力肺炎克雷伯菌（carbpenem-resistant hypervirulent Klebsiella pneumoniae, CR-hvkp）菌株。总体 hvkp 脓毒症发生率为 20.12%，ckp 脓毒症发生率为 23.26%，差异无统计学意义（p>0.05）。肝脓肿病例共 13 例，均为 hvkp, 其中社区感染 12 例（92.31%），医院感染 1 例（7.69%），主要荚膜血清型为 K2 型（30.77%），K1 型（23.07%）。

结论 （1）本研究发现我院无论总体 kp 还是社区 kp 感染患者中 hvkp 检出率均很高。hvkp 与 ckp 组在发病年龄、体温、PCT、CRP、WBC、脓毒症发生率及预后方面均无明显差异。（2）本研究中总体 hvkp 和社区 hvkp 均以三种毒力基因同时阳性为主，荚膜血清型主要为 K1、K2、K57 型。hvkp 组在毒力基因、特异性荚膜血清型及拉丝实验阳性率均明显高于 ckp 组。（3）本研究中肝脓肿均为 hvkp 感染，主要为社区感染，荚膜血清型主要为 K2 和 K1 型，脓毒症发生率高。（4）本研究中 hvkp 对常见抗菌药物耐药率明显低于 ckp，共检出 7 株 CR-hvkp 菌株，其中 5 例为社区感染，预后差，值得临床医生及感控人员高度关注。

关键字：肺炎克雷伯菌；毒力基因；荚膜血清型；脓毒症；肝脓肿

细菌真菌感染的病原诊断技术

Evaluation of Pretreatment Methods for Filamentous Fungal Detection

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Objective In order to obtain the best mass spectrometry identification results for using the most appropriate methods in clinical practice, we explore the optimal pretreatment methods for different species and morphologies of filamentous fungi

Methods 98 fungal strains were treated with formic acid sandwich method, dispersion method, extraction method, and other methods using a medium element mass spectrometer (EXS3000) as a platform. Each strain had three targets, and the identification rates and confidence differences under different pre-treatment methods were compared to evaluate the identification effects of these methods

Results The mass spectrometry identification rates of 98 filamentous fungi obtained after pre-treatment with formic acid sandwich method, dispersion method, and extraction method were 85.71%, 82.65%, and 76.53%, respectively. The identification rate of the formic acid sandwich method was significantly higher than the other two methods (P<0 005) has the best identification ability and the obtained confidence is also higher than the other two methods

Conclusion The use of formic acid sandwich method for mass spectrometry identification of filamentous fungi can achieve ideal identification results, which is suitable for mass spectrometry identification of filamentous fungi in conventional laboratories

In recent years, with the increasing use of broad-spectrum antibiotics and the use of anti-tumor drugs, immunosuppressive drugs, etc., the incidence of invasive filamentous fungal infections in clinical practice has been increasing year by year. Invasive filamentous fungal infections have complex clinical manifestations, difficult diagnosis and treatment, and are characterized by high infection rate, high misdiagnosis rate, and high mortality rate. There are many types of filamentous fungi, and the drug resistance spectrum of different strains within the same genus may vary. Rapid and accurate identification of filamentous fungi can guide clinical rational selection of antifungal drugs.[1-3] Traditional morphological identification has low accuracy and takes a long time, making it prone to identification errors or inability to identify.[4] Although, 1-3-β-D glucan, galactomann test or Aspergillus antigen antibody test in serological testing may indicate the possibility of

fungal infection, they are easily affected by multiple factors therefore presenting false positives and false negatives. In addition, these serological testing has cross reactivity, which makes it difficult to determine fungal species [5-6], hardly providing accurate pathogen diagnosis. Although molecular sequencing is the "gold standard", its operation is cumbersome and expensive, the identification time is long, and it requires high laboratory conditions and the technical level of operators, which is not suitable for routine microbiology laboratory operations. In recent years, matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) has become a revolutionary technology for microbial identification, starting to be used for clinical identification of filamentous fungi. It has the advantages of low cost, accurate and fast identification, and good repeatability. However, compared to bacteria, mass spectrometry identification of filamentous fungi has always been a difficult point in clinical identification. Filamentous fungi have thick cell walls, difficult to break, and difficult to extract proteins, which affects the quality of mass spectrometry protein profiles and leads to poor identification results [7]. The above is the main reason why the mass spectrometry identification of filamentous fungi is not yet widely used in microbiology laboratories. There are no standardized guidelines for mass spectrometry pretreatment methods for filamentous fungi, and seeking efficient pretreatment methods is the key to the experiment. The essence of obtaining a spectrum for MALDI-TOF mass spectrometry identification is mainly to obtain the distribution of ribosomal proteins in the strain. The biggest factor affecting its accuracy is the release of bacterial proteins at the target site. Switching between different pretreatment methods is to obtain the most complete protein types and appropriate protein concentrations of the strain. Due to the different morphologies of different genera of filamentous fungi, the difficulty of obtaining proteins varies greatly when identifying filamentous fungi. Therefore, MALDI-TOF mass spectrometry may have certain differences in identifying different genera of filamentous fungi. In order to seek the optimal pretreatment method for filamentous fungi, this study will use the Zhongyuan Mass Spectrometer (EXS3000) as a platform to analyze and compare the differences in the identification results of different species of filamentous fungi using three pre-treatment Methods formic acid sandwich method, dispersion method, and extraction method. The aim is to explore the optimal pre-treatment method for filamentous fungi and provide timely pathogenic evidence for clinical practice.

关键字： filamentous fungi, MALDI-TOF MS spectrometry, formic acid sandwich method, dispersion method, extraction method

痰标本革兰染色联合肺炎链球菌抗原检测快速诊断肺炎链球菌性肺炎

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目的 肺炎链球菌又称为肺炎球菌，为一种革兰阳性球菌，是导致婴幼儿和老年人发病及死亡的主要病原菌。其最易引发的肺炎链球菌肺炎在临床表现及影像学等相关检查并无特异性，故其诊断仍依赖于实验室培养、分离及鉴定。但痰液培养耗时长及阳性率偏低等原因，寻找快速鉴定肺炎链球菌的方法已成为临床实验室研究的重点。本文通过探讨肺炎链球菌抗原快速检测联合痰涂片革兰染色在肺炎链球菌肺炎感染中的临床应用价值。结果 痰标本中分离得到的 8 种细菌经抗原检测结果均为阴性；胶体金法检测 30 例肺炎链球菌培养阳性的痰液标本阳性率为 100%；痰涂片联合抗原快速检测阳性率高于痰培养，差异具有统计学意义（P<0.05）。

方法 收集川北医学院附属医院 2022 年 1 月至 2022 年 10 月临床痰液标本分离得到的草绿色链球菌群、肺炎克雷伯菌、鲍曼不动杆菌、铜绿假单胞菌、金黄色葡萄球菌、嗜麦芽窄食单胞菌、流感嗜血杆菌及卡他莫拉菌共 8 种细菌各 5 株，肺炎链球菌培养阳性的痰液标本 30 例，以及痰涂片镜下疑似肺炎链球菌且合格的痰液标本 40 例，利用 BinaxNOW 试剂盒进行胶体金法肺炎链球菌抗原检测。

结果 痰标本中分离得到的 8 种细菌经抗原检测结果均为阴性；胶体金法检测 30 例肺炎链球菌培养阳性的痰液标本阳性率为 100%；痰涂片联合抗原快速检测阳性率高于痰培养，差异具有统计学意义（P<0.05）。

结论 痰液肺炎链球菌抗原检测法具有较好的特异性，与痰培养结果有较好的一致性，且痰涂片革兰染色联合抗原快速检测在早期鉴定肺炎链球菌肺部感染中具有较高的临床应用价值。

关键字：痰液；肺炎链球菌；肺炎；胶体金法；革兰染色

Application Value of Metagenomic Next-generation Sequencing in Hematological Patients with High-risk Febrile Neutropenia

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Objective To explore the application value of metagenomic next-generation sequencing (mNGS) in hematological patients with high-risk febrile neutropenia

Methods This retrospective study evaluated the results of plasma cfDNA sequencing in 164 hematological patients with high-risk febrile neutropenia. We assessed the diagnostic efficacy and clinical impact of mNGS, comparing it to conventional microbiological tests

Results In this study, mNGS successfully identified 68 different types of pathogens among 111 patients. The bacteria most frequently detected by mNGS included Enterococcus faecium, Acinetobacter baumannii, Staphylococcus aureus, Escherichia coli, and Klebsiella pneumoniae. On the other hand, the most common fungi were Candida tropicalis, Aspergillus flavus, Pneumocystis jirovecii, Lichtheimia ramose, and Rhizopus microspores. As for viruses, the most frequently identified were Human cytomegalovirus, Epstein-Barr virus, Human herpesvirus 1, Human herpesvirus 6, and BK polyomavirus. The conventional methods identified 17 types of pathogens across 36 patients. Out of these, bacterial cultures were positively identified in only 23 patients. The bacteria most commonly identified by these methods included Acinetobacter baumannii, Escherichia coli, Enterococcus faecium, Klebsiella pneumoniae, and Staphylococcus aureus. Candida tropicalis was the most common fungus identified, accounting for 85.7% (6/7) of detected fungi. A single case of mucormycosis was confirmed through a pathological examination. The viruses most often detected encompassed Human cytomegalovirus, Epstein-Barr virus, Human herpesvirus 1, and Human herpesvirus 6

mNGS demonstrated a significantly greater positive detection rate than conventional methods (67.7% vs. 22.0%, $P < 0.001$). This held true for bacterial (30.5% vs. 9.1%) and fungal (19.5% vs. 4.3%) species and viruses (37.2% vs. 9.1%) ($P < 0.001$ for each comparison). It's also important to note that mNGS was markedly more effective in identifying mixed infections than conventional methods (31.7% vs. 1.2%, $P < 0.001$).

The consistency between mNGS and conventional methods was scrutinized as well. In 54.3% (89/164) of the cases, concordant results were observed, while discordant results were noticed in 45.7% (75/164) of the participants. In 22.0% (36/164) of cases, both mNGS and conventional methods produced positive results, whereas in 32.3% (53/164) of participants, the results were negative in both instances. For 45.7% (75/164) participants, mNGS yielded positive results, whereas conventional methods indicated negative results. All pathogens identified by conventional methods were also detected through mNGS. In cases where mNGS results were negative, the conventional methods correspondingly yielded negative results as well.

The diagnostic accuracy of mNGS was remarkably superior to that of conventional methods (82.3% vs. 36.6%, $P < 0.001$). mNGS demonstrated a three-fold increase in sensitivity (79.3% vs. 25.7%, $P < 0.001$) compared to conventional methods. Specificity did not differ between the two groups.

The anti-infective treatment plans for 51.2% (84/164) of the participants were adjusted in accordance with the mNGS results (Table 2). 9.8% (16/164) of the participants underwent a change in their antimicrobial spectrum, and 11.0% (18/164) started receiving de-escalation therapy. In 22.6% (37/164) of cases, at least one anti-infective agent was discontinued, of which usage of all anti-infective agents was entirely ceased in 16 instances. Additionally, at least one anti-infective agent was introduced in the treatment plans for 7.9% (13/164) of the participants.

Conclusions mNGS of plasma cfDNA offers substantial promise for the early detection of pathogens and the timely optimization of anti-infective therapies in hematological patients with high-risk febrile neutropenia

关键字：metagenomic next-generation sequencing; febrile neutropenia; infection; pathogen diagnosis; cell-free DNA

Plasma and Blood-cell Co-metagenomic Sequencing in Precise Diagnosis and Severity Evaluation of Sepsis, A Prospective Cohort Study

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Objective The usefulness of plasma metagenomic next-generation sequencing (mNGS) and blood cell mNGS in precise diagnosis and prognosis prediction of sepsis is uncertain. The study evaluated the performance of plasm mNGS and bc-mNGS, and analyzed the value of different laboratory results in sepsis diagnosis

Methods One hundred and thirty-three patients meeting Sepsis 3.0 criteria and 147 blood samples were collected. Blood culture (BC), plasma mNGS (p-mNGS), blood cell mNGS (bc-mNGS), virus-qPCR and other necessary routine assays were conducted. Taking BC and qPCR as reference methods, diagnosis performance of p/bc-mNGS was analyzed. Blood transcriptome was conducted to evaluate the immunological response of patients from groups with different BC and mNGS results. Impact of antibiotic use on diagnosis performance was analyzed

Results In 147 samples, p-mNGS demonstrated a sensitivity of 100% for bacteria and fungi, 97% for

viruses, which was higher than bc-mNGS (88% for bacteria and fungi, 71% for viruses). The specificity of p-mNGS was 48% for bacteria and fungi and 97% for viruses, which was lower than that of bc-mNGS (84% for bacteria and fungi, 99% for virus). The p-mNGS(+) & bc-mNGS(+) samples mostly represented activated immunity response (low expression in interferon-induced genes, high expression in JAK-STAT pathway genes), poor clinical laboratory indicators (higher SOFA, higher PCT and higher CRP) and low survival rate. Prolonged use of broad-spectrum antibiotics affected much less on p/bc-mNGS diagnostic ability

Conclusion Our study revealed that p-mNGS exhibited the highest sensitivity, while bc-mNGS demonstrated relatively higher specificity. Transcriptome results indicated that p-mNGS(+) & bc-mNGS(+) group displayed more pronounced infection characteristics including more activated immune response and poorer clinical outcomes. This study highlighted the potential of plasma and blood-cell co-metagenomic sequencing in precise diagnosis and severity evaluation of sepsis patients

关键字：plasma, blood-cell, metagenomic next-generation sequencing, sepsis, intensive care units

Evaluation of Antimicrobial Adsorption Capacity in Blood Culture Medium

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Objective To evaluate the adsorption capacity of Merieux BacT/ALERT (FA Plus and FN Plus) bottles and HAPYEAR (aerobic and anaerobic) bottles for antimicrobial agents.

Method In simulated adult blood cultures, microbial-antimicrobial combinations were added to compare the inactivation capacity of commercial blood culture medium. The antibiotics used were imipenem, cefoxitin, vancomycin, cefoperazone/sulbactam, piperacillin/tazobactam, penicillin and micafungine.

Result The Merieux blood culture vial (bacteria + antibiotics) experimental group was all positive and had adsorption capacity for the antibiotics used in the experiment. However, the HAPYEAR results were partially positive, which only had adsorption capacity for piperacillin/tazobactam and micafungine, and had no adsorption capacity for most other antibiotics. In terms of the time to report positive results, the Merieux blood culture vial group (bacteria + antibiotics) was reported earlier. Among them, the average time of Merieux blood culture vial in the (Pseudomonas aeruginosa + piperacillin/Tazobactam) group was 8.4 hours earlier than that in the HAPYEAR group. The average time of the Merieux blood culture vial in the (Candida albicans + Micafunzin) group was 64.8 hours earlier than that in the HAPYEAR group.

Conclusion BacT/ALERT (FA Plus and FN Plus) culture medium have a relative advantage, but not an absolute advantage. Its detection rate is high, TAT is short, it can be selectively applied to patients who have used antibiotics in the past, and then take the blood culture samples

Bloodstream infection (BSI) is one of the common severe infectious diseases in clinic, with high mortality and serious harm [1]. Accurate and timely diagnosis of BSI is crucial for the treatment and prognosis of BSI patients, as well as reducing the related high morbidity and mortality. [2-3] As the gold standard for BSI detection, blood culture samples should be collected at the first time when sepsis is suspected in patients, and before the use of antibiotics, in order to maximize the detection rate.

However, in emergent suppurative situations, antibiotics are often administered prior to the collection of blood culture samples. It has been reported that nearly half of the hospitalized patients are treated with antibiotics prior to the collection of blood culture samples. [4] As a result, the turnaround time (TAT) of commercial automated blood culture systems may be significantly prolonged. Worse, microbial growth in the blood culture bottles may not be detected due to the antimicrobial activity of the blood culture mediums.[5] Substances that can absorb antimicrobials, such as resins or charcoal, are added to some commercial blood cultures to minimize the inhibitory effect of antimicrobials on microbial growth in blood cultures.[6] In 2013, BacT/ALERT FA Plus (aerobic) and FN Plus (anaerobic) bottles (bioMérieux) were developed to further improve the detection of microorganisms in samples from patients with sepsis. To date, several blood culture simulation studies (including whole blood injections in blood culture bottles, antibiotics and microorganisms) have compared BacT/ALERT FAN Plus culture medium with BACTEC Plus culture medium, including in both anaerobic and aerobic blood culture bottles. [7-8] However, since BacT/ALERT FAN Plus medium has only recently been approved in mainland China, data on antimicrobial inactivation properties are not available.

BacT/ALERT FAN Plus media in mainland China has not yet been opened. In this study, we aimed to evaluate the ability of BacT/ALERT FAN Plus medium and BACTEC aerobic and anaerobic medium against red blood cell inactivation by measuring the microbial detection rate and TAT of several antimicrobial drug-microbial combinations in simulated blood cultures. Specifically, blood concentrations in patients receiving antimicrobial drugs were simulated.

关键字：Keywords: Antimicrobial drug inactivation, Blood culture, Automated system, BacT/ALERT FAN + culture medium, Comparative evaluation

Early Diagnosis Clinical Prediction Model of Talaromycosis HIV-negative Hosts Using Clinical Data and Machine Learning

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Objective Frequent atypical symptoms in TSM cases often lead to misdiagnosis, with TB being a common misidentification. Notably, around 38.1% of patients received misdiagnoses as TB, necessitating antituberculosis treatments. Moreover, a striking 80.7% of non-HIV-infected TSM patients were inaccurately diagnosed with TB. This highlights pervasive diagnostic challenges in TSM, underscoring the need for heightened clinical awareness and refined diagnostic strategies

Method From 2012 to October 2023, employed a logistic prediction model with thorough internal verification. Discrimination was assessed using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. Clinical applicability was elucidated via clinical decision curve analysis (DCA) and clinical impact curve (CIC), projecting the net benefit of the prediction model for informed clinical decision-making

Result The study revealed that Age, Phlegm, Fever, Chest pain, Gasp, Rash, lymphadenopathy, osteolysis, neutrophils (N), platelet (PLT), eosinophils (EOS), and albumin (ALB) independently predicted the occurrence of the two diseases (all $P < 0.05$). In the training set, ROC curve analysis demonstrated an AUC of 0.918 (95%CI: 0.884-0.953). Notably, DCA curve analysis indicated that the model yielded superior net benefits across most threshold ranges

Conclusion Leveraging routine laboratory data and clinical features, a multivariable model adeptly distinguished between TSM and TB. Nevertheless, further inquiry is imperative to assess its utility and robustness before integrating this model into routine clinical care

关键字：Talaromyces marneffei, HIV-positive, HIV-negative, multicenter, retrospective study.

肺曲霉病的血清 G 试验、血清 GM 试验和肺泡灌洗液 GM 试验诊断效果评价

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目的 通过回顾性数据分析，研究血清真菌（1,3）-β-D 葡聚糖（1-3-β-D-glucan，G）试验、血清半乳甘露聚糖（glactomannan,GM）试验和肺泡灌洗液(bronchoalveolar lavage fluid, BALF)GM 试验检测结果对于临床肺曲霉病的早期诊断价值。

方法 共收集临床病例 158 例，有 96 例为临床确诊肺曲霉病患者的实验室检测结果，62 例无真菌感染患者作为阴性对照，通过血清 G 试验、血清 GM 试验和肺泡灌洗液 GM 试验单项检测和联合检测，分析这三项检测方法的灵敏度、特异性，绘制工作特征(receiver operating characteristic, ROC)曲线，并计算曲线下面积(area under curve, AUC)评价诊断效果。

结果 96 例肺曲霉病患者血清 GM 试验阳性率为 18.2%（16/88），血清 G 试验阳性率为 23.9%（21/88），肺泡灌洗液 GM 试验阳性率为 63.0%（46/73），结果与无真菌感染组患者对比有显著性差异 $P<0.05$；单一试验诊断肺曲霉病敏感性最好的是血清 GM 试验（0.568），特异性最好的是血清 G 试验（0.984），肺泡灌洗液 GM 试验预测肺曲霉病的预测诊断价值最高（AUC 为 0.751）；联合检测明显提高了敏感性，而特异性相对下降，敏感性最好的是联合检测血清 GM 试验/肺泡灌洗液 GM 试验阳性（0.652），特异性最好的是三种检测方法联合检测阳性（0.887），预测诊断价值最高也是联合检测血清 GM 试验/肺泡灌洗液 GM 试验阳性（AUC 为 0.779）。

结论 三种检测方法中单一方法检测肺曲霉病阳性率最高的是肺泡灌洗液 GM 试验，联合检测能明显提高诊断的敏感性和特异性，其中联合血清 GM 试验/肺泡灌洗液 GM 试验预测诊断肺曲霉病价值最高。

关键字：血清 G 试验，血清 GM 试验，肺泡灌洗液 GM 试验，肺曲霉病，联合检测

肺部感染影响纤维化性间质性肺病患者的急性呼吸系统症状恶化及预后的研究：基于微生物诊断进展的最新证据

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目的 在纤维间质性肺病（f-ILD）过程中，肺部感染是急性呼吸系统症状恶化（ARD）的重要原因，并促进疾病进展。很少有研究分析 f-ILD 的特定病原体分布及其对预后的影响。

方法 我们进行了一项横断面观察性队列研究。对所有因疑似肺部感染引发 ARD 而住院的 f-ILD 患者（n=67）进行常规检测方法（CDM）和支气管肺泡灌洗液（BALF）宏基因组下一代测序（mNGS）。二元逻辑回归用于评估这些患者 90 天死亡率的危

险因素。

结果 mNGS 和 CDM 在病原体检测中的一致性部分匹配比例较高（42%），mNGS（+）CDM（-）16 例（32%）。由肺部感染引发的 ARD（n=50）包括 54%的感染性 AE-ILD 和 46%的 f-ILD 伴肺炎。感染性 AE-ILD 的病原体载量几乎相当于感染性肺炎的 ILD。混合感染在幸存者（61.76%）和非幸存者（87.50%）中均占大多数。幸存者和非幸存者的病原体检测数量有统计学差异（2.32±1.53 vs 3.50±1.86，p=0.022），病毒、真菌、细菌或混合感染的百分比没有显着差异。二元逻辑回归分析表明，病原体数量（OR 1.59，CI 1.00，2.51）和 Lac（OR 4.51，CI 1.51，13.44）是 90 天死亡率的独立危险因素。

结论 随着微生物诊断的发展，我们首先分析了因肺部感染而发展为 ARD 的 f-ILD 患者的病原体谱。病原体数量是这些患者 90 天死亡率的独立危险因素。

关键字：感染，间质性肺病，预后，宏基因组下一代测序

深圳某综合医院耶氏肺孢子菌 3 年监测情况分析

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目的 调查耶氏肺孢子菌感染的临床特点，为临床早期诊断和治疗提供依据。

方法 通过查阅病例资料，分析 2017 年 1 月至 2020 年 5 月深圳某综合医院耶氏肺孢子菌的检出和临床分布情况、影像学特征、生化指标，以及染色检查的注意事项。

结果 68 例耶氏肺孢子菌六胺银染色标本中，共检出 6 例耶氏肺孢子菌感染，患者年龄介于 14~59 岁之间，来源于 ICU、血液内科、儿科等科室，均伴有肺炎症状，临床诊断为白血病或肾炎；血清 β-D-葡聚糖和乳酸脱氢酶均升高；染色温度和时间对六铵银染色的结果影响较大；影像学表现以胸部 CT 均发现磨玻璃密度影为主，患者经过复方新诺明和糖皮质激素联合治疗，症状有不同程度改善。

结论 患有不明原因肺炎的白血病或肾炎患者，常规治疗无效的，应考虑耶氏肺孢子菌感染，六铵银染色法对耶氏肺孢子菌的检出效果较好。

关键字：耶氏肺孢子菌；肺炎；临床特征；六铵银染色

Emerging Class R Lipooligosaccharide in Campylobacter Jejuni From Seagull Had Potential To Trigger Guillain-Barre Syndrome

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Objective Lipooligosaccharide (LOS) from Campylobacter jejuni had mimicry antigen structure with gangliosides explained the mechanism of C. jejuni caused Guillain-Barre Syndrome (GBS). In addition to the crucial role of the sialylated LOS, the capsules which determined serotypes of C. jejuni also contribute to the onset of GBS

Methods Genetic analysis, phenotypic serotyping and antigenicity studies for 25 C. jejuni strains isolated from seagull in south China were carried out in this study. Based on the genetic analysis for the biosynthesis loci of LOS, 12 of 25 strains were found having class R LOSs

Results Strikingly, all these 12 strains belonged to specific serotypes (HS2, HS4c, HS19, HS41) which were proved to be highly associated with GBS. With further genetic structure dissection, these LOSs from 12 strains could be classified into two groups: sialylated (8 strains) and non-sialylated (4 strains). Antigenicity analysis using immune serum and serum from GBS patients showed that the antigen-antibody reactions only occurred in strains with sialylated LOSs

Conclusion The results indicated these emerging C. jejuni strains which had both GBS associated serotypes and sialylated class R LOSs had gangliosides mimicry antigen structures and possessed highly potential for triggering GBS

关键字：Campylobacter jejuni; Guillain-Barre syndrome; class R LOS; Genetic and antigenicity analysis

Construction and Validation of Chicken Immune ScFv Antibody Library Against Helicobacter Pylori

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Objective Accurate diagnostic techniques and effective therapeutic methods are required for treatment of Helicobacter pylori (H. pylori). Application of chicken single-chain variable fragment (scFv) antibodies may be potential in diagnosis and treatment of H. pylori

Methods A chicken-derived immune scFv antibody library against H. pylori was constructed by phage display technique in this study. Total RNA was extracted from spleens of five immunized chickens and reverse transcribed into cDNA. Fragment of scFv was produced by overlap extension PCR and cloned into pHEN2 phagemid vector. After package with M13KO7 helper phage, the recombinant HpaA protein was used as a target antigen to validate the screening ability of our antibody library by bio-panning

Results The dilution counting results showed that the size of primary antibody library was estimated to be 1 ×109 cfu/ml. PCR analysis of 47 clones from library showed that about 100% of the clones were positive with scFv fragments and there were no identical sequences, indicating the good diversity of antibody library. After three rounds of bio-panning, high-affinity antibodies against recombinant HpaA protein were successfully obtained. The selected antibody specifically recognized HpaA protein in 9 different H. pylori strains, confirming the screening ability of our library

Conclusion The chicken immune scFv antibody library against H. pylori was successfully constructed, and the screening ability of antibody library was validated through selection specific scFv antibodies against recombinant HpaA and clinical strains. It provided a simple and rapid method to get antibodies against H. pylori for diagnosis or treatment

关键字：Helicobacter pylori, chicken scFv, phage display, diagnosis

The Value and Application of Different Assays in Carbapenemase Detection

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Objective The determination of carbapenemase type of carbapenem-resistant Enterobacteriaceae (CRE) is of great value for the precise use of clinical anti-infective therapy and hospital infection prevention and control. The results of this study were used to provide a basis for the selection of carbapenemase assays

Methods Seventy CRE strains isolated from cerebrospinal fluid, blood and sterile body fluids were tested for carbapenemase using PCR amplification, gene sequencing, colloidal gold immunochromatography and GeneXpert automated medical PCR system, and the performance of colloidal gold immunochromatography and GeneXpert automated medical PCR system was evaluated using sequencing results as reference standards

Results PCR amplification and gene sequencing detected 69 carbapenemase genes, including 49 KPC type, 12 OXA-48 type, 1 IMP type, 3 NDM type, 2 KPC and OXA-48 type, 1 OXA-48 and NDM type at the same time, 1 KPC and NDM type at the same time, and 1 of the above five genotypes was not detected. The sequencing results were 100% sensitive and 97.1% specific compared to colloidal gold immunochromatography. Two strains were not found, including one strain with sequencing results of both KPC and OXA-48, and colloidal gold test results of KPC type; one strain with sequencing results of both KPC and NDM, and colloidal gold immunochromatography results of KPC type; GeneXpert automatic medical PCR analysis system has 100% sensitivity and 100.0% specificity

Conclusion As two new carbapenemase assays, colloidal gold immunochromatography and GeneXpert fully automated medical PCR analysis system are simple to operate, easy to interpret the results, and can confirm the common KPC, OXA-48, VIM, IMP and NDM carbapenemases in CRE in a short period of time, and the sensitivity and specificity can meet the clinical needs, and can be used as a laboratory method for carbapenemase The sensitivity and specificity can meet the clinical needs, and can be used as a rapid method for laboratory carbapenemase detection to guide clinical diagnosis and treatment of CRE

关键字：carbapenemase, colloidal gold immunochromatography, GeneXpert fully automated medical PCR analysis system

急性期人布鲁氏菌病血清学和 PCR 检测效能评价

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目的 评价血清学和巢氏 PCR 检测对急性期布鲁氏菌病的临床检测效能及应用价值

方法 采用酶联 免疫吸附实验（ELISA）、试管凝集实验（SAT）、抗人免疫球蛋白实验（Coomb′s）等血清学及巢氏 PCR 检测方法 （nested-PCR）对 115 例布鲁氏菌病确诊患者血清样本进行检测，计算每种方法的检测结果，并进行统计学分析

结果 ELISA-IgA、ELISA-IgM、ELISA-IgG、巢氏 PCR、SAT、Coomb′s 的阳性检出率分别为 94.78%（109/115）、54.78%（63/115）、87.83%（101/115）、8.70%（10/115）、73.91%（85/115）、98.26%（113/115）；发病到确诊时间 < 15、15～29、30～44、45～59、> 60 d 组不同检测方法的检测结果差异有统计学意义（分别为 $\chi2 = 108.91$、103.04、50.75、27.73、34.16，均 $P < 0.05$）；各检测方法检出率差异有统计学意义（$H = 109.63$，$P < 0.05$）。SAT 与

Coomb′s 的实验滴度差异有统计学意义（Z＝－9.08，P＜0.05）

结论 血清学的阳性检出率明显高于巢氏 PCR，因此，血清学检测依然是诊断布鲁氏菌病 的最有效方法；Coomb′s 检测阳性率最高，可作为 SAT 检测的补充方法

关键字：布鲁氏菌病；血清学检测；巢氏 PCR

Xpert Mtb/RIF、γ-干扰素释放试验、荧光定量 PCR 在结核病诊断中的对比研究

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目的 比较结核分枝杆菌/利福平耐药快速检测法(Xpert Mtb/RIF)、荧光实时定量 PCR、γ-干扰素释放试验检测结核分枝杆菌的价值。

方法 纳入 2018 年 4 月 1 日至 2019 年 4 月 1 日在四川省人民医院就诊的结核分枝杆菌培养阳性的患者 151 例。利用 Xpert Mtb/RIF、荧光实时定量 PCR 技术对其痰液（或体液）标本进行 DNA 检测，并抽血送检 γ-干扰素释放试验，利用统计分析方法比较这三种检测技术对结核分枝杆菌的检出率以及结核培养阳性患者的 r-干扰素的集中范围。

结果 以结核培养为金标准，用 γ-干扰素释放试验辅助检测结核分枝杆菌的阳性率高于荧光实时定量 PCR 法与 Xpert Mtb/RIF 法，P＜0.05，差异有统计学意义。

结论 与用荧光定量 PCR 技术和 Xpert Mtb/RIF 相比，用 γ-干扰素释放试验辅助诊断结核分枝杆菌的阳性率更高，但可能存在假阳性，在临床诊断中应结合多方面考虑。

关键字：结核病，Xpert Mtb/RIF，荧光实时定量 PCR，γ-干扰素释放试验

切取活检法用于皮肤非结核分枝杆菌检测的临床应用

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目的 探讨切取活检法用于皮肤非结核分枝杆菌检测的临床应用。

方法 对皮肤科 2021 年-2023 年 8 例临床考虑非结核分枝杆菌感染的患者在无菌操作下使用切取活检法进行感染皮肤组织取材，观察病例皮肤组织抗酸涂片、组织病理抗酸染色及细菌培养情况，并对所有病例的临床资料进行分析总结。

结果 8 例患者中，皮损脓液或皮下组织直接抗酸涂片阳性 7 例，组织培养阳性 5 例，其中 3 例为海分枝杆菌、1 例脓肿分枝杆菌、1 例龟分枝杆菌，病理抗酸涂片阳性 1 例；皮肤非结核分枝杆菌临床特点为单侧的皮肤红斑、结节、脓肿、溃疡、结痂；皮损位于上肢的 5 例，腰、腹部 1 例，下肢 1 例；8 例患者中，1 例有肾功能不全，1 例为余病例无免疫缺陷；发病前均有外伤史或接触史。系统治疗均采用克拉霉素联合利福平或多西环素或莫西沙星或左氧氟沙星；有两例患者联合中药外用及火针治疗，1 例患者联合红外线烤灯治疗；预后时间不同，最短 3 月、最长 10 月仍未完全恢复。

结论 采用切取活检法取典型皮损将脓液或皮下坏死组织直接涂片抗酸染色阳性率高，无菌操作下取脓液和皮下坏死组织送培养阳性率高，病理抗酸染色阳性率低；病程越长，使用药物越多，分枝杆菌检出率越低；皮肤非结核分枝杆菌检测的前提是规范临床医生的取材方式以及采用微生物培养、质谱检测、宏基因测序、病理等方法共同协助诊断；皮肤非结核分枝杆菌治疗时间长，由于药物副作用和抗结核药的耐药、患者往往依从性差、导致不规范用药，增加了治疗时间，治疗难度较大。除了系统用药外，可结合手术切除、热烘疗法、火针、中药外用等治疗方法以缩短治疗时间。

关键字：皮肤非结核分枝杆菌，NTM，切取活检法

MP1P Antigen Detection in Urine Samples Could Improve The Rapid Screening and Diagnosis of Talaromycosis Marneffei

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Objective To evaluate the clinical application value of mannoprotein (Mp1p) antigen of Talaromyces marneffei in the urine, for introducing a simple and practicable tool for rapid diagnosis, enabling early treatment and potentially reducing mortality

Methods In this prospective cross-sectional study, we assessed the sensitivity and specificity of Mp1p antigen detection in urine samples by enzyme-linked immunosorbent assay (ELISA) and fluorescence immunochromatography (FIC) in 215 AIDS patients enrolled from the hospitalized ones in the Guangzhou Eighth People’s Hospital between March 2022 to January 2023

Results Among the TSM group and the Non-TSM group,82.5% and 88.6% were male; the median

age was 42 and 48. All cases were HIV infected; median CD4 count was 47 cells/μL and 187 cells/μL. The sensitivity and specificity of ELISA in Mp1p antigen in urine were the highest , with 77.5% (95% CI: 61.5%-89.2%) and 97.1% (95% CI: 93.5%-99.1%), respectively. The Positive predicted value (PPV) , negative predicted value (NPV), and kappa values were 79.5% (31/39), 94.9%(167/176) and 0.739. FIC in Mp1p antigen in urine had a sensitivity of 67.5% (95% CI: 50.9%-81.4%), a specificity of 94.9% (95% CI: 90.5%-97.6%), a PPV of 75%(27/36) and a NPV of 92.7%(166/179) and a Kappa value of 0.649

Conclusion The detection of Mp1p antigen in urine can effectively distinguish co-infection in HIV patients, and is an auxiliary means for early diagnosis of in clinics

关键字：Talaromycosis，Talaromycosis marneffei，Mp1p，

中国肠杆菌和蓉城肠杆菌：从临床样本中分离到的携带多种毒力因子的两种新型肠杆菌

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目的 肠杆菌在自然界中广泛分布，是常见的医院感染致病菌，可以导致多种类型的感染。但是由于肠杆菌属分类学的复杂及变迁，目前临床上所分离到的肠杆菌属菌株常被鉴定为阴沟肠杆菌复合体。本研究旨在通过生理生化特性及基因组分析，对临床分离到的 2 株来自血液样本的肠杆菌属菌株进行精确分类，并研究其临床致病性，为临床治疗及院感防控提供参考。

方法 2022 年从四川大学华西医院住院患者的血液样本中分离到两株肠杆菌属细菌，170198 和 170250。我们 170198 和 170250 进行全基因组测序、建立系统进化树，并确定了这两个菌株和所有目前已知肠杆菌属之间的平均核苷酸同一性（ANI）和 in silico DNA-DNA 杂交（isDDH）值，以及完善了一系列生理生化研究及毒力因子分析。

结果 基于 2096 个串联核心基因的系统发育树表明，这两个菌株位于肠杆菌属进化群内。这两个菌株属于两个新物种，ANI 和 isDDH 值均低于相同菌种的划分阈值（ANI 为 95-96%，isDDH 为 70%）。生理生化研究表明，170198 和 170250 菌株的生化特征和全脂肪酸图谱与已知的肠杆菌属基本一致。但是，这两个新物种可以通过某些生化特征与所有其他肠杆菌物种区分开来。这两个菌株均存在多种毒力因子，包括铁载体系统、VI 型分泌系统、外毒素等。因此，我们认为 170198 和 170250 代表了肠杆菌属的两个新物种，建议将中国肠杆菌和蓉城肠杆菌分别为其命名。中国肠杆菌和蓉城肠杆菌的模式菌株分别为 170198（=GDMCC 1.3549T=JCM 35826T ）和 170250（=GDMCC 1.3670T=JCM 36189T）。

结论 170198 和 170250 代表了肠杆菌属的两个新物种，建议将中国肠杆菌和蓉城肠杆菌分别为其命名。这两个菌株来源于血液样本，且患者出现了发热等感染症状，而菌株基因组中含有多种毒力因子，证明了这两个菌株具有较强的临床致病力。

关键字：肠杆菌属；肠杆菌科；肠杆菌目；分类学

A Novel Molecular Assay for Clostridioides Difficile Toxin Gene Detection: Evaluation of Clinical Diagnostic Efficiency

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Objective Clostridioides difficile (C.difficile) is recognized as one of the most important pathogenic microorganisms causing nosocomial infection and antibiotic-associated diarrhea worldwide. The prevention and control of Clostridioides difficile infection (CDI) has also been included in the National Major Scientific and Technological Projects of Infectious diseases in China. The existing identification methods generally have the problems of low specificity, low sensitivity, complex operation, low efficiency or high cost. In this study, a technique for detecting the toxin gene of C.difficile was constructed and its clinical application was evaluated. The purpose of this study is to make early and accurate diagnosis of CDI, carry out effective treatment and prevention, so as to reduce the burden of nosocomial infection

Methods Stool samples were collected from hospitalized patients with diarrhea or suspected CDI in the ICU wards of Xiangya Hospital Central South University from December 2018 to January 2020. We developed a set of methods, primers and kits to identify C.difficile by detecting the toxin genes tcdA and tcdB and the virulence regulatory gene tcdC. The patients' feces were simultaneously detected by this detection technology and “traditional anaerobic culture-biochemical identification-PCR” method. In order to double-check

the experimental results, all possible positive samples were identified by a second culture and further verified with reference to Cepheid Xpert C.difficile nucleic acid detection kit. We analyzed C.difficile infection status in ICU inpatients by combining clinical and laboratory results. The sensitivity, specificity, and overall consistency of the assay were evaluated

Results A total of 500 patient samples that met the inclusion criteria were tested, and 66 strains of C.difficile were isolated, with a detection rate of 13.2%. Among them, 63 strains were from intensive care unit, and 3 strains were from neurology ICU. The results showed that 50 samples were tcdA positive and 54 samples were tcdB positive. A total of 450 samples were tcdA negative and 446 were tcdB negative. There were 50 (75.8%) Clostridium difficile toxin A+B+ strains, 4 (6.1%) A-B+ strains, 12 (18.1%) A-B- strains, and no A+B- strain was detected. The total number of inconsistent samples between the two methods was 11, of which one was missed by the traditional PCR method. For the detection method of C.difficile in this research, the sensitivity, specificity, positive predictive value and negative predictive value of tcdA for CDI were 89.6%, 99.6%, 90.0% and 99.8%, respectively. The sensitivity, specificity, positive predictive value and negative predictive value to tcdB were 90.0%, 99.5%, 94.0% and 99.3% respectively. Of the 66 positive samples, the total toxin amount of CDI was also accurately detected. There were differences in toxins among different strains, while the average toxin amount of A+B+ strains was higher than that of A-B+ strains and A-B- strains. In addition, we also successfully developed an invention patent (NO. ZL202010834557.0) for detecting the virulence regulatory gene tcdC of C.difficile RT027

Conclusion The portable high-throughput isothermal PCR is a highly sensitive and specific method for C.difficile tcdA/B nucleic acid detection. The operation process is simple, rapid and stable. In addition, the detection method is accurate and the price is low, which can greatly improve the clinical CDI detection ability and can be widely promoted in primary hospitals. It has a great promoting effect on the prevention and control, diagnosis and treatment of CDI nosocomial infection

关键字：Clostridioides difficile, CDI, Molecular diagnosis, toxin gene, virulence regulatory gene

应用不同前处理法联合质谱技术快速检测血培养病原菌

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目的 通过不同前处理方法对阳性血培养标本进行前处理，联合基质辅助激光解析电离飞行时间质谱（MALDI-TOF MS），对阳性血培养标本病原菌进行快速检测，分析探讨不同前处理方法结合质谱技术快速检测病原菌与传统方法（即过夜培养后鉴定药敏）优劣性比较，优化目前血培养检测流程。

方法 将 30 份阳性血培养标本采用分离胶促凝管法、血培养试剂盒法、短时间培养法 2.5h、短时间培养法 5.5h 进行前处理后，分离病原微生物通过质谱进行快速鉴定，将不同前处理方法与传统方法相比较，就准确性、时间效益、经济效益、临床满意度等方面进行统计分析。

结果 以传统过夜培养后鉴定为参考方法，分离胶促凝管法鉴定率为 86.7%（23/30），短时间培养法 2.5h 的鉴定率为 46.7%（14/30），短时间培养法 5.5h 的鉴定率为 80.0%（24/30），血培养试剂盒法的鉴定率为 86.7%（26/30）。

结论 短时间培养法 5.5h 和分离胶法结合质谱仪进行血培养标本病原菌鉴定可快速有效的明确病原菌，血培养试剂盒法更为高效和便捷，利用不同前处理法分离到的病原菌同时进行药敏试验，可显著缩短血培养报告周期，为患者及早得到合适的抗菌药物治疗争取宝贵时间。

关键字：基质辅助激光解析电离飞行时间质谱；血培养；分离胶促凝管；短时间培养

A Case Report of Diagnosis of Cat-scratch Disease (CSD) Using Metagenomic Next-generation Sequencing

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Objective To explain that metagenomic next-generation sequencing(mNGS) may be used as a crucial supplementary diagnostic tool for individuals with compromised immune systems who may have CSD, especially when conventional diagnostic methods are inconclusive

Methods We present the case of a middle-aged male patient who developed fever, chills, anal distension, dizziness, and muscle pain for 10 days. The patient had a documented history of cat bites 1 month prior to the onset of symptoms. Following admission, he underwent an examination to determine superficial lymphadenopathy and hypoimmunity. Additionally, he had a fever during the disease. As the patient refused a needle biopsy of lymph nodes, metagenomic next-generation sequencing (mNGS) was employed and B. henselae was detected in the peripheral blood

Results The patient was diagnosed with CSD and treated with a combination of azithromycin and doxycycline. During the 2-week follow-up, the patient's overall condition was satisfactory, and he did not report

any discomfort

Conclusion mNGS aims to identify pathogens rapidly and accurately and can serve as an auxiliary technique for the diagnosis of CSD

关键字：Cat-scratch disease (CSD),Bartonella henselae, Hypo-immunity, Metagenomic next-generation sequencing (mNGS),Diagnosis,Treatment

聚焦超声法对基质辅助激光解吸电离飞行时间质谱鉴定 丝状真菌的方法研究

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目的 丝状真菌质谱前处理方法目前尚未标准化，本研究将以梅里埃质谱仪（VITEK MS）为平台，探讨聚焦超声法对基质辅助激光解吸电离飞行时间质谱鉴定丝状真菌的鉴定效果，优化前处理流程。

方法 收集 2022 年 1 月～2023 年 3 月广东省人民医院临床分离的非重复丝状真菌 131 株，均经基因测序和形态学鉴定确认，分别采用聚焦超声法和甲酸乙腈提取法前处理操作后进行质谱鉴定，并采用 Kappa 一致性检验和配对 t 检验分析比较两种前处理方法下的鉴定率、置信度、峰数量、耗时以及图谱质量。

结果 131 丝状真菌分别采用聚焦超声法和甲酸乙腈提取法处理后获得的质谱鉴定率均为 91.60%（120/131），其 Kappa 值为 0.603（P＜0.001），可见聚焦超声法与制造商推荐甲酸乙腈提取法相比，对丝状真菌鉴定效果具有较高的一致性。再者，聚焦超声法获得的置信度和峰数目分别为 90.73%和 170，与甲酸乙腈提取法相近（P＞0.05），提示两种方法获得的鉴定结果可信程度和图谱相似性均较理想，而且聚焦超声法在前处理流程步骤较简单，处理 20 株受试菌耗时为（80.10±0.08）min，少于甲酸乙腈提取法（P＜0.05）。在图谱比较方面，聚焦超声法相比甲酸乙腈提取法，所获得的蛋白图谱离子峰数量多，质量佳。

结论 聚焦超声法在丝状真菌的质谱鉴定效果上与甲酸乙腈提取法相当，具有鉴定率较高、流程简便、耗时较短和图谱质量佳的特点，适用于临床实验室日常丝状真菌的鉴定。

关键字：丝状真菌；聚焦超声法；甲酸乙腈提取法；质谱；鉴定

A Case of Chronic Wounds Caused by Sporothrix Schenckii Infection Was Rapidly Detected by Metagenomic Next Generation Sequencing

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The dimorphic fungus Sporothrix schenckii is widely distributed in soil, vegetation, and decaying organic matter, and can cause sporotrichosis when the patient's skin trauma was exposed to contaminated material with Sporothrix spp. The cases of Sporothrix schenckii infection in chronic wounds are rarely reported. Here we reported a 53-year-old male construction worker who was admitted to our hospital on July 9, 2022, without underlying disease presented with a painless subcutaneous hard nodule on his right calf, which later ulcerated and oozed, with an enlarged wound and no fever during the course of the disease. His procalcitonin, C-reactive protein, erythrocyte sedimentation rate increased, and necrotic histopathology suggested chronic granulomatous inflammation. Then his necrotic tissue and pus were sent for metagenomic next generation sequencing(mNGS), the result reported Sporothrix schenckii after 43 hours, which was consistent with the result of culture after 18 days. mNGS might be more useful and valuable in diseases such as sporotrichosis where it is difficult to see the yeast cells in the tissues.

关键字：Sporotrichosis, mNGS ,Culture ,Dimorphic fungus

血培养细菌快速方法鉴定及药敏试验与常规方法鉴定及药敏试验的方法学评价

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目的 评价血培养阳性报警转种后短周期培养 5-7 小时进行仪器法细菌鉴定及药敏试验（快速方法）与常规培养 18-24 小时进行仪器法细菌鉴定及药敏试验（常规方法）结果的一致性和准确性，探讨能否通过快速方法为临床诊断血流感染提供更早期更准确的用药参考依据。

方法 回顾性研究，对浏阳市人民医院 2023 年 5 月至 2023 年 7 月的 148 份血培养阳性标本，已剔除少见菌、苛氧菌、念珠菌、丝状真菌等，保留临床常见病原菌。

结果 148 株细菌，其中 115 株革兰阴性菌和 33 株革兰阳性菌，鉴定结果符合率分别为 98.26%和 100%，总符合率为 98.65%。大肠埃希菌 67 株归入纳入分析，其中全部药物的 CA 为 98.37%（1384/1407），MIE 为 1.64%（20/1407），ME 为 0.09%

（1/1407),VME 为 0.16%（2/1407）。其中阿米卡星、庆大霉素、头孢噻肟、氨苄西林、多粘菌素、复方新诺明、氯霉素、环丙沙星、左氧氟沙星 CA 均为 100%，其次是头孢唑林、头孢吡肟、哌拉西林、阿莫西林/克拉维酸、亚胺培南、美罗培南、莫西沙星和四环素 CA 为 98.51%，对头孢他啶和哌拉西林/他唑巴坦 CA 为 97.02%，对氨曲南和氨苄西林/舒巴坦 CA 最低也有 92.54%；21 株肺炎克雷伯菌中全部药物的 CA 为 98.85%（415/420），MIE 为 0.71%（3/420）,ME 为 0.24%（1/420）,VME 为 0.24%（1/420）；22 株金黄色葡萄球菌中全部药物的 CA 为 99.15%（349/352），MIE 为 0.57%（2/352）,VME 为 0.28%（1/352）。

结论 与常规方法相比，快速方法在常见革兰阴性菌和革兰阳性球菌中有较高的鉴定和药敏结果符合率以及较低的错误率，能够成为临床血流感染抗菌药物药敏试验的一种新的快速的替代方法，对危急重症血流感染患者快速及时救治有较大的临床应用价值。

关键字：血培养；药敏试验；快速方法；常规方法

Metagenomic Next-generation Sequencing in Identifying Non-tuberculous Mycobacteria Infections at A Tertiary Hospital in China

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Objective High sensitivity and rapidity of pathogen detection makes metagenomic next-generation sequencing (mNGS) as a promising diagnostic technology in identifying non-tuberculous mycobacteria (NTM). As majority of NTMs are environmental commensals and few species cause clinical NTM infections, the clinical value of mNGS positive results needs to be explored

Methods Screening the mNGS results performed from May 2019 to June 2023 at a tertiary hospital in China, we analyzed the clinical data of patients with NTM positive results by mNGS and followed them up until February 2024

Results 73 patients with NTM positive results by mNGS were finally enrolled with the detection rate of 5.1%. 68.5% of patients suffered from chronic diseases. Six patients were detected with multiple NTMs. The predominant isolates were M. abscessus (38.8%), M. intracellulare (18.8%,) and M. avium (13.8%). Majority (83.6%) isolates were identified in bronchoalveolar lavage fluid (BALF). One patients was diagnosed with disseminated infection caused by M. Colombia. 34.2% of patients received anti-NTM treatment with a median treatment time of 39.4 months. The treatment was based on macrolides, mainly in combination with anti-tuberculosis drugs (84.0%) and aminoglycosides (52.0%). Among the patients who did not receive targeted treatment, 56.3% of patients prioritized treatment of other pathogens due to the relatively low abundance of NTMs, and 31.2% had NTM positive results caused by colonization or contamination

Conclusion mNGS facilitates the clinical diagnosis of NTM infections, enabling early implementation of treatment. Due to the long course of treatment, it is necessary to comprehensively evaluate whether patients with positive NTM results for mNGS should start treatment based on traditional culture, radiology, clinical symptoms, general physical condition, and patient willingness

关键字：metagenomic next-generation sequencing (mNGS), non-tuberculous mycobacteria (NTM), NTM-pulmonary disease, treatment, diagnosis

CRISPR-Cas12a 联合 Multi-RCA 实现结核分枝杆菌 RpoB 基因的 POCT 法

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目的 滚环扩增（RCA）是一种简单、高效的等温扩增技术，多用于 RNA 及单链 DNA(ssDNA)扩增，尚未应用于双链 DNA（dsDNA）。CRISPR-Cas 系统先前多用于基因编辑，但其反式切割活性的发现使其在分子快速诊断方面具有巨大潜力。鉴于结核病（TB）对全球卫生健康的严重威胁，且现有 TB 诊断方法存在高成本、操作复杂和耗时长等缺点。本研究联合 CRISPR-Cas12a 系统和多重滚环扩增（Multi-RCA）技术，实现对结核分枝杆菌（MTB）rpoB 基因的高效扩增，并达到现场快速检测（POCT）的目的。

方法 首先建立 Taq-Multi-RCA-Cas12a 和 T4-Multi-RCA-Cas12a 一步及分步法，随后我们优化了酶的用量、锁环探针浓度、扩增时间等条件，并通过紫外灯照射，直接用肉眼读取结果，实现 MTB 的 POCT 检测。最后评估了该方法的灵敏度及特异性，并与“金标准”测序进行比较。

结果 T4-Multi-RCA-Cas12a 一步法检测限为 102pM，分步法检测限为 10pM；Taq-Multi-RCA-Cas12a 一步法检测限为 10pM，分步法检测限为 1pM。该方法可在 3h 内鉴定 MTB，且与其它临床常见菌无交叉反应。该方法的灵敏度、特异性、阳性预测值和阴性预测值分别达到了 100%、96.93%、92.60%及

100%。

结论 综上所述，Taq-Multi-RCA-Cas12a 和 T4-Multi-RCA-Cas12a 技术在鉴定 MTB 方面表现出卓越的即时检测性能，可在简易的恒温设备，如水浴锅中，快速检测 rpoB 基因保守序列并通过紫外灯照射，人眼直接读取结果。该技术不仅实现 MTB 的 POCT 检测，而且拓展 Multi-RCA 在扩增 dsDNA 方面的应用，在检测其他临床病原体 DNA、病毒 DNA 以及循环肿瘤 DNA 等 dsDNA 具有巨大的潜力。

关键字：MRCA，CRISPR-Cas12a，结核分枝杆菌，POCT

流式液相多重蛋白定量技术检测细胞因子在血流感染早期诊断中的研究

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目的 评估流式液相多重蛋白定量技术检测细胞因子（IFN-γ、 IL-2、IL-4、IL-6、IL-10、IL-17A 和 TNF-α）在单一病原菌血流感染患者中的早期诊断能力，初步分析细胞因子区分 G+菌、G-菌和念珠菌血流感染的潜在价值。

方法 回顾性收集河南省某三甲医院 2023 年 3 月-2023 年 10 月血培养阳性的单一细菌菌血症和单一念珠菌血症患者共 139 例，其中 G+菌感染患者 43 例，G-菌感染患者 83 例，念珠菌血症患者 13 例，同期健康体检者 27 例作为正常对照组。采用流式液相多重蛋白定量技术检测 IFN-γ、 IL-2、IL-4、IL-6、IL-10、IL-17A 和 TNF-α，比较各组患者的外周血细胞因子水平。

结果 三组血流感染患者的 IL-4、IL-6 和 IL-10 与正常对照组相比具有明显差异（P<0.05）。G-菌组的 IL-6 和 IL-10 高于正常组（P<0.05），IL-6 和 IL-10 联合诊断 G-菌血流感染的曲线下面积（ACU）为 0.688(0.586-0.79)。G+菌组的 IL-4 低于正常组（P<0.05），IL-4 诊断 G+菌血流感染的 ACU 为 0.700(0.577-0.822)。念珠菌血症组的 IL-10 高于正常组（P<0.05），IL-10 诊断念珠菌血症的 ACU 为 0.802（0.666-0.938）。而 G-菌组与 G+菌组相比，G-菌组与念珠菌血症组相比，G+菌组与念珠菌血症组相比，7 种细胞因子水平均无统计学意义。

结论 细胞因子 IL-4、IL-6 和 IL-10 在血流感染早期诊断中具有一定价值，但是不能有效区分 G+菌、G-菌和念珠菌血流感染，需联合其他感染指标综合判断。

关键字：细胞因子，血流感染，念珠菌血症

PCR、LAMP、PCT 在细菌性痢疾诊断中的应用价值 及与免疫指标的相关性

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目的 探究聚合酶链反应（PCR）、环介导等温扩增法（LAMP）、降钙素原（PCT）在细菌性痢疾诊断中的应用价值及与免疫指标的相关性。

方法 收集 2019 年 5 月~2022 年 5 月我院收治的 110 例细菌性痢疾患者粪便标本为观察组，同时选择同期 50 例健康体检者为对照组，均使用 PCR、LAMP、PCT 进行联合检验，对 PCR、LAMP、PCT 三种技术的特异性、灵敏度进行评价，并检验两组的免疫指标水平。

结果 观察组与对照组使用 3 种检测志贺菌阳性差异有统计学意义（P<0.05）；以临床诊断为标准，PCR、LAMP、PCT 的灵敏度分别为 62.56%、58.72%、60.26%，特异度分别为 71.67%、75.00%、74.17%，准确度分别为 59.11%、62.22%、59.44%。观察组 CD3+、CD4+、CD4+/CD8+水平均低于对照组，组间差异有统计学意义（P＜0.05）。

结论 联合应用 PCR、LAMP、PCT 法检测细菌性痢疾可提高临床诊断准确性。免疫指标水平可对细菌性痢疾中志贺菌检测提供临床依据，可辅助上述检测方法进行检测。

关键字：PCR；LAMP；PCT；细菌性痢疾；诊断；免疫指标

呼吸机相关性肺炎患者免疫指标和细菌学特征的改变的相关性研究

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目的 本研究旨在探讨和鉴定呼吸机相关肺炎(VAP)相关的预后免疫因素，并进一步检测耐药病原菌，为 VAP 的临床防治策略建立理论指导。

方法 研究对象为 2019 年 7 月至 2022 年 11 月在本院住院的使用呼吸机的患者 478 例。细菌鉴定系统采用 ATB 和 VITEK 鉴定系统。药敏试验采用 K-B 法或 VITEK 系统。根据细菌种类定义的细菌耐药性：金黄色葡萄球菌对甲氧西林的耐药性；甲氧西林、头孢他啶或亚胺培南对铜绿假单胞菌的耐药性；产广谱 β-内酰胺酶和头孢菌素对肠杆菌科细菌的耐药性。外周血单核细胞与异硫氰酸荧光素(FITC)、藻红蛋白(PE)、PE-花青素 5.5(PEcy5.5)和外

周蛋白叶绿素蛋白单抗共同孵育后进行循环免疫反应分析。用 FC500 软件对约 10,000 个淋巴细胞进行检测，以确定 CD3+、CD4+、CD8+、CD3CD16+CD56+、CD19+、CD4+CD25+CD127+、CD8+CD28 和 CD8+CD28+淋巴细胞的百分比。

结果 在 478 例使用呼吸机的患者中，约有 103 例发生 VAP(21.5%，103/478)。对 103 例 VAP 患者的病原菌分布及耐药性进行检测分析。VAP 组死亡 35 例，并发脓毒症 43 例。与非 VAP 组相比，VAP 组 CD3+(P=0.012)、CD3+CD4+(P=0.024) 和 CD8+CD28+(P=0.017)T 细胞比例显著升高，提示免疫应答更为严重。多因素回归模型分析显示，气管切开(P=0.013)、机械通气时间 7d(P=0.02)、吸入和反流(P=0.011)是≥发生的独立危险因素。

结论 根据细菌培养和药敏试验结果，合理选择抗生素，加强对重症监护病房患者的监护，可有效控制 VAP 的发生，改善患者预后。

关键字：免疫因素、病原体分析、呼吸机相关性肺炎

The Impact of Rapid Microbial Identification Report on The Clinical and Health Economics of Hospitalized Patients with Bloodstream Infection

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Objective To evaluate and compare the impact of rapid microbial identification using VITEK MS with routine microbial identification reports on the use of antibiotics, clinical outcomes, and health economics in hospitalized patients with bloodstream infection

Methods This study is a research using pre-test and post-test control group design. During the period from March 2020 to October 2021, the clinical microbiology laboratory underwent a series of improvement measures, including the performance of Bact/Alert FA and FN PLUS blood culture bottles with the VIRTUO Microbial Detection System (bioMerieux), MALDI-TOF VITEK MS (bioMerieux) for rapid microbial identification, and the sending of bacterial identification reports to clinical physicians through information systems and providing medical education related to blood culture to clinical medical staff. And we set the patients admitted from March 2019 to February 2020 before optimizing the blood culture process as the pre-optimization group, and the patients admitted from November 2021 to October 2022 after optimizing the blood cultrue process as the post-optimization group. Compare the impact of optimizing the blood culture process on the use of antibiotics, clinical outcomes, and health economics between the pre-optimization group and the post-optimization group

Results A total of 446 patients were included in the pre-optimization group, and 413 patients were included in the post-optimization group. Compared with the pre-optimization group, the post-optimization group reduced the identification report time by 40.7h($p<0.001$), the time from admission to the first targeted antibiotic treatment was reduced by 28.7h($p<0.001$), the average hospitalization time was shortened by 5.9 days($p<0.001$), the average antibiotics cost was saved by 7300yuan ($1021)($p<0.001$), and the average hospitalization cost was saved by 24078yuan ($3368)($p<0.001$)

Conclusion The combination of MALDI-TOF MS and a series of optimization measures significantly shortened the time of microbial identification, and accelerated the initialization time of antibacterial targeted therapy, and brought the health economic benefits

关键字：microbial identification; blood culture; economic anlaysis; bloodstream infections

Revolutionizing The Diagnosis of Severe Pneumonia: A Comparative Study of MPCR, NGS, and MALDI-TOF MS in Pathogen Identification and Clinical Outcome Improvement

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Objective The accurate and rapid diagnosis of bacterial and fungal pathogens is crucial for the effective management of severe pneumonia, a leading cause of morbidity and mortality worldwide. This study evaluates the efficacy of advanced diagnostic technologies, including multiplex PCR (mPCR), next-generation sequencing (NGS), and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), in identifying pathogens in severe pneumonia cases

Methods We conducted a prospective study involving 1,250 patients with clinically diagnosed severe pneumonia across five hospitals from January 2019 to December 2022. Specimens were analyzed using mPCR, NGS, and MALDI-TOF MS, with culture methods serving as the standard reference. Sensitivity, specificity,

time-to-diagnosis, and the impact on clinical outcomes were assessed

Results mPCR identified bacterial or fungal pathogens in 85% of the samples, with a sensitivity and specificity of 92% and 95%, respectively. NGS offered a broader pathogen detection spectrum, identifying pathogens in 95% of cases, with 89% sensitivity and 98% specificity. MALDI-TOF MS accurately identified 90% of cultured pathogens within 2 hours of specimen receipt. The average time-to-diagnosis from sample collection was 2 hours for MALDI-TOF MS, 5 hours for mPCR, and 24 hours for NGS. Early pathogen identification (within 6 hours of hospital admission) and subsequent targeted antimicrobial therapy were associated with a 25% reduction in ICU stay duration and a 20% decrease in 30-day mortality compared to standard culture methods

Conclusion Advanced diagnostic technologies, especially MALDI-TOF MS and NGS, significantly improve the timely and accurate identification of bacterial and fungal pathogens in severe pneumonia. Early and precise pathogen diagnosis facilitates targeted treatment, substantially reducing ICU stays and mortality rates. Implementing these technologies in clinical settings could revolutionize the management of severe pneumonia, highlighting the importance of investing in diagnostic infrastructure and training

关键字：severe Pneumonia, diagnostic Technologies, mPCR, NGS, MALDI-TOF MS, pathogen Identification

Development of A Multiplex Molecular Point-of-Care Test for Rapid Detection of Nontuberculous Mycobacteria

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Objective There has been a growing awareness of the escalating prevalence of infections caused by Non-tuberculous mycobacteria (NTM). However, the clinical presentation and laboratory tests between Mycobacterium tuberculosis and NTM can be similar and hard to differentiate. Rapid and accurate diagnostic tools for NTM are absent. The objective of this study was to develop a direct molecular and point-of-care method for NTM identification from sputum, facilitating prompt clinical decision-making

Methods The assay targets the intergenic transcribed spacer (ITS) region between the 16S rRNA and 23S rRNA genes of mycobacteria using a pan-mycobacterial primer set. Species-specific probes were designed to identify 8 NTM species, including Mycobacterium avium, Mycobacterium intracellulare, Mycobacterium abscessus, Mycobacterium kansasii, Mycobacterium gordonae, Mycobacterium scrofulaceum, Mycobacterium marinum/Mycobacterium ulcerans and Mycobacterium fortuitum (Mycobacterium ulcerans and Mycobacterium marinum complex were not differentiated) and the M.tuberculosis complex (MTBC). A "fluorescence-melting temperature" two-dimensional labeling analysis-based multicolor melting curve analysis was developed to achieve multiple detections

Results The multicolor melting curve analysis correctly identified 9 reference mycobacterial strains and showed no cross-reaction with other non-mycobacterial strains. Analytical performance was rigorously assessed using a diverse panel of clinical samples, demonstrating a sensitivity of 95% and specificity of 98% compared to 16S rRNA sequences. Furthermore, the point-of-care device exhibited a limit of detection as low as 10 genomic copies per reaction, underscoring its remarkable analytical sensitivity. Processed with a sputum pretreatment and performed in a fully automatic nucleic acid amplification instrument, it allows the identification of clinically relevant 9 Mycobacterium species in a single reaction within 2.5 h

Conclusion Considering its rapidity, accessibility, and accuracy, we present a significant stride in the field of addressing the pressing challenges associated with NTM detection. It has potentially contributed to the ability to recognize NTM and enabled clinicians to institute appropriate treatment regimens

关键字：POCT，multiplex molecular test，Non-tuberculous Mycobacteria

AIDS 合并马尔尼菲蓝状菌感染的临床特征

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目的 研究获得性免疫缺陷综合征（AIDS）合并马尔尼菲蓝状菌（TM）感染的临床特征及预后危险因素。

方法 回顾性分析我院 2014 年 10 月至 2022 年 9 月确诊为 AIDS 合并 TM 感染的临床特征，根据预后分为好转组和恶化组，采用非条件 Logistic 回归分析筛选出预后的独立危险因素并建立预测模型。

结果 133 例 AIDS 合并 TM 感染患者，主要表现为发热（93.23%）、贫血（78.2%），咳嗽（48.12%）、消瘦（43.61%）、浅表淋巴结肿大（42.86%）和合并卡氏肺囊虫病患者（32.46%)。表现为低白蛋白血症（99.25%）和不同程度肝功能损害，以 AST 升高（69.17%）为主。114 例（88.37%）患者 CD4+T 淋巴细胞＜50 个细胞/ul。好转组 103 例，恶化组 30 例，好转率为 77.44%，单因素回归分析发现 AIDS 合并 TM 感染预后不良危险因素有：白细胞、中性

粒细胞、降钙素原、肌酐、尿素氮、肝大。保护因素：白蛋白、白球比。多因素回归分析发现：白蛋白、尿素氮是影响 AIDS 合并 TM 感染预后的独立危险因素，建立二元 Logistic 回归模型方程为 ln(p/1-p)=1.308-0.107×ALB+0.28×BUN，曲线下面积为 0.825（95%：0.733-0.916）。

结论 AIDS 合并 TSM 主要表现为发热、贫血、咳嗽、消瘦、淋巴结肿大，低白蛋白血症、AST 升高，CD4+绝大多数＜50 个。白蛋白、尿素氮是 AIDS 合并 TSM 预后不良的独立危险因素。

关键字：AIDS，TSM，临床特征，预后危险因素，预测模型

Positively Charged Magnetic Multilayered Quantum Dot Guides Label-free and Ultrasensitive Detection of Multiple Pathogenic Bacteria on Immunochromatographic Strip

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Objective Immunochromatographic assay (ICA) is a simple and effective point-of-care testing technology, but it still not able to achieve the ultrasensitive and accurate detection of multiple pathogenic bacteria due to the following two reasons: i) the interference of complex components in real-world samples and ii) lacking of suitable high-affinity antibodies for pathogens. Until now, a universal ICA method that allows the multiplex and sensitive monitoring of different bacteria by using non-antibody-modified nanotags has not been reported

Methods Herein, we propose a label-free fluorescent ICA mediated by a positively charged magnetic multilayered quantum dot (Fe@MQD-P+) with a unique combination of broad-spectrum binding ability of cationic polymer to bacteria, superior fluorescence signals of numerous QDs and magnetic enrichment ability of Fe3O4 core. The Fe@MQD-P+ tag was used as the universal bacteria capture tool for the rapid and efficient magnetic enrichment of three different pathogens including Pseudomonas aeruginosa (P. aeruginosa), Escherichia coli O157:H7 (E. coli O157:H7), and Salmonella typhimurium (S. typhi) and the capture efficiencies were reaching up to above 90%. Three kinds of monoclonal antibodies were separately immobilized onto the three test lines of ICA strips to ensure the specific and multiplex detection of three target pathogens

Results The established Fe@MQD-P+-based ICA allowed the multiplex and ultrasensitive detection of the three target bacteria via one three-channel ICA strip within 20 min. The LODs of our method reached 50, 100, and 100 cells/mL for P. aeruginosa, E. coli O157:H7, and S. typhi, respectively, which are 50 times more sensitive than those from traditional AuNP-based ICA methods. The excellent stability and specificity of the proposed ICA in real environmental and clinical specimens were also demonstrated

Conclusions This work is the first to report the combined use of cationic polymer labelling and ICA to fabricate rapid, sensitive and universal detection method for bacteria. We believe that our proposed Fe@MQD-P+-based ICA could serve as a promising tool for rapid screening of various pathogenic bacteria with simplicity, high speed, and sensitivity

关键字：fluorescent ICA; bacteria; label-free; multiplex detection

Phenylboronic Acid-Modified Magnetic Nanozyme Enables Simultaneous and Ultrasensitive Detection of Respiratory Bacteria on Immunochromatographic Assay

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Objective Highly pathogenic respiratory pathogens, such as Streptococcus pneumoniae (S. pneumoniae) and Pseudomonas aeruginosa (P. aeruginosa), are always a great threat to human health and result in million deaths each year globally. The early clinical symptoms (e.g., cough, fever) caused by respiratory bacteria are similar to those induced by common respiratory viruses, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus and influenza B virus, which brings difficulty to control the epidemic spread and guide clinical treatment. A simple technique for rapid, sensitive, and simultaneous diagnosis of respiratory bacteria is urgently needed

Methods We developed a highly stable colorimetric immunochromatographic assay (ICA) on the basis of 4-mercaptophenylboronic acid (MPBA)-modified magnetic nanozyme (Fe-Au@Pt) for ultrasensitive and multiplex detection of respiratory bacteria in complex specimens. The Fe-Au@Pt nanozyme with a well-defined core-satellite structure, strong magnetic responsiveness, superior catalytic activity, and numerous binding sites was prepared through the adsorption of one layer of bimetallic Au@Pt nanoparticles (~5 nm) onto monodispersed Fe3O4 nanosphere (~180 nm) via using polyetherimide (PEI) as linkers. MPBA was modified onto the Fe-Au@Pt surface to provide boronic acid groups for effective broad-spectrum bacterial capture. By combining with antibodies-modified ICA strip, the Fe-Au@Pt-MPBA can effectively enrich S. pneumoniae and P. aeruginosa from sample solution and enable ultrasensitive colorimetric detection by combining with magnetic separation and enzymatic deposition signal amplification

Results The proposed nanozyme-based ICA method excellent detection performance for S. pneumoniae and P. aeruginosa, including high capture rate (> 90%) to the target pathogens, short testing time (< 25 min), low detection limit (< 20 cells/mL), and good reproducibility (relative standard deviation < 12.2 %). The sensitivity of the proposed assay is at least 20 and 200 times higher than those of traditional enzyme-linked immunosorbent assay and AuNP-based ICA strip, respectively. The clinical utility of the proposed assay was validated through the diagnosis of 26 real clinical respiratory tract specimens

Conclusion Given its advantages of simple operation, visual observation, and high sensitivity, our Fe-Au@Pt-MPBA-based ICA method could be developed as a user-friendly clinical testing technique for on-site and real-time diagnosis of bacterial samples

关键字：magnetic nanozyme, immunochromatographic assay, respiratory bacteria

微滴数字 PCR 在疑似脓毒血症患者病原学诊断中的应用

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目的 脓毒症是一种时间依赖性疾病，病死率和残疾率高，及时准确的病原学诊断至关重要。传统的病原菌鉴定耗时长、阳性率低，迫切需要一种快速、灵敏的病原体检测方法。本研究旨在探讨微滴数字 PCR（ddPCR）在疑似脓毒血症患者病原学诊断中的价值。

方法 选取 2023 年 9 月-2024 年 3 月某院收治的疑似脓毒血症患者，抽取静脉血采用 ddPCR 方法检测血液标本中的 13 种病原体，同时进行血培养、宏基因组二代测序（mNGS）。通过与血培养、mNGS 诊断结果进行比较，评估 ddPCR 方法的诊断效能。

结果 47 例患者血样中，血培养法阳性 7 例（14.8%），mNGS 法阳性 19 例（40.4%），ddPCR 法阳性 15 例(31.9%)。与血培养相比，ddPCR 的敏感性为 80.5%，特异性为 62.5%。在检测阳性率方面，ddPCR 阳性率（31.9%）显著高于血培养阳性率（14.8%），$p<0.05$；但低于 mNGS（40.4%），$p>0.05$。在检测病原菌种类方面，ddPCR 检出的病原体（12 种）多于血培养（5 种），$p<0.05$；少于 mNGS（21 种），$p<0.05$。ddPCR 与血培养的阳性一致性为 70.2%，阴性一致性为 95.6%；ddPCR 与 mNGS 的阳性一致性为 90.5%，阴性一致性为 87.4%。在检测时长方面，ddPCR 耗时（5.7±0.8 h）低于血培养（72.5±11.4 h），$p<0.05$；ddPCR 耗时也低于 mNGS（50.6±8.2 h），$p<0.05$。

结论 ddPCR 是一种灵敏、快速、准确的方法，在疑似脓毒症患者中表现出良好的病原学诊断性能。在检测耗时方面明显低于血培养和 mNGS，总体检出率明显高于血培养，但病原菌检出种类低于 mNGS。ddPCR 技术能准确、快速地反映临床疾病的进展情况，为抗生素的使用提供指导，为患者的预后评估提供更准确的依据。

关键字：脓毒症，微滴数字 PCR，宏基因组二代测序，血培养，病原学

Metagenomics Next Generation Sequencing (mNGS) Reveals Emerging Infection Induced by Klebsiella Pneumonia

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Objective The increasing emergence of hypervirulent Klebsiella pneumoniae (hv-Kp) and carbapenem-resistant K. pneumoniae (CR-Kp) poses a serious and substantial problem to the antibiotic applicability and public health. An expanding repertoire of newly identified CR-hvKp challenges the last resort of tigecycline and polymyxin to combat infections. However, the transmission and co-occurrence of the corresponding antimicrobial resistance (AR) and virulence determinants are largely unknown. This study aims to investigate the dissemination and dynamics of CR-Kp and its antibiotic resistance in one hospitalized patient

Methods Metagenome next-generation sequencing (mNGS) was conducted for different specimens collected from this inpatient. CR-Kp strains were examined by antibiotic susceptibility and string testing. Antimicrobial and virulence genes were therefore annotated by using whole genome sequencing (WGS)

Results We report a clinical case infected with a variety of CR-Kp isolates. The co-occurrence of KPC-2 and NDM-1 in this patient was revealed. These CR-Kp isolates such as BALF2, Sputum T1 and T3 were respectively classified into ST11 and ST147. The genetic signature (iuc operon) of hyper-virulence were identified in strain T1, although string testing indicated its intermediate virulence

Conclusion Multiple infections of CR-Kp isolates were revealed by mNGS, and their issemination was attributed to plasmid variations, mgrB inactivation and integrative conjugative elements (ICEs). Furthermore, our finding largely suggested one likely convergence to from CR-hvKp, different from acquisition of carbapenem-resistance in hvKp. Together, mNGS combined with WGS benefit the clinical diagnosis and anti-infection therapy, and facilitate a better understanding

of genetic variants conferring antimicrobial and virulence properties

关键字：Carbapenem and polymyxin resistance; Klebsiella pneumoniae; Metagenome sequencing; Horizontal gene transfer

结核性胸腔积液中 sFasL 的来源和功能

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目的 初步确定 TPE 患者胸水 sFasL 的细胞来源及其对活化的 CD4+T 细胞的影响，探讨其在 TPE 发生与发展中的作用。

方法 采集健康人的外周血，通过 Ficoll 密度梯度离心法分离外周血单个核细胞(PBMCs)，使用卡介苗(BCG)刺激后，采用流式细胞术检测各种细胞 (CD4+ ， CD8+ ， CD14+ ， CD19+) 上膜型 FasL(mFasL)的表达，采用 ELISA 检测细胞培养基上清液中 sFasL 的浓度。接着磁珠分选法分选 CD14+单核细胞，并用巨噬细胞集落刺激因子(GM-CSF)将其诱导成巨噬细胞，然后加入 BCG 刺激之后，采用实时荧光定量 PCR(qRT-PCR)检测 FasL、金属蛋白酶(MMPs) 和解聚素金属蛋白酶(ADAMs)等分子的表达。另外，以 BCG 刺激人单核源性巨噬细胞，用于刺激同源的 CD4+T 细胞进行共培养，然后用流式细胞术检测 CD4+T 细胞的凋亡情况。之后用 TPE 患者的胸水培养 CD3 和 CD28 活化后的 CD4+T 细胞，并加入抗 sFasL 抗体，以流式细胞术检测 CD4+T 细胞凋亡情况。最后，在含有 10%胎牛血清的培养基中加入外源性的重组 sFasL，培养活化的 CD4+T 细胞，采用流式细胞术检测 CD4+T 细胞凋亡情况。

结果 流式细胞术结果显示，BCG 刺激 PBMC 后的 CD4+T 淋巴细胞(P=0.002)、CD8+T 淋巴细胞(P=0.01)、CD14+T 单核细胞(P=0.014)及 CD19+B 细胞(P<0.0001)中 mFasL 均高于 PBS 组。ELISA 结果显示，BCG 刺激 PBMC 后的上清中 sFasL 浓度较 PBS 组高(P<0.0001)。qPCR 结果发现 MMP2、MMP7、MMP9、ADAM10、ADAM17 等分子表达变化不大。通过 BCG 刺激 M0 细胞，进一步发现细胞内 mFasL(P<0.0001)及培养上清中 sFasL 的浓度均较 PBS 组高(P=0.0007)。TPE 患者胸水培养活化 CD4+T 细胞较正常培养基培养后凋亡率更高，而当加入抗 sFasL 的单克隆中和抗体后其凋亡率增高；另外加入外源性的重组 sFasL 培养活化的 CD4+T 细胞的凋亡率降低。

结论 辅助性 T 细胞、细胞毒性 T 细胞、B 细胞和单核细胞都可能是 sFasL 的来源。TPE 患者胸水 sFasL 的主要功能可能是抑制活化的 CD4+T 凋亡。

关键字：结核性胸腔积液，可溶性 Fas 配体，外周血单个核细胞，CD4+T 细胞，凋亡

细菌真菌感染的治疗

头孢哌酮钠舒巴坦钠与哌拉西林钠他唑巴坦钠治疗复杂性尿路感染的安全性与有效性

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目的 复杂性尿路感染(Complicated urinary tract infections，cUTIs)为存在全身症状或同时伴有复杂合并疾病（如肾盂肾炎、前列腺炎或尿脓毒症综合征）的尿路感染，多发生于生殖泌尿道结构或功能异常或通过导尿管感染的患者。本文是探究头孢哌酮钠舒巴坦钠和哌拉西林钠/他唑巴坦钠是治疗复杂性尿路感染(cUTIs)的安全性与有效性。

方法 选择空军军医大学第一附属医院在 2019 年 1 月—2021 年 11 月收治的成人 cUTIs 患者 213 例为研究对象，其中 103 例患者给予头孢哌酮钠舒巴坦钠，110 例患者给予哌拉西林钠/他唑巴坦钠。判定标准为抗菌药物治疗后的临床治愈率、微生物清除率、抗菌药物总治疗时间、有效抗菌药物治疗时间、住院时间、尿路感染复发率、再住院率、全因病死率。

结果 两组基线特征无统计学差异，引起 cUTIs 的病原菌分布相似。安全性方面，除了尿路感染复发率，哌拉西林钠/他唑巴坦钠组抗菌药物治疗总持续时间、有效抗菌药物治疗持续时间和住院天数均高于头孢哌酮钠舒巴坦钠组。全因死亡率两组无显著差异。有效性方面，头孢哌酮钠舒巴坦钠组的临床治愈率和微生物清除率均高于哌拉西林钠/他唑巴坦钠组。在不良事件发生率方面，头孢哌酮钠舒巴坦钠组稍高。

结论 采用头孢哌酮钠舒巴坦钠和哌拉西林钠/他唑巴坦钠治疗产 ESBL 和氨基-R 肠杆菌科细菌引起的 cUTIs 具有安全性和有效性。

关键字：复杂性尿路感染； 产超广谱 β-内酰胺酶； 抗菌药物治疗； 头孢哌酮钠舒巴坦钠； 哌拉西林钠/他唑巴坦钠

影响免疫功能健全和免疫功能低下患者隐球菌病治疗和预后的因素：一项为期 10 年的回顾性研究

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目的 总结了免疫功能正常和免疫功能受损的肺隐球菌感染患者的治疗过程和预后，并分析相关因素。

方法 采用卡方检验检验分类变量的差异，采用独立样本 t 检验比较连续变量的差异。

结果 共有 243 名患者纳入分析。免疫功能正常患者的中位治疗时间为 207 天，而免疫功能受损患者的中位治疗时间为 253.5 天。免疫功能正常患者肺部感染好转的中位时间为 32.5 天，免疫功能低下患者为 34.5 天。弥漫性肺部浸润（p=0.008*）和 CRP（p=0.024*）是影响免疫功能正常患者病情好转天数超过 4 周的重要因素，而年龄（p=0.033*）和中性粒细胞计数（p=0.038*）则是影响免疫功能受损患者病情好转天数超过 4 周的重要因素。在免疫力受损的患者中，血清荚膜抗原滴度≥1::40（p=0.013*）是导致疗程延长超过 9 个月的不利因素。26/98（26.53%）名免疫功能正常的患者在治疗结束后血清抗原检测结果未转为阴性，他们的血清抗原检测结果明显低于 14/29（48.28%）名免疫功能低下的患者（P=0.027*）。所有接受手术切除的患者预后良好。

结论 肺影像学示弥漫性浸润的免疫功能受损患者的治疗天数更长，病情好转时间更长。免疫功能受损患者的血清抗原水平越高，治疗时间越长。免疫功能受损患者的血清抗原检测不易转阴。

关键字：肺隐球菌病；免疫抑制；治疗；预后；荚膜抗原滴度

播散型荚膜组织胞浆菌感染致继发性噬血细胞性淋巴组织细胞增多症一例并文献复习

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目的 本研究旨在探讨播散型荚膜组织胞浆菌感染（DH）合并继发性噬血细胞性淋巴组织细胞增多症(HLH)的诊断与治疗策略。方法 本文通过分析重庆医科大学附属第一医院于 2023 年 2 月 26 日收治的一例播散型荚膜组织胞浆菌感染合并继发性噬血细胞性淋巴组织细胞增多症患者的诊疗过程，并结合相关文献进行复习。

方法 收集病例、查阅文献、总结分析

结果 病例为一名 67 岁老年男性患者，在 1 个月前于中国广西壮族自治区旅游返家（重庆市）三天后出现发热、厌食症状，伴随乏力和体重减轻，在病程中反复高热，表现出全血细胞减少，铁蛋白升高，NK 细胞活性下降，肝脾肿大等 HLH 的临床特征，通过骨髓穿刺涂片镜检、外周血 mNGS、影像学检查确诊为播散型荚膜组织胞浆菌病。患者接受小剂量地塞米松诱导治疗（5mg/次、次/d 静脉推注

14d 后续用 2.5mg/次、次/d 静脉推注 7d）和两性霉素 B 脂质体（起始 17mg/次、次/d，3 天内逐渐加量至 100mg/次、次/d 静脉滴注 21d）续用伊曲康唑（200mg/次、次/12h 口服）的抗真菌治疗，三个月后的复查胸部 CT 显示病灶基本吸收。

结论 播散性荚膜组织胞浆菌感染伴噬血细胞性淋巴组织细胞增多症患者，治疗策略应以针对原发疾病为主，辅以激素诱导治疗，同时避免使用免疫抑制药物以减轻感染，从而改善患者预后。

关键字：播散型组织浆菌病；噬血细胞性淋巴组织细胞增多症；不明原因发热；呼吸困难；肝脾肿大

我国诺卡菌脑脓肿诊治策略及预后分析

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目的 诺卡菌脑脓肿极为罕见，仅占所有颅内脓肿的 1-2%，但死亡率很高，达 30%。受病例数的限制，诺卡菌脑脓肿研究均为回顾性研究，且大多局限于病例报告或小病例系列的研究，目前尚无我国诺卡菌脑脓肿研究数据，本研究描述了我国诺卡菌脑脓肿临床特点、诊治方案及预后因素，以帮助临床识别诺卡菌脑脓肿，提高诊治水平。

方法 详细记录我中心新诊断的 1 例诺卡菌脑脓肿诊治经过，同时检索 1998 年到 2023 年已报道确诊诺卡菌脑脓肿中国患者，进行统计分析。

结果 共 29 例诺卡菌脑脓肿患者，平均年龄 51.7 岁，44.8%患者免疫功能低下。肺部和皮肤感染是最常见的非颅脑部位。磁共振成像显示额叶是最常见的受累部位，75%呈多灶性分布。降钙素原大多无明显升高，脓液培养阳性率最高，质谱分析或宏基因检测有助病原菌的筛查。分离出最常见的微生物是皮疽诺卡菌，其次是亚洲诺卡菌。17 例患者仅接受抗菌药物治疗，9 例患者同时接受内科和外科治疗，比较手术组与非手术组之间的治愈率无统计学差异。96%患者接受以甲氧苄氨嘧啶-磺胺甲恶唑（TMP-SMX）为主的双联抗生素治疗。23 例患者疾病控制，3 例死亡，3 例疾病进展。诺卡菌脑脓肿误诊率极高为 85.7%，高龄及未接受 TMP-SMX 治疗为预后高危因素。

结论 诺卡菌是免疫功能低下宿主脑脓肿的重要病因，疑似感染患者应尽早行脓液抽吸培养，根据药敏选择适当的抗菌方案，推荐治疗方案中含有 TMP-SMX 可改善预后。

关键字：诺卡菌，脑脓肿，治疗， 危险因素

Efficacy and Safety of Plasma Concentration-optimized Polymyxin B Therapy in Treating Carbapenem-resistant Gram-negative Bacterial Infections

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Objective Polymyxin B (PMB)-based combination therapies are used to treat serious carbapenem-resistant gram-negative bacterial (CR-GNB) infections. This observational study investigated the relationship between PMB concentration and clinical efficacy and safety

Methods PMB regimens were optimized through therapeutic drug concentration monitoring (TDM) and area under the concentration-time curve (AUC). Logistic regression was used to analyze the relationships between variables with clinical efficacy and 30-day mortality factors were analyzed by Cox regression. The sensitivity and specificity of Cmin and AUC for the occurrence of acute kidney injury (AKI) were determined by ROC curve analysis

Results In all, 191 samples were tested from 130 patients. The clinical effectiveness of PMB was 65.4%. Multivariate logistic regression analysis revealed that lung infection, continuous renal replacement therapy (CRRT), and C-reactive protein (CRP) were independent factors significantly associated with efficacy. AKI occurred in 14.6% of the patients during treatment; age > 73 years (OR: 3.63; 95% CI: 1.035-12.727; P = 0.044), Cmin greater than 2.3 μg/mL (OR: 7.37; 95% CI: 1.571-34.580; P = 0.011), combined vancomycin (OR: 9.47; 95% CI: 1.732-51.731; P = 0.009), and combined piperacillin-tazobactam (OR: 21.87; 95% CI: 3.139-152.324; P = 0.002) were independent risk factors. The identified PMB cut-offs for predicting AKI were Cmin = 2.3 μg/mL and AUC = 82.0 mg· h/L

Conclusion PMB-based combination regimens have good efficacy in treating CR-GNB infections, especially bloodstream infections, but have been unsatisfactory for lung infections. Cmin ≥ 2.3μg /mL and AUC ≥ 82.0 mg· h/L may increase PMB-associated AKI incidence. PMB dose should be adjusted based on TDM to ensure efficacy

关键字：Polymyxin B (PMB); Therapeutic drug concentration monitoring (TDM); Carbapenem-resistant gram-negative bacteria (CR-GNB); Clinical efficacy; Acute kidney injury (AKI)

多黏菌素类治疗碳青霉烯耐药菌所致重症感

染临床研究进展

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目的 本文对多黏菌素类药物治疗碳青霉烯耐药菌所致感染的临床研究进行综述，旨在为临床合理应用多黏菌素类药物提供参考。

方法 本文主要在 Pubmed、Web of Science 和会议论文等搜索主题词“colistin”或者“polymyxin”，主要收集并整理了截止至 2023 年 3 月 15 日部分文献，并就多黏菌素类药物敏感性、药动学及药效学、临床应用、不良反应等方面的研究进展进行综述。

结果 多黏菌素类药物是治疗碳青霉烯耐药菌所致感染的最后一道防线，目前国内有三种多黏菌素类药物可用于临床，分别是注射用多黏菌素 E 甲磺酸钠、硫酸多黏菌素 B、注射用硫酸黏菌素。作为一类时间浓度依赖型抗生素，多黏菌素类药物治疗窗窄，临床应用时需进行治疗药物浓度监测以减少肾毒性和神经毒性等不良反应。此外，针对不同的感染部位，需选择合适的多类黏菌素药物，必要时联合局部用药。而对于不同的碳青霉烯耐药菌，联合用药与否以及选择哪种联合抗感染药物，仍需更有论证强度的临床研究进行进一步探讨。

结论 多黏菌素类药物对治疗碳青霉烯耐药菌所致重症感染具有独特价值，但存在药物敏感性折点争议、剂量与用法有差异、药动学与药效学研究不足等问题，仍需进一步研究，以期在发挥此类药物的最佳疗效的同时，尽可能减少其耐药性和毒性。

关键字：多黏菌素；耐碳青霉烯类细菌；感染；临床研究

59 例咽峡炎链球菌群脑脓肿临床特征分析

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目的 总结归纳咽峡炎链球菌群（SAG）感染脑脓肿患者的临床特征，为该病的临床诊断与治疗提供参考依据。

方法 收集 2016 年 1 月－2023 年 10 月广东三九脑科医院 59 例咽峡炎链球菌群脑脓肿患者的临床信息进行回顾性统计分析。

结果 59 例脑脓肿患者中男 52 例（88.1%）、女 7 例（11.9%），年龄为（42.34±18.94 岁）。根据病原菌分为三组，分别为中间链球菌组 32 例（54.24%）、星座链球菌组 21 例（35.59%）与咽峡炎链球菌组 6 例（10.17%）。中间链球菌组平均年龄（36.75±20.06 岁）明显低于星座链球菌组平均年龄（50.43±16.17 岁）（P＜0.05）。临床症状常见头痛（64.4%）、肢体无力（35.6%）与发热（30.5%），中间链球菌组与星座链球菌组相比发热概率更大（P＜0.05）。脓肿数量以单发多见（83.1%），好发于大脑顶叶（39.0%）与额叶（39.0%）。白细胞计数（11.87±4.08×109/L）、中性粒细胞占比（77.45±1.16%）与降钙素原（0.41±1.16 ng/mL）明显增高，普通培养与革兰染色的检出率较高（98.3%与 89.8%）。中间链球菌组更倾向于单独感染（90.6%），而星座链球菌患者发生混合感染的概率更大（57.1%），存在显著性差异（P＜0.05）。糖肽类（万古霉素）+碳青霉烯类（美罗培南）联合方案在经验性与目标性用药中均最常用（55.93%与 35.59%）；未发现对利奈唑胺、氯霉素、青霉素、头孢曲松、头孢吡肟、头孢噻肟、万古霉素等抗菌药物产生耐药的菌株。

结论 引起脑脓肿的 SAG 以中间链球菌和星座链球菌为主，两种菌导致的脑脓肿患者年龄、症状与感染模式有所区别；SAG 在临床未出现耐药的情况，临床可根据药敏结果合理评估和调整抗感染方案。

关键字：脑脓肿；咽峡炎链球菌群；咽峡炎链球菌；中间链球菌；星座链球菌

Standard Dose May Be Better! The Multicenter Study of Tigecycline in Patients with Liver Failure

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Objective For patients with liver failure complicated by serious multidrug-resistant gram-negative bacterial infections, high-dose (HD) tigecycline is required to prevent treatment failure, despite the recommendation of halving the dose for patients with severe liver impairment in the package insert. This study aimed to

evaluate the effectiveness and safety of different tigecycline doses in patients with liver failure

Methods This multicenter retrospective cohort study included 192 patients with Child-Pugh grade C liver function. The patients were divided into label-dose (LD), standard-dose (SD), and HD groups (30, 94, and 68 patients, respectively). The primary outcome was all-cause in-hospital mortality

Results Intergroup comparisons indicated no statistical difference in all-cause mortality. The microbial clearance rate was the lowest in the LD group, with no significant impact on coagulation function. The paired-sample comparison revealed significant improvements in infection indicators and notable deterioration in coagulation function following tigecycline treatment in the SD and HD groups. Despite the HD group requiring the highest daily fibrinogen infusion, coagulation function remained significantly impaired. Multivariate survival analysis indicated that a high dose, prothrombin time (PT) prolongation after treatment, and bloodstream infections were independent risk factors for patient death, whereas microbial eradication served as an independent protective factor. Subgroup analysis demonstrated that the microbial eradication cut-off value for the SD group was 9 days, with a cut-off of 8-9 days for the occurrence of coagulation dysfunction

Conclusion Even for patients with liver failure, using standard dose tigecycline and managing the treatment course effectively can still benefit patients

关键字：Tigecycline, liver failure, Child-Pugh C, label dose, standard dose

The First Case of Fungal Pleural Infection Caused by Microascus Gracilis after COVID-19 Pneumonia in China

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Objective We present a case of pleural infection caused by M. gracilis with pulmonary aspergillosis in an immunocompromised man after COVID-19 pneumonia

Methods To further understand the characteristics of the pathogen isolated from the patient, we identified the strain through mycological characteristics, matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) mass spectrometry (MALDI-TOF MS) and internal transcribed spacer (ITS)-based sequencing, and performed in vitro drug susceptibility testing against common antifungal agents. Moreover, we assessed lymphocyte subsets and programmed cell death protein 1 (PD-1) expression in peripheral blood and pleural effusion to monitor the efficacy of therapy with thymosin-α-1 and intravenous immunoglobulin

Results Filamentous fungi isolated from pleural fluid were identified as M. gracilis based on classical morphology, mass spectrometry and molecular biology methods. Although the susceptibility results in vitro revealed that multiple antifungal agents were inactive against the strain, the patient was cured according to the antifungal strategy of caspofungin combined with posaconazole for 5 weeks and then terbinafine plus posaconazole for sequential therapy. Adjuvant immunomodulatory treatment successfully increased the levels of CD3+ T and CD4+ T cells while decreasing the levels of CD3+PD-1+ and CD4+PD-1+ T cells in both peripheral blood and pleural effusion

Conclusion The immunocompromised host with opportunistic M. gracilis infection, rapid and accurate recognition through direct microscopic testing with calcofluor white and MOLDI-TOF MS, is the key to achieving a definite diagnosis, and a combination of antifungal therapy with immunomodulatory therapy is vital for improving survival

关键字：Microascus gracilis, Scopulariopsis, Microascus, Pleural effusion, COVID-19, Pneumonia

Infective Endocarditis Due To High-Level Gentamicin-Resistant Enterococcus Faecalis Complicated Multisystemic Complications in An Elderly Patient

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Infective endocarditis (IE) caused by aminoglycoside-resistant Enterococcus is of considerable public health concern. The problem is especially pronounced in elderly patients who are at an increased risk of renal impairment during antibiotic therapy, thereby limiting the options for pharmacological intervention. Furthermore, the propensity of older patients to present with various comorbidities contributes to a heightened mortality rate. This case report describes the clinical course of an elderly male patient who presented with fever, ankle edema, and lumbosacral pain and further diagnosed with infective endocarditis (IE) caused by a high-level gentamicin-resistant Enterococcus faecium, as evidenced by blood cultures and echocardiographic imaging. The patient was complicated by peripheral and cerebral arterial emboli, a secondary infection of the spine, and ensuing heart failure, marking a grave clinical scenario. After an initial 10-day treatment with vancomycin and ceftriaxone, the patient suffered renal impairment, prompting a switch to bactericidal therapy with ampicillin plus ceftriaxone. Aortic valve replacement surgery

was also performed during this period. The patient ultimately attained clinical cure. This case underscores the importance of early and precise diagnosis, the selection of appropriate antibiotics, and timely surgical intervention to improve the prognosis of elderly patients with IE.

关键字：Endocarditis, Bacterial; Enterococcus faecalis; Aminoglycoside Resistance; Ampicillin plus ceftriaxone; Geriatrics

群体感应信号分子 farnesol 在大鼠外阴阴道假丝酵母菌病模型中抗真菌免疫应答及黏膜修复作用的研究

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目的 通过建立外阴阴道白假丝酵母菌病(Vulvovaginal candidiasis, VVC)大鼠模型来评估 farnesol 对阴道白假丝酵母菌免疫应答及阴道黏膜修复作用的影响。

方法 将 24 只 2~3 月龄的雌性 SD 大鼠分别随机分为正常对照组(假手术组)，VVC 感染模型组，farnesol 治疗组及制霉菌素治疗组(阳性对照组)，每组 6 只。建立 VVC 大鼠模型，farnesol 组动物每日阴道予以 50μM farnesol 一次，制霉菌素组每日阴道予以 1.05×104 IU/kg 制霉菌素片一次，连续 7d。停药后取大鼠阴道分泌物，计算病原体清除率，取阴道标本进行 HE 染色观察急慢性炎症指标及阴道黏膜修复变化，采用免疫组化法检测 IFN-γ、IL-4 及 IL-17 表达变化，透射电镜检测阴道组织超微结构的变化。

结果 结果表明，停药 4 天后制霉菌素(阳性对照组)的转阴率最高为 100%，其次为法尼醇组为 83.3%，感染模型组的转阴率最低为 0%。HE 结果表示，farnesol 组阴道粘膜平均厚度(119.29±18.78μm vs. 74.47±28.90μm)及黏膜层数(10.3±1.62 vs. 7.93±2.16)明显高于模型组(P＜0.05)，与正常对照组及制霉菌素组相似(P＞0.05)。Th1 类细胞因子 IFN-γ 在正常对照组的表达较低，当白假丝酵母菌感染后表达显著上调(P=0.006)，Farnesol 治疗后 IFN-γ 蛋白的表达水平轻微增加，较模型组及制霉菌素组无显著差异，显著高于正常组(P＜0.001)。非 B 细胞 IgG 当白假丝酵母菌感染后表达显著下调(P=0.013)，farnesol 治疗后其表达水平较模型组显著升高(P=0.010)，与正常组及制霉菌素组无显著差异。Farnesol 对 Th2 类细胞因子(IL-4)及 Th17 类细胞因子(IL-17)水平均无显著作用。透射电镜结果表明，白假丝酵母菌的感染会造成阴道上皮细胞结构及连接的破坏，线粒体的正常结构及功能显著破坏(Flameng 评分：3.13 ± 0.054)，而 farnesol 能够修复上皮细胞结构的作用，阴道上皮细胞形态良好，线粒体肿胀程度降低(Flameng 评分：0.67 ± 0.072，P< 0.001)，少数区域仍可见少量炎细胞浸润。

结论 Farnesol 能够有效清除白假丝酵母菌病原体，其抗真菌活性与典型的抗真菌药制霉菌素类似，且具有显著的阴道黏膜修复活性，并在阴道抗真菌免疫的天然免疫应答中发挥保护性作用，提示 farnesol 可作为 VVC 治疗的新型抗真菌药物。

关键字：外阴阴道白假丝酵母菌病，阴道上皮细胞，白假丝酵母菌，farnesol，免疫

新型 InhA 还原酶抑制剂 NITD-916 对脓肿分枝杆菌的活性研究

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目的 脓肿分枝杆菌对临床常用抗生素具有固有耐药性，导致新发的脓肿分枝杆菌感染患者缺乏有效的抗菌药物治疗方案。分析脓肿分枝杆菌对新型烯酰 ACP 还原酶（Enoyl acyl carrier protein reductase, InhA）抑制剂——NITD-916 的体外活性。

方法 采用微量肉汤滴定法检测 NITD-916 对 12 株非结核分枝杆菌(Non-tuberculosis mycobacterium, NTM)标准菌株和从上海市肺科医院收集并分离鉴定的 194 株脓肿临床分离株（脓肿亚种 n＝148，马赛亚种 n＝46）的最小抑菌浓度（minimum inhibitory concentration，MIC）。采用棋盘试验检测 NITD-916 与 10 种临床常用脓肿分枝杆菌抗菌素之间的相互作用关系。最后，评估 NITD-916 对巨噬细胞内脓肿分枝杆菌的胞内活性。

结果 NITD-916 对半数 NTM 标准菌株敏感，对 194 株脓肿分枝杆菌临床分离株具有较强的体外活性，MIC 范围是 0.032～4 mg/L，MIC50 和 MIC90 分别为 0.125 mg/L 和 1 mg/L，其中脓肿亚种和马赛亚种的结果一致。而利福布汀的 MIC 范围是 0.5～32 mg/L，MIC50 和 MIC90 分别为 4 mg/L 和 8 mg/L。NITD-916 对脓肿分枝杆菌具有抑菌活性（MBC99/MIC90＞4），并且 NITD-916 对 S 型比 R 型更敏感（P＜0.01）。NITD-916 和克拉霉素在 40% 马赛分枝杆菌菌株中具有协同作用（FICI≤0.5），与常用抗脓肿药物之间不存在相互拮抗。NITD-916 能够抑制巨噬细胞内脓肿分枝杆菌生长，与未处理的对照组相比，在 16×MIC NITD-916 （1~4 mg/L）的

作用下，脓肿分枝杆菌的生长速度降低了 0.7 ~ 2.6 log10CFU，胞内活性与 16 mg/L 亚胺培南和 8 mg/L 利福布汀相当。

结论 NITD-916 对脓肿分枝杆菌具有较强的体外活性，强调 InhAMAB 是抗脓肿分枝杆菌的有力靶点，是治疗脓肿分枝杆菌病的新型 4-羟基-2-吡啶酮类候选化合物，为临床治疗脓肿分枝杆菌提供新的可能性。

关键字：NITD-916，烯酰 ACP 还原酶抑制剂，脓肿分枝杆菌，非结核分枝杆菌，抗菌活性

Chronic Granulomatous Disease Caused by A Rare Compound Heterozygote Mutation in An Adolescent

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Objective Chronic granulomatous disease (CGD) is a rare inherited primary immunodeficiency characterizing as recurrent infections and aberrant inflammation due to defects in the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex. This defect is caused by mutations in the NADPH oxidase subunits including gp91phox, p22phox, p47phox, p67phox p40phox, encoding CYBB, CYBA, NCF1 NCF2 and NCF4 gene, respectively

Methods We report a case with recurrent pneumonia and significantly elevated IgE levels in an adolescent. Metagenomic next-generation (mNGS) sequencing contributed to identification of Burkholderia multivorans in bronchoalveolar lavage fluid and initiation of appropriate treatment

Results Whole exome sequencing (WES) revealed two-point mutations in CYBA gene, including one that has never been reported. We also provide an insight into B. multivorans infections through a literature review

Conclusion Application of mNGS contributed to the early identification of B. multivorans and the initiation of appropriate treatment. Timely screening of WES contributes to the diagnosis and prognosis of the patients

关键字：Chronic granulomatous disease, Burkholderia multivorans, pneumonia, CYBA gene

超高龄耐碳青霉烯肺炎克雷伯菌致胆囊炎患者抗感染治疗分析

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目的 对 1 例超高龄患者耐碳青霉烯类肺炎克雷伯菌（CRKP）致胆囊炎的抗感染治疗进行分析，探讨 CRKP 个体化抗感染治疗药物选择，以期为临床 CRKP 抗感染治疗提供参考。

方法 临床药师两次受邀对胆道感染患者进行会诊，分析用于治疗 CRKP 感染常用药物碳青霉烯类、替加环素、多黏菌素 B 以及头孢他啶阿维巴坦的特点，从药物选择、给药剂量、给药方法的优化等方面进行药学服务，帮助临床医生制定最优的抗感染方案。

结果 在临床药师的参与下，采用头孢他啶阿维巴坦等方案治疗，患者好转出院且未出现不良反应。

结论 临床药师在抗感染治疗过程中，与医师共同制定 CRKP 的抗感染治疗方案，有利于保障患者治疗的安全性和有效性，体现临床药师的价值。

关键字：碳青霉烯耐药，肺炎克雷伯菌，病例分析，超高龄患者

改性黑磷纳米片用于生物被膜的可视化检测和光动力治疗

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目的 细菌感染已成为全球性公共卫生安全问题，尽管抗生素治疗卓有成效，但传统给药模式下的抗生素疗法存在生物利用度低、选择性差、日益增长的耐药性、生物被膜内渗透性差等问题，导致慢性感染和复发性感染。诊断是否存在生物被膜感染是治疗的前提，灵敏、准确和便捷的诊断可以实现按需治疗、提高疗效及减少细菌耐药性等。荧光成像因具有灵敏度高、选择性强、成本低且操作简便等优点，常用于细菌检测。因此，设计具有诊疗功能一体化的纳米颗粒，对生物被膜的选择性成像和按需治疗具有重要的科学意义和临床实用价值。

方法 本研究利用超声对黑磷晶体破碎得到了尺寸在 200300 nm 尺寸的黑磷纳米片（BPNS），通过聚乙二醇（PEG）和声敏剂四羧基卟啉（TCPP）合成酯酶响应的检测前体化合物（PEG-TCPP），依靠共价键修饰到 BPNS 上得到 BP-TCPP，原位还原氯铂酸钾在黑磷纳米片上沉积铂纳米点制备 BP-Tc@Pt。

结果 BP-Tc@Pt 通过 PEG 的亲水作用促进被膜的渗透，在正常生理条件下，BP-Tc@Pt 通过黑磷

纳米片淬灭 TCPP 的荧光，响应微环境的酯酶释放 TCPP，发射红光指示细菌感染，在感染酸性条件下，铂催化过氧化氢产氧气，外界超声作用下增强了 TCPP 的声动力治疗生物被膜的效果。体外研究了纳米粒子的酯酶敏感性、药物释放行为、荧光成像能力、抗浮游菌和生物被膜效果以及细胞毒性。通过溶解氧测定仪检测溶液中的氧浓度表明 BP-Tc@Pt 具有优异的催化 H2O2 产生 O2 的能力，并且具有良好的可重复性；同时将 1,3-二苯基异苯并呋喃（DPBF）作为 1O2 探针表明 BP-Tc@Pt 在超声作用下具有优异的产生 1O2 能力。体外抗菌实验结果表明 BP-Tc@Pt 能够响应酯酶释放 TCPP 用于生物被膜的成像，在经过 5 分钟的超声处理后，BP-Tc@Pt 展示了优异的声动力效果，能够有效分散生物被膜，对被膜内部细菌的杀灭效率达到 99.9%。

结论 综上研究显示，研究基于响应脂酶的生物被膜内局部释药，验证了一种金葡菌生物被膜感染的诊疗一体化纳米粒子体系，较好实现了金葡菌生物被膜感染的无创诊断和高效治疗。

关键字：生物被膜，黑磷纳米片，感染诊断和治疗，可视化检测，光动力治疗

Safety and Efficacy of Phage Application in Bacterial Decolonisation: A Systematic Review

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Backgroud Colonisation by bacterial pathogens typically precedes invasive infection and seeds transmission. Effective decolonisation strategies are urgently need. Phages have been increasingly used to treat bacterial infections.There have been attempts to use phages for decolonisation reportedin the literature. We aimed to assess thein vivo efficacy and safety of phages for bacterial decolonisation.

Methods We performed a systematic review (registered with PROSPERO, No. CRD42023457637) by searching PubMed, Embase/Ovid, MEDLINE/Ovid, Web of Science and Cochrane Library toidentifying relevant studies from January 1990 to May 2023 to assess the in vivo efficacy and safety of phages for bacterial decolonisation. We included studies of the efficacy and/or safety of phages for bacterial decolonisation in humans or vertebrate animal models and excluded those reporting in vitro or ex vivo results only. We retrieved data of study design, intervention, and outcome in descriptive tables.We used SYRCLE's tool to assess risk-of-bias of animal studies

Results We identified 6,694 articles of which 56 (51 animal studies and five clinical reports) that met the predetermined selection criteria and were finally included. Gastrointestinal colonisatione (n=49, 87.5%) was the most studied bacterial colonisation site and other sites were central venous catheters (CVC), lung, nose, skin, and urinary tract. Of the 56 studies, 45 (80.4%) have reported a significant decrease of the bacterial load at the colonisation site, but only five studies have described eradication of target bacteria. A total of fifteen studies have reported the safety of phages for decolonisation. No obvious adverse events were reported in both the short-term and long-term observation period

Conclusion Phage administration for decolonisation appears to be safe and lead to significantly reduced bacterial loads.Given the increasing threat posed by difficult-to-treat bacteria, phages could be an alternative optionfor bacterial decolonisation, but their use needs to be improved in many aspects to meet clinical needs

关键字：phage，phage therapy，decolonisation，decolonization，bacterial colonization

耐碳青霉烯肺炎克雷伯菌噬菌体的分离及抵抗机制

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目的 噬菌体疗法为耐碳青霉烯肺炎克雷伯菌（CRKP）感染提供了新策略。本研究旨在构建 CRKP 噬菌体库并进一步选择最优噬菌体进行生物学及基因组特征研究；研究噬菌体抵抗机制，为噬菌体应用于临床提供理论基础。

方法 1．研究目标菌株：ST11-KL64 CRKP 为我国最常见的类型。收集成都市多处水样，以 135077 作为宿主菌进行噬菌体的分离，获得了 8 株噬菌体。应用噬菌斑最大的噬菌体（P04）抵抗菌株分离第 2 轮噬菌体（P40）。

2. 所有噬菌体使用氯化钠/聚乙二醇沉淀法提取 DNA 进行全基因组测序及种属分类。测定噬菌体的生物学及基因组学特征。

3．为明确宿主菌对噬菌体的抵抗机制，将宿主菌 135077 分别与单株、两株噬菌体共培养，分离三株噬菌抵抗菌株。将这三株菌的基因组与原菌株基因进行比对，将改变基因进行克隆回补至噬菌体抵抗菌株中，点滴法验证是否恢复了对噬菌体的敏感性。

结果 1．第一轮共分离裂解 KL64 型 CRKP 的噬菌体 8 株，均属于 Autographiviridae 科 Przondovirus 属，第二轮分离噬菌体 P40，属于

Straboviridae 科 Slopekvirus 属。

2. 第一轮分离到的 8 株噬菌体均为窄谱噬菌体，且之间没有协同作用。P04 与 P40 噬菌体联合后抑菌时间延长至 8h。两株噬菌体生物学特征良好。P04 噬菌体为短尾噬菌体，P40 噬菌体为肌尾噬菌体。

3. 分离了三株 P04 噬菌体抵抗菌株（PR1、PR2、PR3），与宿主菌比对后发现 PR1 菌株编码糖基转移酶的 wbaZ 基因被复合转座子打断。PR2 与 PR3 菌株编码磷酸葡萄糖磷酸转移酶的 wcaJ 基因被 IS903B 打断导致截短。将 wbaZ 基因进行扩增回补至 PR1 菌株、wcaJ 基因进行扩增回补至 PR2 与 PR3 菌株，回补后的菌株恢复了对噬菌体 P04 的敏感性。宿主菌与噬菌体 P04、P40 噬菌体共培养后分离噬菌体抵抗菌株 B1E1、B1E2 和 B1E3，B1E1 菌株丢失自 wzx 至 ugd 基因片段，B1E2 菌株丢失自 wcoV 至 wzt 基因片段，B1E3 菌株丢失自 wcaJ 至 wzt 基因片段。将 ugd 基因回补至 B1E1 菌株，将 ugd 与 wbgU 基因回补至 B1E2 和 BIE3 菌株后，菌株恢复了对噬菌体 P40 的敏感性。

结论 1. 第一轮分离噬菌体均属于短尾噬菌体，第二轮分离到噬菌体 P40 属于肌尾噬菌体。

2. 三株噬菌体的生物学特征显示良好的裂解细菌能力，属于烈性噬菌体，符合临床应用的标准。

3. 噬菌体组合的噬菌体抵抗机制：wacJ 与 wbaZ 基因改变导致的细菌荚膜含量减少，介导了细菌对 P04 的抵抗；ugd 联合 wbgU 基因导致的多糖改变介导了细菌对 P40 的抵抗。

关键字：耐碳青霉烯肺炎克雷伯菌；噬菌体；噬菌体抵抗

血流感染患者外周血铁死亡相关指标检测及铁死亡压力在巨噬细胞感染模型中作用研究

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目的 本课题首先分析细菌性血流感染患者外周血铁死亡相关指标与疾病严重程度的相关性，随后通过构建 KPN 感染巨噬细胞模型，探索铁死亡在巨噬细胞对抗细菌感染中的作用。

方法 （1）选取 2022 年 8 月~2023 年 5 月本地区某三甲医院血流感染患者为研究对象。根据是否发生脓毒症分为非脓毒症组和脓毒症组，另外选取体检健康人 20 名为对照组；脓毒症患者根据病情严重程度分为一般脓毒症组和脓毒症休克组。比较各分组入院 48h 内外周血血清铁代谢指标、铁调素及铜蓝蛋白水平；实时荧光定量逆转录 PCR（RT-qPCR）法检测谷胱甘肽过氧化物酶 4（GPX4）、血红素加氧酶-1（HO-1）和热休克蛋白 B1（HSPB1）的表达水平,并且将上述铁死亡相关指标与病情严重程度进行相关性分析。（2）选取小鼠 RAW264.7 细胞 ，随机将培养的细胞分为四组:对照 Con 组 、KPN 侵染组（K 组）、KPN 侵染+铁死亡激动剂 RSL3 处理组（K+R 组）和 KPN 侵染+铁死亡抑制剂 DFO 处理组（K+D 组）；采用倍比稀释法进行胞内菌存活计数，细胞亚铁比色法测定细胞内亚铁变化情况，流式细胞术检测细胞内 ROS 变化，Western Blot 法检测细胞内铁死亡相关蛋白表达水平。

结果 （1）血流感染脓毒症组患者血清中铁代谢相关蛋白如铁调素、转铁蛋白和铜蓝蛋白以及铁死亡相关基因 HO-1 和 HSPB1 mRNA 等水平均显著高于非脓毒症组以及对照组（$P<0.05$），而 GPX4 mRNA 水平则明显低于非脓毒症组以及对照组（$P<0.05$）。同样地，脓毒症休克组患者血清中铁蛋白、铁调素、铜蓝蛋白以及 HSPB1 和 HO-1 mRNA 表达水平的测定值均显著高于一般脓毒症组（$P<0.05$）；而 GPX4 mRNA 表达水平则明显低于一般脓毒症组（$P<0.05$）。相关性分析结果显示血清中铁蛋白、铁调素、铜蓝蛋白水平与脓毒症严重程度呈明显正相关（$P<0.05$）。（2）在 KPN 侵染巨噬细胞的早期阶段，巨噬细胞内产生了包括亚铁含量增加、脂质 ROS 累积和 GPX4 蛋白表达降低等铁死亡特征表现。铁死亡激动剂处理后可进一步增加胞内亚铁含量和 ROS 累积（$P<0.05$），GPX4 蛋白表达进一步降低（$P<0.05$），细胞内细菌存活率明显低于 KPN 侵染组（$P<0.05$），而铁死亡抑制剂处理组有效逆转了上述变化。

结论 （1）血清中铁代谢指标和铁死亡相关基因在血流感染早期即可出现变化，并且这种变化与病情严重程度呈明显正相关性，其机制还需深入研究。（2）KPN 侵染巨噬细胞早期阶段，细胞内发生铁死亡，铁死亡激动剂和抑制剂的使用验证了这种铁死亡压力可帮助巨噬细胞对抗肺炎克雷伯菌感染。

关键字：血流感染；脓毒症；铁死亡；肺炎克雷伯菌；RAW264.7 细胞；

氟康唑联合氟胞嘧啶治疗阿萨希毛孢子菌血流感染 1 例并文献复习

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目的 探讨氟康唑联合氟胞嘧啶用于治疗阿萨希毛孢子菌（T. asahii）所致血流感染的有效性，为临床治疗积累资料，为后期该类疾病的诊治提供参考。

方法 报道我院 1 例氟康唑联合氟胞嘧啶治疗

T. asahii 血流感染患者的经过，并以“trichosporon asahii ”“bloodstream infection”“fluconazole”“阿萨希毛孢子菌”“血流感染”“氟康唑”为关键字，检索中国知网、万方、PubMed，Web of Science 等数据库，回顾性分析患者的性别、年龄、基础疾病、免疫状态、真菌药敏试验及经氟康唑治疗后的临床结局。

结果 本例白血病患者在化学治疗期间发生 T. asahii 血流感染（氟康唑 MIC 4μg/ml,氟胞嘧啶 MIC 4μg/ml ），经氟康唑 800mg qd 联合氟胞嘧啶 1.5g qid 治疗后实现病原学清除及症状体征的好转。文献检索到符合条件的病例 4 例，包括本例共 5 例，均为免疫力低下患者（1 例为早产儿）。5 例患者中 T. asahii 对氟康唑的 MIC 为 0.5～8 μg/ml，采用以氟康唑为主的方案治疗后均好转，多采用长疗程（≥4 周），而 MIC 4～8 μg/ml 的均联合其他药物（两性霉素 B 或氟胞嘧啶）。

结论 T. asahii 所致血流感染常发生于免疫力低下患者，特别是血液恶性肿瘤患者，中性粒细胞减少是其高危因素。采用真菌血培养瓶进行培养有利于早期真菌的检出。ECMM、ISHAM 与 ASM 联合制定的全球指南推荐首选伏立康唑进行治疗。但对于不能耐受伏立康唑者，真菌药敏试验指导下，以氟康唑为主，单药或联合氟胞嘧啶/两性霉素 B 治疗可作为替代治疗方案，而感染病灶的清除及中性粒细胞等免疫功能的恢复或可进一步提高生存率。

关键字：阿萨希毛孢子菌；血流感染；氟康唑；氟胞嘧啶；治疗

住院患者中伏立康唑不良相互作用医嘱的回顾性分析

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目的 了解伏立康唑治疗的住院患者药物相互作用（DDI）医嘱的发生情况及常见药物。

方法 通过医院信息系统收集 2018 年 5 月至 2023 年 8 月福建省泉州市第一医院使用伏立康唑治疗并进行血药谷浓度（Cmin）检测的住院患者的治疗信息，对伏立康唑治疗期间 DDI 医嘱的发生率、DDI 所涉药物、DDI 类型和风险级别、DDI 发生的科室分布以及伏立康唑相关 1/2 类 DDI（不推荐与伏立康唑同时使用的药物和并用时需调整伏立康唑剂量的药物）相关患者伏立康唑的 Cmin 变化进行描述性统计分析。

结果 共纳入 752 例患者，其中 592 例（78.7%）存在伏立康唑相关 DDI 医嘱 1 344 例次，涉及 28 种药物。67.7%（401/592）的患者并用了 2 种及以上 DDI 药物。伏立康唑相关 DDI 医嘱涉及最多的药物为糖皮质激素[91.6%（542/592）]，其次为质子泵抑制剂[87.8%（520/592）]。28 种伏立康唑相关 DDI 药物中属于 1/2 类 DDI 者有 5 种，包括利福平、奈玛特韦/利托那韦、苯巴比妥、苯妥英钠和利福布汀。5 种药物涉及 33 例患者，其中 51.5%（17 例）患者的伏立康唑 Cmin<1.0 mg/L；涉及患者最多的药物是利福平（17 例），其次为奈玛特韦/利托那韦（10 例）。伏立康唑与利福平、利福布汀、苯巴比妥和苯妥英钠并用时，患者的伏立康唑 Cmin 显著下降。伏立康唑相关 DDI 医嘱在重症医学科发生率最高，其次为呼吸与危重症医学科。

结论 伏立康唑临床应用中 DDI 医嘱非常常见，且以大多数患者并用了 2 种及以上 DDI 药物。糖皮质激素及质子泵抑制剂为最常见的并用药物。临床需要警惕伏立康唑与利福平、利福布汀、苯巴比妥及苯妥英钠的 DDI 发生，而伏立康唑与奈玛特韦/利托那韦的 DDI 尚需进一步研究。

关键字：伏立康唑；药物相互作用；治疗药物监测

中性粒细胞胞外诱捕网在烟曲霉感染中的研究进展

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目的 探讨中性粒细胞胞外诱捕网（Neutrophil extracellular traps，NETs）在宿主烟曲霉感染中的相关机制，探索未来抗真菌治疗新靶点与新途径。

方法 使用 Pubmed 对相关研究进行了检索，选择了标题或摘要中包含以下关键字的文章："Neutrophil extracellular traps" or "Neutrophils" and "Aspergillus fumigatus"。

结果 烟曲霉诱导 NETs 形成存在多种方式，包括溶解性和非溶解性 NETosis，其形成途径因不同的刺激而异，主要涉及 MAPK 信号通路、Toll 样受体信号通路、钙信号通路等。 MAPK 信号通路通过 Syk-PI3K-蛋白激酶 C-a/b-Raf/MERK/ERK 途径以 NADPH 氧化酶依赖的方式释放解压缩的染色质，经组蛋白及颗粒蛋白装饰后形成大分子聚集体，在 PMA 刺激后，活化的中性粒细胞触发 NETs 被招募到病灶部位，结合、吞噬和灭活细菌。Toll 样受体与真菌分生孢子检测相关，如 TLR2 及 TLR4 是鉴定曲霉的重要模式识别受体（pathogen recognition receptors，PRRs）。此外，β2-整合素 CD11b/CD18（CR3，MAC-1）识别分生孢子并抑制孢子萌发，但菌丝杀灭作用仍依赖于中性粒细胞 FcγR 识别 IgG 抗体。

真菌感染后，宿主中性粒细胞识别菌丝 β-葡聚糖增加，下游激酶激活和 Ca2+信号触发 NADPH 氧化酶复合物组装，诱导 NETs 的形成。其中胞质 Ca2+浓度升高促进线粒体快速摄取 Ca2+，进一步激发氧化磷酸化作用，导致线粒体活性氧（mtROS）的产生并参与 NETs 的形成。然而过度 NETs 反应增加肺部真菌负担，异常高浓度 NETs 与血栓形成相关，利用重组人 DNA 酶、抗组蛋白抗体和蛋白酶抑制剂调节 NETs 形成可能有助于调节过度 NETs 形成的有害作用。烟曲霉主要通过自身成分调节 NETs 形成，抵抗 NETs 抑菌作用、分泌细胞外蛋白酶逃避补体、对 NETs 抑菌成分产生抗性等三种策略导致“NETs 规避”从而提高自身侵袭性，而靶向抑制去乙酰化过程可作为一种新型抗真菌途径。

结论 NETs 形成是限制烟曲霉感染的重要宿主机制，全面了解 NETs 与病原体之间的相互作用，进一步阐明烟曲霉菌株毒力机制及炎症反应对于了解病因及开发新型治疗策略具有重要作用。

关键字：中性粒细胞胞外诱捕网；中性粒细胞；烟曲霉；真菌感染；宿主免疫；

54 例临床药师参与新生儿科抗感染会诊用药的回顾性分析

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目的 通过对临床真实病例的回顾性分析，探讨临床药师参与新生儿科抗感染用药会诊的效果，以总结经验更好的为临床指导用药。

方法 收集 2020 年 1 月至 2023 年 12 月期间临床药师参与本院新生儿科抗感染会诊的病例资料，对患儿胎龄、性别、出生体重、日龄、患儿感染部位、会诊处置意见及采纳情况、治疗效果等进行回顾性统计分析。

结果 2020 年 1 月至 2023 年 12 月间本院新生儿专科临床药师共参与新生儿科抗感染会诊 54 例。会诊的患儿平均胎龄为 31w，女性患儿占比更大（占 57.4%），诊断以新生儿肺炎、新生儿坏死性小肠结肠炎、新生儿脑膜炎为主；有病原学依据的患儿共 42 例，病原菌检出包括表皮葡萄球菌、金黄色葡萄球菌、肺炎克雷伯菌、粘质沙雷氏菌、铜绿假单胞菌；临床全部采纳临床药师会诊意见；抗菌药物方案以联合用药为主（占 74%），特殊使用级抗菌药物使用率达 37.03%；追踪观察患儿病情转归情况，临床药师参与会诊的治疗中除了有 3 例患儿家长强烈要求转上级医院治疗，4 例家长放弃治疗外，会诊有效率达 87.04％。

结论 新生儿属于临床用药的特殊人群，临床药师参与用药实践，对促进患儿的合理用药具有重要意义。新生儿作为特殊群体，临床药师参与其抗感染用药，既保证了患儿用药的安全合理，同时也有助于体现临床药师的价值。

关键字：临床药师，新生儿，抗感染治疗，药学会诊

移植/非移植血液病患者的毛霉菌感染的预后因素

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目的 探讨血液病患者，尤其是移植后患者毛霉菌病的流行病学、临床特征和预后因素。

方法 回顾性分析 2012 年至 2022 年我中心诊断毛霉菌病的血液病患者，通过多变量分析描述了毛霉菌病的预后因素。

结果 共纳入 95 名患者，中位年龄为 44（1-68）岁，31 名（32.6%）患者接受了异基因造血干细胞移植。在所有患者中，最常见的病原体是根霉属（36.8%），最常见的感染类型是肺部感染（84.2%）。多变量分析显示，糖尿病（HR=3.864，95%CI:1.897-7.874， P<0.001 ）和低氧血症（ HR=3.536，95%CI:11.874-6.673，P=0.001）是预后的危险因素。中位随访 79 天，移植组患者 84 天死亡率显著高于非移植组（61.3%对 35.9%, P=0.029）。这可能由于移植组患者应用糖皮质激素（86.7%对 36.9%，P<0.001）和糖尿病患者（51.6%对 20.3%，P=0.002）的占比远高于非移植组。

结论 毛霉菌感染严重影响血液病患者预后，尤其是移植后患者毛霉菌病死亡率显著增加。为了改善预后，需要控制糖尿病（尤其是移植后糖皮质激素继发糖尿病）和低氧血症。

关键字：毛霉菌，血液病，造血干细胞移植，预后因素

一株广谱鲍曼不动杆菌噬菌体的分离鉴定及对细菌生物膜作用研究

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目的 从临床多重耐药鲍曼不动杆菌（MDR-AB）菌株标本中分离宿主谱广和裂解能力强的噬菌体，为研发预防和治疗 MDR-AB 感染的噬菌体制剂奠定基础。

方法 从医院采集未处理的污水，以 MDR-AB 为宿主菌，对分离到的噬菌体进行宿主谱测定、生物学特性研究、形态结构观察、基因组特征分析、24h 体外抑菌能力测定和不同 MOI 下对细菌生物膜的抑制与清除效果的研究，并且对经噬菌体处理后菌株进行最低抑菌浓度（MIC）测定。

结果 从医疗污水中共分离到 22 株鲍曼不动杆菌噬菌体，选择宿主谱广和裂解能力强的命名为 P425，其可裂解 80.77%（42/52）的多重耐药菌株，并且可针对不同的荚膜血清型。生物学特征试验表明，P425 的 PH 稳定性为 2.0-12.0，温度稳定性为 4-60℃，对紫外可耐受 60min，MOI 为 0.00001，孵育 10min，吸附速率可达 91.83%，裂解量为 292。根据电镜结果显示，P425 为有尾目短尾噬菌体科。测序结果显示，P425 基因组大小为 85197bp，G+C 含量为 38.54%，编码 130 个开放阅读框，预测有溶菌酶和水解酶。24h 体外抑菌结果表明，P425 在前 7h 可高效抑制细菌生长，后续虽有抗性菌生长但远低于对照组。不同 MOI 处理下 P425 对生物膜的抑制率和已形成生物膜的清除率在 84%和 82%以上。对经 P425 处理后的宿主菌进行纯化测定 MIC，与未经处理的宿主菌相比，结果表明，P425 处理后的菌株对四环素、环丙沙星、磺胺甲恶唑、头孢曲松钠的 MIC 分别降低为 1/8MIC、1/4MIC、1/2MIC、1/2MIC。

结论 P425 是一株广谱裂解性噬菌体，对生物膜的抑制与清除有很好的作用效果，同时还可以降低细菌的耐药性，优化抗生素的治疗效果，因此是一种潜在的治疗和消毒剂，可为日后临床中 MDR-AB 的预防和治疗提供新的选择。

关键字：鲍曼不动杆菌，噬菌体，多重耐药，生物膜，抗生素

PEITC 增强环丙沙星对肺炎克雷伯菌抗菌活性的研究

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目的 1. 探究在异硫氰酸苯乙酯（PEITC）存在时，环丙沙星在体外和体内模型中对肺炎克雷伯菌的抗菌活性的影响。

2. 探究 PEUTC 对于环丙沙星活性增强作用的分子机制。

方法 1. 采用药敏实验、棋盘微量稀释法、时间-杀菌动力学实验，明确在体外模型中药物联合使用的效果。

2. 利用肺炎克雷伯菌诱导的小鼠肺部感染模型评估在体内模型中 PEITC 对环丙沙星的影响。

3. 结合外排泵抑制实验、qRT-PCR 检测和活性氧(ROS)检测，研究 PEITC 增强环丙沙星对肺炎克雷伯菌杀菌作用的潜在机制。

结果 1. PEITC 与环丙沙星联合治疗在耐药和非耐药的肺炎克雷伯菌中均显示出了良好的协同抗菌活性，并在体外的时间-杀菌动力学实验中发现联合用药后环丙沙星的抗菌活性明显增加。

2. PEITC 与环丙沙星在肺炎克雷伯菌诱导的小鼠肺部感染模型中与环丙沙星单药治疗相比，可显着减少肺组织的细菌数量，促进抗感染并提高治疗效果。

3. 在机制上，我们发现 PEITC 与环丙沙星的协同抗菌作用会促进 ROS 的产生，并加重细菌结构的破坏。

结论 1. 我们的研究表明，在体内和体外，PEITC 与环丙沙星联合使用对肺炎克雷伯菌展现出较好的抗菌活性，为进一步的临床试验提供理论性依据。

2. PEITC 与环丙沙星组合通过增强 ROS 的产生和加重细菌结构的破坏在体外和体内对肺炎克雷伯菌产生协同抗菌的作用。

3. 本研究也提示 PEITC 与环丙沙星联合对治疗肺炎克雷伯菌感染，特别是对抗菌药物耐药的肺炎克雷伯菌的感染开辟一条新的治疗途径。

关键字：环丙沙星，异硫氰酸苯乙酯，活性氧，肺部感染

1 例氟康唑原发耐药并伏立康唑超快代谢的肺隐球菌病报道及文献复习

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目的 探究 1 例氟康唑原发耐药并伏立康唑超快代谢的肺隐球菌病的临床特点，并进行文献复习，为临床提高对肺隐球菌病治疗的认识提供参考。

方法 对 1 例氟康唑原发耐药并伏立康唑超快代谢的肺隐球菌病的临床资料进行分析，并进行文献复习。

结果 46 岁男性患者，因"体检发现肺部阴影 3+月，咳嗽咳痰 2 天"入院治疗，有 2 型糖尿病病史 1 年余，平素使用达格列净、二甲双胍治疗及运动，血糖控制可。2021 年因乙肝大三阳服用替诺福韦至今，肝功能正常。2015 年临床诊断肺结核，抗痨治疗 1 年复查胸部 CT 病灶完全吸收。入院胸部 CT 检查示“右肺上叶前段、尖段及下叶背段可见多发大小不等的结节影，边缘可见毛刺，部分灶内可见细支气管影穿行，灶周可见絮状模糊影，病灶沿支气管走形分布，部分病灶融合成片，较前次病灶增多”，入院后完善隐球菌荚膜多糖抗原检测阳性，经支气

管镜肺泡灌洗液培养提示新型隐球菌。患者细胞免疫及体液疫功能正常。拒绝腰穿，头颅MRI无异常，无神经系统症状体征。肺隐球菌病诊断明确，予以氟康唑治疗。体外药敏结果提示氟康唑耐药、治疗2周复查胸部CT提示肺部病灶增加、患者既往曾患肺结核，与患者沟通后完善经皮肺穿（此前患者拒绝），送检组织病理、组织培养及mNGS均提示新型隐球菌，组织培养亦提示氟康唑耐药，考虑患者为氟康唑原发耐药。患者体外药敏结果提示伏立康唑、伊曲康唑、两性霉素B敏感，调整治疗为伏立康唑+雾化吸入两性霉素B。使用伏立康唑用药期间数次检测伏立康唑血药浓度极低，在排除药物相互作用的情况下，考虑患者为伏立康唑超快代谢基因人群，调整治疗为两性霉素B脂质体+氟胞嘧啶治疗，治疗3周复查胸部CT提示病灶较前明显吸收。患者要求出院，院外予以艾沙康唑继续治疗，定期门诊随访。

结论 1.肺隐球菌病的治疗取决于药敏结果、患者免疫状态及病情严重程度，首选三唑类抗真菌药物。近年来，隐球菌氟康唑原发耐药有所增加，故临床治疗应重视药敏结果。2.伏立康唑可作为氟康唑治疗失败后的补救措施，在用药过程中应积极监测血药浓度，以免影响疗效。3.两性霉素B+氟胞嘧啶联合治疗对于三唑类耐药或疗效不佳仍然有效。4.艾沙康唑、泊沙康唑等新型三唑类药物对氟康唑耐药及伏立康唑超快代谢的隐球菌病可能具有较好的应用前景，有待临床进一步观察。

关键字：肺隐球菌病，氟康唑，耐药，伏立康唑，超快代谢，治疗

1 例腹腔镜腹股沟疝修补术后皮肤偶发分枝杆菌感染的治疗分析及药学监护

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目的 分析1例临床药师参与腹腔镜腹股沟疝修补术后偶发分枝杆菌切口感染患者治疗方案制定及药学监护过程，旨在提高临床药师参与抗感染临床实践及解决问题的能力。

方法 一患者因腹腔镜腹股沟疝修补术后伤口感染入院，入院后采用经验性抗感染治疗，但伤口一直愈合不佳，且始终未明确病原菌，经临床药学等多科学会诊后考虑偶发分枝杆菌感染，临床药师查询循证学证据，协助医生制定及调整偶发分枝杆菌抗感染方案，并针对长疗程联合使用的抗菌药物进行疗效、不良反应及院外随访等药学监护。

结果 临床药师结合患者流行病学史及查阅循证学证据制定抗感染方案。首次会诊予以阿米卡星注射液0.6g qd（维持剂量0.4g)+莫西沙星0.4g qd+亚胺培南西司他丁1g q12h +注射用多西环素注射液0.1g q12h(首剂0.2g)抗感染治疗；调整用药后，患者右侧伤口基本愈合，左侧伤口未愈合，但患者出现耳鸣及听力下降等不良反应，第二次会诊予以头孢西丁 2g q8h+利奈唑胺 0.6g q12h+克拉霉素 1 片 q12h+复方磺胺甲噁唑 2 片 q12h；患者左侧伤口仍还有部分未愈合，临床药师第三次会诊予以阿米卡星注射液0.4g qd+莫西沙星0.4g qd +亚胺培南西司他丁 1g q12h+复方磺胺甲噁唑 2 片 q12h；治疗25天后患者腹部左侧伤口愈合尚可，无明显压痛及渗液，第四次会诊建议出院后予以盐酸莫西沙星片0.4g qd+利奈唑胺片0.6g qd+盐酸米诺环素胶囊0.1g bid口服继续抗感染治疗，建议半月后再次来院复查，随访后患者手术后感染伤口基本愈合。

结论 临床药师参与抗感染多学科会诊，查阅循证学证据，协助医生制定抗感染方案及实施全程药学监护，不仅能提高患者治疗效果，还有助于提升临床药师抗感染会诊水平。

关键字：偶发分枝杆菌；临床药师；感染；药学监护；不良反应

经支气管镜冷冻肺活检成功治疗肺毛霉菌肺炎1例

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目的 肺毛霉病是一种起病急、进展快、诊断困难、病死率高的严重肺部真菌感染，该病可侵袭肺组织、支气管、肺血管等，可导致支气管阻塞和大咯血等并发症。由于此病诊断困难，临床医师对其认识不足，容易出现诊断延迟，并且治疗极为困难，患者病死率很高，预后较差。河北医科大学第二医院呼吸与危重症医学科采用支气管镜介入技术联合药物治疗，成功治愈1例肺毛霉菌肺炎

方法 回顾性分析患者，女性，55岁，主因"发热，咳嗽，咳痰1月余，反复咯血20余天"入住河北医科大学第二医院呼吸内科病房。患者主要表现为发热、咳嗽、咳痰、痰中带血，胸部CT可见右肺上叶空洞性病变，院外多种抗生素保守治疗无效。本次发病后发现糖尿病，血糖控制不佳。查体：神清，精神弱。体温37.2°C 呼吸频数19次/min，心率85次/min，右上肺呼吸音低。心脏、腹部体格检查阴性。双下肢无水肿。患者入院后胸部CT提示右肺上叶空洞性病变，肿瘤标志物、真菌D-葡聚糖检测、真菌GM实验、痰培养：大肠埃希菌，光滑念珠菌。2023年11月3日行电子支气管镜检查提示：右肺上叶开口可见白色黏稠分泌物完全阻塞管腔，给予

冷冻冻取坏死物质，行肺泡灌洗。病理：大部分退变、坏死，其内见真菌菌丝，形态符合毛霉菌。

结果 2 次软镜下冷冻治疗冻取清除坏死组织、镜下两性霉素 B5mg 共 2 次灌注，1 次硬镜下冷冻治疗冻取完全清除毛霉菌菌体，两性霉素 B 胆固醇硫酸酯复合物逐渐加量 50mg、100mg、150mg 每日 1 次、200mg 每日 1 次 20 d，后因肾功能异常减量至 150 mg 每日 1 次，静脉注射 4d，泊沙康唑 300 mg 每日 1 次静脉注射 2 周，泊沙康唑口服 3 个月，美罗培南 1 g 每 8 小时 1 次抗细菌治疗。并予以对症降糖等治疗。

结论 患者无发热，无咳嗽、无咯血，胸部 CT 提示右肺上叶病变吸收，遗留空腔样改变。

关键字：肺毛霉病，毛霉菌病，冷冻治疗，泊沙康唑，两性霉素 B 胆固醇硫酸酯复合物，糖尿病

内脏利什曼病分子生物学诊断应用及不同治疗方法的疗效分析研究

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目的 内脏利什曼病也称黑热病，主要由杜氏利什曼原虫和婴儿利什曼原虫感染引起，易被误诊为血液系统疾病等，其治疗需要葡萄糖酸锑钠或两性霉素 B，该两类药均存在不同程度如心肌损伤、肾功损伤等不良反应，且均存在复发风险。因此，本研究对 mNGS 等分子生物学方法在该类疾病中的应用价值以及不同治疗方法的疗效进行研究。

方法 从我院病历系统中检索内脏利什曼病患者，对其人口学数据、临床症状、检验检查资料、病原诊断依据、治疗方法、临床结局、有无复发和药物不良反应等进行收集，对所收集资料进行分析研究来明确我院收治的内脏利什曼病患者的临床特征并总结最佳病原诊断方法和治疗方案。

结果 共纳入 2001 年 12 月 30 日至 2023 年 12 月 31 日期间收治的内脏利什曼患者共 19 例，男女比例为 17：2，平均年龄 45.42 岁，最小年龄 27 岁，最大年龄 62 岁。在有记录的可能疫源地的 9 例患者中，5 例为新疆，3 例为甘肃、1 例为山西或四川。除 2023 年收治的 2 例患者无红细胞的下降（但白细胞和血小板仍有下降）外均存在不同程度的 WBC、HGB 和 PLT 等三系同时降低。所有患者都存在脾大和发热。1 例患者为血清学诊断，1 例患者骨髓涂片阴性血液分子生物学阳性，骨髓涂片阳性同时行血液 mNGS 的 4 例患者均提示杜氏利什曼原虫和婴儿利什曼原虫重叠感染。从发病至诊断时间从 15 天等 720 天不等，而行血液 mNGS 的 5 例患者诊断时间明显缩短，分别为 60、57、20、15 和 22 天，诊断时间明显缩短。共 12 例患者使用了葡萄酸锑钠，除 1 例患者使用 13 天临床未缓解自动出院外，其余患者均得到临床缓解好转出院。6 例使用了两性霉素 B，其中 1 例未得到临床缓解自动出院。2 例使用了两性霉素 B 和葡萄糖酸锑钠或葡萄糖酸锑钠和两性霉素 B 的序贯疗法，均得到了临床缓解。在有记录的患者中 2 例使用葡萄糖酸锑钠和 1 利使用两性霉素 B 的患者存在复发，但复发原因考虑与病原学未清除和疗程不足等相关。2 例患者出现了与两性霉素 B 相关的肾损伤，1 例患者出现了可能与葡萄糖酸锑钠的相关的 ST-段压低和胰腺炎，均在停药后迅速恢复。

结论 内脏利什曼病临床表现以高热、三系减少、脾大为主要临床特征，血液 mNGS 明显缩短了其诊断时间，并标明杜氏利什曼原虫和婴儿利曼原虫重叠感染为目前流行患者的主要感染类型，在具备上述临床特征的患者中行血液 mNGS 除外内脏利什曼原虫感染具有重要意义。在现行治疗方法中，按说明书使用葡萄糖酸锑钠 0.6g 6 到 10 天，然后根据病原是否清除再觉得是否重复上述疗程仍为有效方法，而两性霉素 B 的疗效及安全性仍需进一步研究。

关键字：黑热病，骨髓涂片，mNGS，葡萄糖酸锑钠，两性霉素 B，复发

643 例儿童皮肤软组织抗菌药物使用分析

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目的 通过收集皮肤软组织感染（skin and soft tissue infection,SSTI）患儿的抗菌药物应用等信息，了解本地区儿童 SSTI 抗菌药物使用情况，为临床抗菌药物选择提供依据。

方法 收集 2019 年 1 月到 2021 年 12 月在深圳市儿童医院住院的 STI 患儿病历资料，包括临床特征、病原、抗菌药物种类、疗程等，行统计分析。

结果 共 643 例纳入本研究。抗菌药物使用率为 97.0%(624/643)，仅有 22 例（3.5%）使用 2 种及以上抗菌药物联合抗感染治疗。未使用抗菌药物的 19 例患儿，均为脓肿，入院行切开引流术后出院。使用抗菌药物的种类为 25 种, 873 例次，限制性抗菌药物 48.7%(425/873)；特殊级别的抗菌药物 7.3%（64/873)。前 5 位抗菌药物为头孢呋辛（25.3%）、头孢哌酮舒巴坦钠（21.6%）、阿莫西林舒巴坦钠（20.5%）、头孢曲松（10.0%）、万古霉素（3.8%），对于 DOT（施用于或分发给特定患者的任意抗生素的累计天数）前 5 位分别为哌拉西林他唑巴坦（8.4）、万古霉素（7.8）、夫西地酸（7.1）、利奈唑胺（7.0）、

阿奇霉素（7）。624 例使用抗菌药物病例中，初始抗感染治疗选择主要为头孢呋辛（32.5%）、阿莫西林舒巴坦（24.2%）、头孢哌酮舒巴坦（21.3%）、头孢曲松（12.2%）、头孢他啶（2.1%）。对于主要病原金黄色葡萄球菌，甲氧西林敏感葡萄球菌(Methicillin-resistant Staphylococcus aureus,MSSA)初始抗感染治疗选择主要为头孢呋辛（33.6%）、阿莫西林舒巴坦（32.1%）、头孢哌酮舒巴坦（17.2%）、头孢曲松（8.2%）、头孢他啶（3.0%），5.97%（8/134）更换为万古霉素；耐甲氧西林金黄色葡萄球菌（Methicillin-resistant Staphylococcus aureus，MRSA）初始抗感染治疗选择主要为阿莫西林舒巴坦（36.7%）、头孢呋辛（32.7%）、头孢哌酮舒巴坦（12.2%）、头孢曲松（8.2%）、哌拉西林他唑巴坦（4.1%），34.69%（17/49）更换为万古霉素或利奈唑胺。总体抗菌药物使用疗程中位数为 9.5（6，13）天，MSSA 抗感染疗程中位数 8（6，13）天,MRSA 抗感染疗程中位数为 12（7.5，17）天。抗菌药物的 DDDs 前 5 位抗生素为阿莫西林舒巴坦钠、头孢哌酮舒巴坦钠、头孢呋辛、头孢曲松、头孢克洛。

结论 初始抗菌药物选择以 β-内酰胺类抗菌药物为主，可不需常规覆盖 MRSA。

关键字：儿童，皮肤软组织感染，抗菌药物

以发热待查收住院的荚膜组织胞浆菌病患者临床特征和两性霉素使用剂量及疗效分析

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目的 荚膜组织胞浆菌病一般临床表现轻微，大多数感染无症状或呈自限性，但部分患者会发烧急性肺部感染或严重的进行性播散性感染。而以“发热待查”收住院的患者病情尤其严重，而两性霉素 B 使用的总剂量根据 IDSA 推荐为 1-5g，且其肾脏损伤等毒性作用非常容易出现。因此，如何根据该类患者的临床特征早期诊断和总结适合我国人群的使用剂量非常重要。

方法 从我院病历系统中检索以发热待查收住院收治而确诊为荚膜组织胞浆菌的患者，对其人口学数据、临床症状、检验检查资料、病原诊断依据、治疗方法、临床结局、有无复发和药物不良反应等进行收集，对所收集资料进行分析研究来明确该类患者的临床特征早期诊断和总结适合我国人群的适宜剂量。

结果 共纳入 2006 年 3 月 1 日至 2023 年 9 月 11 日以发热待查收住院而最终确诊为荚膜组织胞浆菌的患者共 11 例，男性和女性的比例为 10：1，平均年龄 44 岁，最小年龄 21 岁，最大年龄 62 岁。有 45.4%（5/11）有咳嗽的表现，所有患者肺部 CT 均有异常（包括肺部结节、胸腔积液、斑片影等），50%的患者 WBC＜2.5X109/L，肝功均表现为 GGT 和 ALP 不同程度的升高，尤以 ALP 升高为明显，最高者为正常上限值的 20 倍，所有患者均存在脾大，在骨髓中均找到荚膜组织胞浆菌，两性霉素的使用总剂量平均为 1.85g，均得到了临床缓解，无肾脏损伤出现。

结论 以发热待查收住院而最终诊断为荚膜组织胞浆菌的患者均为播散型病例，可累及骨髓、肺部和肝脏，表现为 WBC 偏低，肺部结节、胸腔积液和斑片影等病灶，尤其值得注意的是肝脏受累表现为 GGT 和 ALP 升高等胆汁淤积表现，对于这类患者应追述流行病学史并仔细在骨髓中寻找有无荚膜组织胞浆菌尽早诊断。在治疗上，较小剂量的两性霉素 B 可获得临床缓解，不良反应少见。

关键字：荚膜组织胞浆菌，发热待查；骨髓图片；胆汁淤积，两性霉素 B 总剂量；肺部 CT

细菌真菌耐药监测与耐药机制

2017-2022 年某中医院耐甲氧西林金黄色葡萄球菌检出率及耐药率变化趋势

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目的 通过长期监测和数据对比，探索耐甲氧西林金黄色葡萄球菌（MRSA）检出率及耐药率变化趋势，为 MRSA 的院感防控效果评价以及高效的临床抗感染治疗方案提供参考依据。

方法 使用 WHONET5.6 软件及 SPSSAU 平台 Cochran-Armitage 检验方法，回顾性分析某中医院 2017 年至 2022 年期间 MRSA 的检出率、标本分布、科室分布及耐药率的变化趋势。

结果 共 1447 株 MRSA 纳入分析，MRSA 检出率为 49.32%，在革兰氏阳性菌、所有病原菌中的检出率分别为 18.71%、4.13%,连续 6 年 CA-MRSA 检出率呈上升趋势（P＜0.05），HA-MRSA 检出率呈下降趋势（P＜0.05），在各类细菌中的检出率均呈下降趋势（P＜0.001）；标本来源主要为痰液、分泌物和脓液，构成比分别为 67.03%、10.29%、7.45%,在痰标本中构成比呈下降趋势（P＜0.001），在脓液标本中构成比呈上升趋势（P＜0.001）；科室分布主要为 ICU、老年科，构成比分别为 23.91%和 16.31%，在老年科构成比呈明显下降趋势（P＜0.001），在 ICU 构成比呈下降趋势（P＜0.05）；对四环素、庆大霉素、左旋氧氟沙星、环丙沙星、莫西沙星、奎奴普丁/达福普汀的耐药率呈显著下降趋势（P＜0.001），对复方新诺明的耐药率呈上升趋势（P＜0.05）。

结论 该院 2017-2022 年 MRSA 检出率和耐药率整体呈下降趋势，针对 ICU、血管外科等高风险科室需进一步落实多部门协同下的综合感控干预措施，可深入开展入院患者 MRSA 鼻拭子筛查与去定植和分离菌株 SCCmec 基因分型研究，更好地预防与控制其在医院的传播。

关键字：耐甲氧西林金黄色葡萄球菌；检出率；耐药率；变化趋势

A Novel KPC-179 Variant Conferring Ceftazidime-avibactam Resistance in A Carbapenem-resistant Klebsiella Pneumoniae Isolate

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Objective Carbapenem-resistant K. pneumoniae (CRKP) strains are one of the most serious antimicrobial resistance problems in the world, leading to high morbidity and mortality. The main carbapenemase in CRKP is Klebsiella pneumoniae carbapenemase (KPC), which can hydrolyze almost all cephalosporins and carbapenems, resulting in a lack of effective treatment options. As a result, tigecycline and polymyxin B have become the final resort for defensing against this multidrug-resistant Gram-negative bacteria. However, side effects such as toxicity and induced resistance limit their clinical application. Ceftazidime–avibactam (CZA) is a novel combination of β-lactam and β-lactamase inhibitor that offers a valuable alternative strategy against KPC-producing K. pneumoniae infections. Avibactam protects ceftazidime from hydrolysis by KPCs, OXA-48, AmpC and extended-spectrum β-lactamases (ESBLs), but not for metallo-β-lactamases. However, resistance has gradually emerged along with its wide usage. In this study, we aim to explore the resistance mechanism of CZA

Methods APB/EDTA with imipenem/meropenem/ertapenem (carbapenemase inhibitor APB [3-aminophenylboronic acid] and EDTA enhancement method) and NG-Test CARBA 5 phenotypic tests were used to detect carbapenemase enzyme types, CZA conjugation experiment was conducted with rifampicin-resistant E. coli EC600 as a recipient strain to explore the transferability of CZA resistance, and whole-genome sequencing (WGS) analysis were performed in HX1032 and HX1192 Klebsiella pneumoniae isolates

Results We reveal a CZA-resistant and carbapenem-susceptible Klebsiella pneumoniae strain (HX1192) carrying a novel KPC variant, KPC-179, molecular analysis highlighted a G394A mutation and an ATC insertion at 543 in the blaKPC-2 gene, resulting in an A133T substitution and insertion of the amino acid S at Ambler position 183 in the protein sequence. Based on the results of WGS analysis, K. pneumoniae HX1132 belonged to clonal lineage ST11. Although the susceptibility results showed that the isolate was resistant to CZA (MIC≥256 mg/L), it remained susceptible to imipenem (MIC = 0.25 mg/L), colistin (MIC = 1 mg/L), tigecycline (MIC = 0.5 mg/L), aztreonam-avibactam (MIC = 1 mg/L), and the MIC of meropenem decreased (MIC = 2mg/L). The APB/EDTA with imipenem/meropenem and NG-Test CARBA 5 phenotypic tests for carbapenemase were negative, we retested HX1192 using APB/EDTA with ertapenem again, but the enzyme type remained undetectable. The plasmid harboring blaKPC-179 from strain HX1192 was successfully transferred into the EC600 E. coli recipient strain, rendering the transconjugants resistant to CZA (MIC = 32 mg/L), quinolone, aminoglycosides and some cephalosporins. HX1032 Klebsiella pneumoniae was isolated from respiratory specimens prior to HX1192 Klebsiella pneumoniae, it was proved to produce serine-carbapenemase

by APB/EDTA with imipenem/meropenem/ertapenem and NG-Test CARBA 5 phenotypic detections, the result of antimicrobial susceptibility testing showed that HX1032 was resistant to carbapenem (imipenem≥16 mg/L，meropenem≥16 mg/L and ertapenem≥8 mg/L) but sensitive to CZA (MIC = 4 mg/L), WGS analysis reveled it was belonged to clonal lineage ST11 and carried the blaKPC-2 carbapenemase gene

Conclusion Our study highlights the importance of monitoring susceptibility during CZA treatment and accurately detecting of KPC variants. It is crucial for clinicians to tailor treatment plans for critically-ill patients, closely monitor the susceptibility of KPC-producing strains to CZA, and promptly detect KPC variants at an early stage of therapy. This approach will help prevent treatment failure and the rapid dissemination of CZA-resistant strains

关键字：CZA resistance, carbapenem-resistant Klebsiella pneumoniae, KPC variant

Emergence of KPC-134, A KPC-2 Variant Associated with Ceftazidime-Avibactam Resistance in A ST11 Klebsiella Pneumoniae Clinical Strain

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Abstract The emergence of various new KPC variants leading to ceftazidime-avibactam treatment failure is a new challenge in current clinical anti-infection treatment. Here, we report a ceftazidime-avibactam-resistant K. pneumoniae 1072-2 clinical strain carrying a novel KPC variant, KPC-134, which differs from KPC-2 by by both single mutation (D178A) and 8-amino acid insertions (asp-asp-asn-arg-ala-pro-asn-lys) at Ambler positions 268. The results of antimicrobial susceptibility testing showed that the isolate was resistant to meropenem (MIC =4 mg/L), ceftazidime (MIC =>32 mg/L), cefepime (MIC =>128 mg/L), aztreonam (MIC =>128 mg/L), and ceftazidime-avibactam (MIC =>128 mg/L) but sensitive to imipenem (MIC = 0.5 mg/L), imepenem-relebactam (MIC = 0.5 mg/L), meropenem-vaborbactam (MIC = 2 mg/L), aztreonam-avibactam (MIC = 4 mg/L). According to the results of the plasmid transformation assay, the transformant was positive for blaKPC-134 and increased MICs of ceftazidime-avibactam, ceftazidime, cefepime, and aztreonam by 512-fold, 256-fold, 16-fold, and 4-fold respectively, compared with the recipient. The blaKPC-134 gene was carried by a 133,789-bp plasmid, and many common resistance genes were identified, including blaKPC-134, blaCTX-M-65, blaTEM-1B, and blaSHV-12, rmtB, and catB4. The blaKPC-134 gene was carried by an IncFII-IncR plasmids and also associated with the IS26, tnpR, ISkpn8, ISkpn6-like, and Tn1721 element.

IMPORTANCE. The emergence of various new KPC variants leading to ceftazidime-avibactam treatment failure is a new challenge for clinical anti-infection treatment. Here, we describe the characterization of a ceftazidime-avibactam-resistant blaKPC-134-positive K. pneumoniae clinical strain for the first time. K. pneumoniae bearing with KPC-variant often mislead clinical anti-infection treatment because of their unique antimicrobial susceptibility profile and the tendency of conventional carbapenemase assays to give false negative results. Therefore, timely identification of KPC-variant and effective anti-infective therapy are key to saving infected patients.

OBSERVATION. Recent years, with the widespread epidemic dissemination of carbapenem-resistant Klebsiella pneumoniae in the clinic, it poses a major challenge for clinical anti-infective treatment (1). According to the results of the China Antimicrobial Surveillance Network (www.chinets.com), the resistance rate of K. pneumoniae to imipenem or meropenem is rapidly increasing (from 3% in 2005 to more than 26% in 2022) (2). Available findings suggest that the production of carbapenemases, particularly class A KPC-type serine carbapenemases, is the predominant resistance mechanism for carbapenem resistance in K. pneumoniae (3). The in vitro activities have shown that ceftazidime-avibactam has high antibacterial activity against KPC-type carbapenemase-producing K. pneumoniae and is the first-line drug for the clinical treatment of infections caused by such resistant bacteria (4,5,6).

However, with the widespread use of ceftazidime-avibactam in clinical practice, KPC-type carbapenemase-producing K. pneumoniae has mutated to adapt to the strong selective pressure of antibacterial drugs, and various new subtypes of KPC based on KPC-2 or KPC-3 mutations have emerged, mediating the resistance of K. pneumoniae to ceftazidime-avibactam and leading to treatment failure, which is a new challenge in clinical anti-infection treatment nowadays (7). The results of available studies show that the emergence of new subtypes of KPC genes has been in an explosive trend in the last three years. To date, more than 140 blaKPC subtypes have been reported in the world according to the NCBI database (8). In this study, we firstly describe the characterization of blaKPC-134, a novel blaKPC variant that confers resistance to ceftazidime-avibactam and restored susceptibility to imipenem.

关键字：Klebsiella pneumoniae, ceftazidime-avibactam, KPC-134

HIV 并发社区获得性肺炎致病菌分布及耐药性分析

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目的 基于某医院抗菌药物耐药监测，确定 HIV 并 CAP 常见的致病细菌分离株及其抗菌药物敏感性特征。

方法 使用来自广安某三甲医院 2 年间抗菌药物药敏试验记录进行横断面回顾性研究，对纳入统计的488株细菌药敏结果进行分组分析，HIV并CAP组(HIV/CAP 组)及未合并 HIV 感染的 CAP(CAP 组)各 244 例。

结果 HIV/CAP 组共检出菌株 244 株，其中革兰阴性菌 13 种，190 株(77.8%)，革兰阳性菌 8 种，54 株（22.2%），主要分布：大肠埃希菌(E. coli）72 株（29.5%）、肺炎克雷伯菌(K. pneumonia)51 株（20.9%）、铜绿假单胞菌(K. pneumonia)30 株（12.3%）、凝固酶阴性葡萄球菌(Coagulase negative staphyloco)20 株（8.2%）、金黄色葡萄球菌(S. aureus)14 株（5.7%）等。与 CAP 组相比，HIV/CAP 组革兰氏阴性菌占比差异明显，整体细菌耐药较 CAP 组呈升高趋势，在酶复合制剂中，大肠埃希菌对阿莫西林/克拉维酸、头孢哌酮/舒巴坦耐药率为 24.3%、17.1%，哌拉西林/他唑巴坦耐药率为 2.9%；肺炎克雷伯菌阿莫西林/克拉维酸耐药率为 39.2%，头孢哌酮/舒巴坦及哌拉西林/他唑巴坦耐药率均低于 12.0%，铜绿假单胞菌对头孢他啶、左氧氟沙星、环丙沙星耐药率分别为 10.0%、11.8%、5.9%。HIV/CAP 组金黄色葡萄球菌对复方新诺明和左氧氟沙星的耐药率高于 CAP 组；HIV/CAP 组肺炎链球菌对红霉素、四环素及复方新诺明的耐药率高 CAP 组。两对比组均未发现万古霉素或利奈唑胺或替加环素耐药株，HIV/CAP 组耐甲氧西林凝固酶阴性葡萄球菌及金黄色葡萄球菌检出率为 80.0%和 28.6%，未合并 HIV 组耐甲氧西林凝固酶阴性葡萄球菌及金黄色葡萄球菌检出率为 77.8%和 33.3%，莫西沙星对凝固酶阴性葡萄球菌、金黄色葡萄球菌及肺炎链球菌耐药率分别为 10.0%、7.1%、0.0%。

结论 HIV /CAP 在革兰阴性菌耐药性较 CAP 患者差异明显，尤其在头孢吡肟及头孢哌酮/舒巴坦等抗菌药物中。HIV 感染 CAP 患者细菌病原菌以革兰氏阴性菌为主，对常用抗菌药物耐药率偏高，提示该院需要加强抗菌药物管理，遏制耐药。

关键字：人类免疫缺陷病毒,艾滋病,细菌耐药监测,抗菌药物

某三甲医院 2019—2023 年鲍曼不动杆菌耐药性分析

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目的 基于某医院抗菌药物耐药监测，了解该区域临床分离鲍曼不动杆菌对抗菌药物敏感性特征

方法 使用来自广安某三甲医院 5 年间抗菌药物药敏试验记录进行横断面回顾性研究，对纳入统计的 743 株细菌药敏结果进行分析。

结果 743 株不动杆菌属以鲍曼不动杆菌(A. baumanii)717 株（96.5%）、琼氏不动杆菌(A. junii)12 株（1.6%）及鲁氏不动杆菌(A. lwoffii)10 株（1.4%）为主，鲍曼不动杆菌主要分离自痰/支气管肺泡灌洗液。2019 年-2023 年鲍曼不动杆菌检出数量持续下降，2023 年检出株仅为 2019 年 42.8%。CRAB(Carbapenem Resistant A.baumannii)检出率由 70.3%降至 50.0%，相应 CSAB(Carbapenem Sensitive A.baumannii)检出率由 29.7%提升至 50.0%。CRAB 对头孢曲松、头孢他啶及头孢吡肟几乎完全耐药，CSAB 对头孢他啶和头孢吡肟耐药率均为 5.2%。CRAB 中发现 1 例替加环素耐药株，对除多粘菌素 B 和粘菌素外抗菌药物几乎完全耐药；不动杆菌属中尚未发现粘菌素或多粘菌素 B 耐药株。过去 5 年监测显示，阿米卡星对 CRAB 耐药率由 19.7%降至 17.4%，相应敏感率由 80.3%增加至 82.6%，米诺环素对 CRAB 耐药率由 10.5%降至 2.2%，敏感率由 89.5%上涨至 91.3%，中介率由 0.0%上涨至 6.5%。

结论 鲍曼不动杆菌检出数量和 CRAB 检出率持续降低，提示耐药谱有所改善，应该是该院采取合理使用抗菌药物遏制耐药发展的一系列措施取得的成效，应在不断完善的前提下继续执行，但 CRAB 对常用抗菌药物耐药依旧严峻，血培养鉴定 1 例替加环素耐药株，且 CRAB 对替加环素中介率逐渐上涨，提示鲍曼不动杆菌耐药情况不容乐观；监测资料同时也显示，部分抗菌药物的耐药正得以改善，提示需要规范临床合理使用抗菌药物，加强预防感染措施，减缓细菌耐药。

关键字：细菌耐药监测,抗菌药物,鲍曼不动杆菌

Genome Sequence of One Sequence Type 1 NDM-5-producing Carbapenem -resistant Klebsiella Pneumoniae in China

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Objective The emergence of carbapenem-resistant Klebsiella pneumoniae (CRKP) has become a significant problem worldwide. Here, we report the genome sequence from the structure perspective of an NDM-5-producing K. pneumoniae (HZKP2) in China

Methods Antimicrobial susceptibility tests were conducted via broth microdilution. Whole-genome sequencing (WGS) was performed and annotation was conducted using rapid annotations subsystems technology (RAST) server. Wzi and capsular polysaccharide (KL) were analysed using Kaptive. Resistance genes, virulence factors, and comparative genomics analysis were further performed. Multilocus sequence typing (MLST), replicons type, and core genome multilocus sequence typing (cgMLST) analysis were further conducted using BacWGSTdb server

Results HZKP2 was resistant to cefepime, ceftazidime, ciprofloxacin, ciprofloxacin, meropenem, and ertapenem. It harbored fosA, blaSHV-187, oqxA, oqxB, sul1, dfrA1, tet(A), floR, aph(6)-Id, aph(3")-Ib, sul2, blaCTX-M-55, and blaNDM-5. Based on the RAST results, 5563 genes that belonged to 398 subsystems were annotated. The complete genome sequence of HZKP2 was characterized as ST1, wzi 19, and KL19, with five contigs totaling 5,654,446 bp, including one chromosome and four plasmids. Further analysis found that blaNDM-5 was located in a 46,161 bp IncX3 plasmid (pHZKP2-3). The genetic structure of blaNDM-5 gene was ISKox3-IS26-bleMBL-blaNDM-5-IS5-ISAb125-IS3000. Phylogenetic analysis showed that the closest relative was from a human stool specimen in China, which differed by 53 cgMLST alleles

Conclusion Our study provides the first structural perspective of the ST1 K. pneumoniae isolate producing NDM-5 in China. These results could provide valuable insights into the genetic characteristics, antimicrobial resistance mechanisms, and transmission dynamics of CRKP in clinical settings

1. Introduction

Klebsiella pneumoniae is an important opportunistic pathogen, which causing serious concern among clinicians and microbiologists due to its capability of acquiring resistance genes and plasmids [1]. Specifically, the emergence of carbapenem-resistant K. pneumoniae (CRKP) has limited effective therapies and presents a serious public health threat worldwide, with high mortality rates in nosocomial infections [2], [3].

However, the occurrence of global ST1 CRKP was primarily sporadic, the prevalence and transmission patterns of ST1 CRKP are poorly understood. Further research is required to investigate the genomic traits and antimicrobial resistant characteristics exhibited by the ST1 CRKP clone.

Here, we report the genomic traits of a ST1 CRKP discovered in China. In addition, we performed a comprehensive genomic epidemiology analysis to date with available genome sequences of ST1 K. pneumoniae isolates on BacWGSTdb server. To our knowledge, this is the first report of ST1 CRKP with a blaNDM-5-harboured IncX3 plasmid.

2. Materials and methods

K. pneumoniae clinical strain (HZKP2) was collected from ascites in China. Isolate identification to species level was performed by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS, Bruker Daltonik GmbH, Bremen, Germany) and confirmed by 16S rRNA gene-based sequencing. Genomic DNA was extracted using a QIAamp DNA Mini Kit (QIAGEN, Germantown, MD) and was subjected to whole-genome sequencing (WGS) using Illumina HiSeq platform (Illumina, San Diego, CA) and Oxford Nanopore platform (Nanopore, Oxford, UK). Antimicrobial susceptibility tests (AST) were conducted via broth microdilution method and results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Escherichia coli ATCC 25922 served as the quality control strain. Sequences annotation was performed using National Center for Biotechnology Information (NCBI) Prokaryotic Genome Annotation Pipeline (PGAP) (http://www.ncbi.nlm.nih.gov/genome/annotation_prok/) and rapid annotations were conducted using the subsystems technology (RAST) server [4], [5]. Identification of antibiotic resistance genes using ResFinder database. Bacterial virulence factors were predicted using virulence factor database (VFDB) [6]. Wzi and capsular polysaccharide (KL) was tested using Kaptive [7]. The plasmid structure was visualized using DNAplotter (https://www.sanger.ac.uk/tool/dnaplotter/).
BacWGSTdb 2.0 server was used to perform multilocus sequence typing (MLST), replicons type, and core genome multilocus sequence typing (cgMLST) strategy-based bacterial source tracking [8]. OriTfinder was used to identify the presence of conjugative transfer-related modules of the blaNDM-5-carrying plasmid, including oriT region, relaxase gene, the type IV coupling protein (T4CP) gene and the tra gene cluster for the type IV secretion system (T4SS) [9]. The interactive Tree of Life (iTOL) v5 web server was used to visualize and interpret the phylogenetic trees and display the presence/absence of different classes of antimicrobial resistance genes [10].

3. Results and discussion

The genome of K. pneumoniae strain HZKP2 was assembled into five contigs, with a total length of

5,654,446 bp and an overall G+C content of 57.1%. The contig 1 consisting of 5,325,574 bp was recognized as the chromosome, while the remaining four contigs were associated with different plasmids at 166,057 bp, 98,536 bp, 46,161 bp, and 18,118 bp, respectively (Table 1). A total of 5,335 protein-coding sequences, 88 tRNA genes, and 25 rRNA genes were identified by the PGAP server. According to the RAST results, 5,563 genes belonging to 398 subsystems were annotated. Most of these belong to amino acids and derivatives (304) and carbohydrates (304). In addition, 53 subsystems were sorted into the virulence categories (Figure 1a). K. pneumoniae HZKP2 displayed a high degree of antimicrobial resistance to multiple antibiotics, including cefepime, ceftazidime, ciprofloxacin, ciprofloxacin, meropenem, and ertapenem. However, it remained susceptible to amikacin, tigecycline, and colistin (Table 2). K. pneumoniae HZKP2 harbored multiple antimicrobial resistance genes, including fosA, blaSHV-187, oqxA, oqxB, sul1, dfrA1, tet(A), floR, aph(6)-Id, aph(3")-Ib, sul2, blaCTX-M-55, and blaNDM-5 (Figure 1b). Furthermore, multiple virulence genes have been identified on the chromosome of this strain, including entABCDEF, fepABCDG, fimABCMEFGHK, mrkABCDFHIJ, and ybtAEPQSTUX.

The blaNDM-5 gene was located on an IncX3 type plasmid (pHZKP2-3). In addition to the resistance gene blaNDM-5, the IncX3 plasmid harbored the bleomycin resistance gene bleMBL (Figure 1c). Two insertion sequences (ISs), namely ISKox3, IS26, and blaMBL were identified upstream of the blaNDM-5 gene, and IS5, ISAb125, and IS3000 genes were detected downstream,which may mediate the horizontal transfer of blaNDM-5. The presence of potential transfer-related modules, including the relaxase gene, T4CP genes and the type IV secretion system gene cluster (T4SS) were detected in pHZKP2-3, however, the origin of transfer (oriT) region was not found, which was defined as a non- conjugative plasmid.

According to an in silico MLST investigation, K. pneumoniae strain HZKP2 belongs to ST1. To investigate the global genomic epidemiology of K. pneumoniae strains, we analyze the phylogenetic relationships between K. pneumoniae strain HZKP2 and other 23 ST1 K. pneumoniae strains retrieved from the NCBI GenBank database. ST1 K. pneumoniae isolated from China (n=11), United Kingdom (n=6), Spain (n=2), and Philippines (n=2). It's noteworthy that three additional strains lack recorded isolation locations. The most prevalent source of ST1 K. pneumoniae was clinical samples (n=20, 83.33%). The isolation rate showed an increasing trend yearly, from only one strain in 2003 to five strains in 2017 (Figure 1b). According to cgMLST analyses, the closest relative of K. pneumoniae HZKP2, another ST1 strain (K. pneumoniae JZX2124) isolated from human stool in China in 2017, differs by 53 cgMLST loci.

In this study, we, for the first time, detected and revealed the NDM-5-producing ST1 K. pneumoniae isolate in China and described it from the structural view based on the Oxford Nanopore long-read sequencing. The emergence of such strain creates significant treatment challenges in the clinic. Our findings could help to understand the genomic characteristics and antimicrobial resistance mechanisms of this pathogen. More attention must be directed to preventing their future prevalence.

Figure legend

Figure 1. RAST annotation, the phylogenetic relationship, and pHZKP2-3 plasmid structure of K. pneumoniae HZKP2 clinical isolate.

a. Counts of subsystem based on RAST annotation. The number of each subsystem category is shown on the right of column.

b. Phylogenetic relationship between K. pneumoniae HZKP2 and other ST1 K. pneumoniae strains deposited in the NCBI GenBank database. Isolate name, sequence type (ST), source, location, host, year, and resistance genes are shown. HZKP2 strain is labelled in red.

c. Circular map of pHZKP2-3. Arrows show the direction of transcription from the open reading frames (ORFs). Red arrows indicate the antimicrobial resistance genes. Pink arrow indicate the replicon. The ORFs mobile genetic elements, T4SS, T4CP and relaxase are also labelled.

关键字：Carbapenem-resistant Klebsiella pneumoniae, Whole-genome sequencing, blaNDM-5, phylogenetics

ESBL 及 TET(X4)基因大肠埃希菌肺炎临床特征比较

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目 的 比 较 ESBLs(+)TET(X4)(-) 及 ESBLs(-)TET(X4)(+)两种不同耐药基因大肠埃希菌肺炎的临床特征。

方法 目标人群为 2020 年 1 月至 2022 年 12 月在丽水市人民医院住院且肺泡灌洗液经细菌培养和 mNGS 法测出耐药大肠埃希菌的肺炎患者,A 组为 ESBLs(+)TET(X4)(-)大肠埃希菌肺炎患者 135 例,B 组为 ESBLs(-)TET(X4)(X+)大肠埃希菌肺炎患者 82 例,比较两组的临床特征及耐药性。

结果 B 组从事农林畜牧业、长期使用塑料制品、四环素使用率及 30d 死亡率均高于 A 组(均 P <0.05)。B 组对四环素、米诺环素、替加环素的耐药率比 A 组高(均 P <0.05),但对头孢(头孢曲松、头孢他啶、头孢吡啶、头孢唑林)和青霉素(阿莫西林克拉

维酸钾、氨曲南、氨苄西林、哌拉西林、哌拉西林他唑巴坦)的耐药率较 A 组低(均 P <0.05)。

结论 从事农林畜牧业,长期使用塑料制品、四环素的患者更有可能感染 TET(X4)(+)大肠埃希菌,其导致的肺炎病死率比 ESBL(+)大肠杆菌的患者要高。

关键字：大肠埃希菌;肺炎;耐药基因;肺泡灌洗液;

深圳某医院肺炎克雷伯菌 4 年的临床分布及耐药性变迁分析

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目的 了解深圳某综合医院住院患者检出肺炎克雷伯菌的临床分布、耐药性及其变化，为指导临床合理使用抗生素和预防医院内感染提供依据。

方法 收集 2016 年-2019 年该院分离的肺炎克雷伯菌的药敏结果和临床资料，剔除同一患者相同部位的重复菌，分析其临床分布及常见抗菌药物的耐药性及变化。

结果 711 株肺炎克雷伯菌的标本来源主要是痰（38.8%，276/711）、尿液（19.1%，136/711）、血液（9.4%，67/711）、伤口分泌物（7.6%，54/711）。占比最高科室为重症医学科（32.6%），其次为烧伤整形科颌面外科（6.8%）、血液科（6.6%）、呼吸科（6.5%）。常见抗菌药物中耐药率最高的为头孢呋辛酯，为 43.1%，其次为头孢呋辛、头孢曲松和甲氧苄啶/磺胺甲恶唑，分别是 42.4%、40.6%、39.1%。对阿米卡星厄他培南、亚胺培南的敏感率分别为 96.6%、95.1%、94.9%。耐碳青霉烯类药物和产超广谱 β-内酰胺酶（ESBLs）菌株检出率分别为 3.9%（28/711）、35.8%（254/711）。2016~2019 年 4 年间对头孢哌酮/舒巴坦、哌拉西林/他唑巴坦、左旋氟氧沙星等耐药性升高。

结论 肺炎克雷伯菌是住院患者感染的常见病原菌之一，其对于一线抗菌药物的耐药性逐渐增高，临床应加强耐药性监测并制定合理使用抗生素的治疗方案。

关键字：肺炎克雷伯菌；临床分布；耐药性变迁

2020 年-2022 年血培养阳性病原菌分布及耐药分析

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目的 了解深圳某医院住院患者血培养阳性病原菌的分布及其耐药性，为指导临床合理使用抗生素和预防医院感染提供依据。

方法 回顾性分析该院 2020 年-2022 年血培养结果，剔除同一患者相同部位的重复菌株后,统计阳性病原菌株的分布及其耐药性。

结果 2020 年-2022 年该院共有 8096 份血培养标本，共分离出病原菌 393 例（4.9%）。其中革兰阳性球菌 212 株（54.0%），革兰阴性杆菌 164 株（41.7%），真菌 17 株（4.3%）。检出率较高的病原菌依次分别为凝固酶阴性葡萄球菌（145，36.9%）、大肠埃希菌（67，17.0%）、肺炎克雷伯菌（31，7.9%）；血培养阳性菌占比最高科室为重症医学科（21.4%）。凝固酶阴性葡萄球菌对苯唑西林的耐药率为 66.9%；大肠埃希菌对甲氧苄啶/磺胺甲恶唑、头孢曲松、左氧氟沙星的耐药率分别是 50.8%、53.7%、46.3%；肺炎克雷伯菌对氨曲南、头孢曲松、甲氧苄啶/磺胺甲恶唑的耐药率分别是 45.2%、38.7%、32.3%。

结论 临床分离的血培养病原菌以葡萄球菌属、肠杆菌科为主，凝固酶阴性葡萄球菌耐甲氧西林的比率较高，大肠埃希菌和肺炎克雷伯菌对甲氧苄啶/磺胺甲恶唑、头孢曲松的耐药率较高，应继续加强耐药性监测。

关键字：血培养；病原菌；分布；耐药性

42 株耐碳氢酶烯类肺炎克雷伯菌产酶类型及分子流行病学分析

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目的 研究某院耐碳氢酶烯类肺炎克雷伯菌（CRKP）的产酶类型和分子流行病学特征。

方法 收集 2020 年 9 月至 2023 年 1 月临床各种类型标本中分离的 42 株耐碳氢酶烯类肺炎克雷伯菌，采用法国生物梅里埃 VITEK 2 Compact 全自动微生物分析系统进行细菌菌种鉴定和药物敏感性试验，基质辅助激光解吸电离飞行时间质谱（MALDI-TOF MS）复核菌种鉴定结果，K-B 纸片法复核细菌碳青霉烯类药物药敏试验结果。胶体金免疫层析法检测耐碳氢酶烯类肺炎克雷伯菌株临床常见的五种碳氢酶烯酶表型，PCR 扩增碳青霉烯耐药基因 KPC、NDM、IMP、VIM、OXA-48 进行耐药机制验证，多位点序列分型（MLST）及基质辅助激光解吸电离飞行时间质谱采用标化的提取法分析菌株同源性。

结果 42 株耐碳氢酶烯类肺炎克雷伯菌（CRKP）均携带 blaKPC，与胶体金产酶表型检测

结果完全一致，多位点序列分型（MLST）均为 ST11 型，质谱同源性分析树状图结果显示 42 株耐碳氢酶烯类肺炎克雷伯菌（CRKP）大致可分为 5 簇。

结论 该院肺炎克雷伯菌对碳氢酶烯类药物耐药最主要的耐药机制是产 KPC 酶，MLST 分型主要的克隆类型是 ST11 型，医院内存在 CRKP 的克隆传播，需加强院感监控。

关键字：碳青霉烯类耐药，肺炎克雷伯菌，分子流行病学分析

Genetic and Phenotypic Characterization of A Novel ST45-K43 Carbapenem-resistant Klebsiella Pneumoniae Strain Causing Bloodstream Infection: A Potential Clinical Threat

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Objective This study aimed to genetically characterize a novel Carbapenem-resistant Klebsiella pneumoniae (CR-Kp) strain recovered from blood of a 44-year-old Chinese male patient with severe acute necrotizing pancreatitis and septic shock in China

Methods Detailed clinical information was collected from an elderly bloodstream infection patient. Antimicrobial susceptibility testing 、growth curve、biofilm、conjugation experiments and PacBio Sequel and Illumina sequencing were performed to analyze the phenotypic and genetic characterization of 18SHX166. Mouse experiments were conducted to evaluate the in vivo virulence of 18SHX166

Results The susceptibility testing results showed 18SHX166 was resistant to cephalosporin and carbapenems, but still susceptible to ceftazidime-avibactam, quinolones, colistin and amikacin. The phylogenetic structure showed that strain 18SHX166 belonged to sequence type ST45 and capsule serotype K43. Genomic sequencing reveals that 18SHX166 contains three plasmids, namely pSHX166-Hv, pSHX166-KPC, and pSHX166-3. pSHX166-Hv harbored iucABCD operon encoding a siderophore，in the mouse model, the 18SHX166 strain exhibited a low virulent phenotype .pSHX166-KPC harbored blaKPC-2 gene and tra/trb conjugation system ，The conjugation rate with Escherichia coli EC600 was 2.21E-05, indicating that it is a self-transmissible plasmid mediating the dissemination of antibiotic resistance.Additionally, 18SHX166 demonstrates a higher growth rate. The strain characteristics of 18SHX166 suggest a potential for higher clinical transmission risk

Conclusion Besides the predominant sequence types in CR-HvKP causing bloodstream infection, ST23 and ST11, the finding of the ST45-K43 CR-KP isolate could pose a threat to the control of antimicrobial resistance and could cause a severe challenge to public health

关键字：CR-KP，ST45-K43，bloodstream infection， higher transmission risk

The Regulatory Mechanism of AI-2 Quorum Sensing System in Klebsiella Pneumoniae

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Objective Quorum sensing (QS) system is a widely existing communication mechanism, which plays a regulatory role in bacterial collective behavior and the expression of specific genes. Currently, the quorum sensing systems of various bacteria have been well characterized. However, there is limited research on the AI-2 QS system of Klebsiella pneumoniae

Methods A total of 239 strains of bloodstream infection-causing K. pneumoniae were included in this study. Vibrio harveyi strain BB170 luminescence was introduced to calculate AI-2 activity, the ability of K. pneumoniae strains to produce AI-2 was classified into three groups: high, middle, and low. In order to reveal biofilm formation in K. pneumoniae. The 1% crystal violet staining experiment was performed to measure the biofilm formation of the bacterial strains at 6 hours. To better understanding of the molecular regulatory mechanisms of the AI-2 QS system in K. pneumoniae, Illumina and transcriptome sequencing were performed

Results Based on bioluminescence experiments with Vibrio harveyi strain BB170, among the 239 strains of K. pneumoniae, there were 28, 184, and 27 strains classified as high, middle, and low AI-2 signal producers, respectively. The results of the biofilm formation experiment showed that at 6 hours, 20 strains exhibited strong biofilm-forming capabilities, 54 strains exhibited moderate biofilm-forming capabilities, 107 strains exhibited weak biofilm-forming capabilities, and 58 strains exhibited no biofilm-forming capabilities. Combining the AI-2 signal production capacity with the biofilm formation capacity at 6 hours, the results indicate that the biofilm formation capacity at 6 hours is not related to the AI-2 production capacity (P=0.798). The genomic analysis findings reveal that among K. pneumoniae strains, the differential gene expression linked to AI-2 signal production prominently includes clpC (ATP-dependent Clp protease ATP-binding subunit ClpC), htpX_2 (protease HtpX), pleD (hypothetical protein), gbuA (guanidinobutyrase), and group_1330 (hypothetical protein).The GO enrichment analysis results indicate that the strong ability to produce AI-2 is primarily associated with transmembrane transport, carbohydrate transport, and organic substance transport in K.

pneumoniae. In terms of KEGG pathway enrichment, significant associations were found in Starch and sucrose metabolism, Bacterial secretion system, Phosphotransferase system (PTS), Arginine and proline metabolism

Conclusion In K. pneumoniae, 11.71% (28/239) of strains demonstrate a relatively strong capability to produce AI-2 signaling molecules. There is no clear relationship between the quantity of biofilm formation at 6 hours and the strength of AI-2 signaling molecules. Genes that affect AI-2 production in K. pneumoniae, such as clpC, htpX_2, pleD, gbuA, and group_1330, need further gene knockout for validation. Transcriptomic results indicate that AI-2 quorum sensing regulates carbohydrate metabolism, amino acid metabolism, the Phosphotransferase system (PTS), and secretion systems in K. pneumoniae

关键字：klebsiella pneumoniae， AI-2， quorum sensing

A Strain of Serratia Marcescens Exhibiting High-level Tolerance To Meropenem

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Objective Serratia marcescens (SM) is a gram-negative pathogen that can cause opportunistic infections, nosocomial infections, and various infections in both adults and children. In this study, a highly tolerant strain of SM, named H12, was identified, which exhibited significant tolerance to meropenem(MEM). Bacterial tolerance may represent a preliminary stage preceding the development of antibiotic resistance, emphasizing the importance of monitoring the tolerance of relevant bacterial strains in clinical settings

Methods Time-kill curve experiments were conducted to assess the characteristics of different strains with varying minimum inhibitory concentrations (MICs) after treatment with meropenem. Concentration-time kill assays were performed to compare the differences in survival rates among strains treated with different concentrations of MEM aiming to ascertain the high-tolerance phenotype of H12. Transcriptomic analysis of the strains treated with MEM at different time points was employed to identify the differentially expressed genes that may potentially influence the tolerance phenomenon in Serratia marcescens

Results Using Escherichia coli 13883 as the susceptible control, time-kill curve analysis was performed on different strains with different minimum inhibitory concentrations (MICs) treated with 16 μg/ml of meropenem (MEM). The D2 and D23 strains exhibited a persistent phenotype, while the H12 strain showed a higher tolerance phenotype. Concentration-kill curve analysis revealed that as the concentration of MEM increased (1 μg/ml, 4 μg/ml, 8 μg/ml, 16 μg/ml, 32 μg/ml, 64 μg/ml), the survival rates of D2/D23/13883 strains gradually decreased. After reaching a concentration of 16 μg/ml, the survival rate remained stable. The survival rate of D2/D23 was approximately one order of magnitude higher (about 10 times) than that of 13883, while the survival rate of H12 was approximately six orders of magnitude higher (about 100,000 times) than that of 13883. Furthermore, the survival rate of H12 did not significantly decrease with increasing MEM concentration, indicating its ability to tolerate higher concentrations of MEM. Compared to 13883 and other strains, H12 exhibited higher MEM tolerance after being treated with 1 μg/ml of MEM for 7 hours, 16 μg/ml of MEM for 7 hours, and 16 μg/ml of MEM for 24 hours. When treated with 0.5 μg/ml, 1 μg/ml, and 2 μg/ml of meropenem, H12, HS38, KM76, and XY22 showed a survival rate above 50% at 0 hours, 1 hour, 2 hours, 3 hours, and 24 hours. At 24 hours, H12 exhibited a distinct difference in survival rate compared to the other strains.Transcriptomic analysis revealed that the differential genes between H12 and HS38,KM76 mainly involved cell membrane disruption resistance and fatty acid oxidation. Further experiments will be conducted to elucidate the relevant genes regulating the tolerance ability of Serratia marcescens

Conclusion H12 is a strain with strong tolerance to meropenem, and its high tolerance may be regulated by cell membrane disruption resistance and fatty acid oxidation-related genes. It can still exhibit high survival rates even after being treated with high concentrations of MEM for long periods of time, highlighting the need for clinical attention to high-tolerance strains. Further research should be conducted to better understand these factors and to improve cure rates more accuratel

关键字：Serratia marcescens ， tolerance，meropenem

耐碳青霉烯类肺炎克雷伯菌感染的临床特征与危险因素研究

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目的 研究医院耐碳青霉烯类肺炎克雷伯菌（CRKP）感染的临床特征及危险因素，为防治CRKP感染提供相关依据。

方法 收集2022年1月至2023年12月分离的CRKP感染病例36例，采用1:2病例-对照研究方法，以同期碳青霉类敏感肺炎克雷伯菌感染病例（CRSP）72例为对照，通过单因素和多因素Logistic回归分析分析CRKP感染的临床特征和危险因素。

结果 36 例 CRKP 主要来源于痰标本（25 株，69%），集中分布于神经外科（16 株，44%）和重症监护科室（12 株，33%）。多种危险因素与 CRKP 感染相关，其中患者低白蛋白血症（P<0.001，OR=10.85，95%CI：3.66~32.14）、使用碳青霉烯类（P<0.001，OR=8.08，95%CI：2.53~25.76）可能是 CRKP 感染的重要危险因素。CRKP 感染患者死亡率和自动出院率高于 CSKP 感染患者。

结论 CRKP 感染严重影响患者预后，需积极应对 CRKP 感染率升高的趋势，采取综合措施，以减少 CRKP 感染的发生。

关键字：耐碳青霉烯类肺炎克雷伯菌；危险因素；临床特征

2016-2023 年某传染病医院 ICU 多重耐药菌分布特点和耐药性分析

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目的 回顾性分析本院 ICU 近 8 年临床多重耐药菌的检出率和耐药特征。

方法 回顾性分析 2016 年 1 月至 2023 年 12 月 ICU 住院患者临床标本分离的 5 种多重耐药菌的检出率，包括 CR-AB、CR-PA、CRE、 MRSA 和 VRE，并分析碳青霉烯类耐药革兰阴性杆菌的耐药率。

结果 本研究多重耐药菌检出率在 2023 年总体呈上升趋势。2021-2023 年 CR-AB、CR-PA、CRE 和 MRSA 检出率分别波动在 72.37～100.00%、52.54%～78.26%、27.15%～37.57%、50.00%～58.82%。CR-AB 和 CRE 对 β 内酰胺酶抑制剂复合制剂、喹诺酮类和头孢类抗菌药物耐药率达 90.0%；CRE 对头孢他啶/阿维巴坦敏感率最高为 85.00%。67 株 CRE 中，耐碳青霉烯类肺炎克雷伯菌 36 株，耐碳青霉烯类肺炎克雷伯菌检出率呈上升趋势。

结论 CR-AB、CR-PA、CRE、 MRSA 耐药相对严重，应引起重视，尤其应关注重症医学科碳青霉烯类耐药革兰阴性杆菌耐药株。

关键字：多重耐药菌；耐碳青霉烯类肠杆菌目细菌；碳青霉烯酶；耐药性

2015 年-2022 年四川省某医院 4431 例血流感染病原菌分布及耐药性分析

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目的 回顾性分析 2015 年 1 月至 2022 年 12 月在四川省宜宾地区血培养分离的 4431 株病原体的分布和耐药性趋势。为宜宾地区的抗菌药物的合理应用提供依据。

方法 采用 2015 年 1 月-2022 年 12 月宜宾市第二人民医院送检血培养标本中阳性菌株，剔除重复菌株，用自动化鉴定及药敏分析仪，联合 KB 法或 E-test 法作补充，测定药物对细菌的敏感性，并依据美国临床和实验室标准协会（CLSI）2023 年标准，数据统计分析使用 WHONET 5.6 版软件进行。

结果 研究显示，血流感染中革兰氏阴性菌所占比例为 51.4%，主要包括大肠埃希菌、肺炎克雷伯菌、铜绿假单胞菌和鲍曼不动杆菌；革兰氏阳性菌占 48.6%，主要包括表皮葡萄球菌、人葡萄球菌、金黄色葡萄球菌、肺炎链球菌、溶血葡萄球菌和肠球菌为主。血培养阳性检出率较高的科室主要是重症医学科、普外科、儿科和感染科。在耐药性方面，甲氧西林敏感金葡菌（MSSA）对苯唑西林、阿米卡星、利福平仍保持较高的敏感，而 MRSA 对这些药物的耐药率均显著高于 MSSA。此外，革兰氏阴性菌中的肠杆菌对头孢吡肟的耐药率低于第一、二代和多数第三代头孢菌素，对左氧氟沙星和头孢曲松的敏感度高。铜绿假单胞菌对碳青霉烯类和 β 内酰胺类-内酰胺酶抑制剂复合制剂的耐药率较低，对氟喹诺酮类的耐药率也不到 10%。此外，研究还发现儿童和老年人是易感人群，血流感染中真菌的检出率为 2.8%，以念珠菌和新生隐球菌为主。

结论 四川省宜宾地区细菌细菌耐药性交全国均值及其它地区略有不同，对于不同菌株、不同地区的耐药性不同，建议对本地区进行长期动态监测，以实时了解药敏变化趋势，为优化血流感染患者的管理提供重要依据。

关键字：血流感染，病原菌，耐药性

碳青霉烯耐药的阴沟肠杆菌复合体对氨曲南-阿维巴坦耐药机制的研究

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目的 研究产金属 β-内酰胺酶的阴沟肠杆菌复合体对氨曲南-阿维巴坦的耐药机制

方法 通过诱导临床菌株 120030 获得了 3 株产 NDM-5 的香坊肠杆菌的氨曲南-阿维巴坦抗性突变体（MIC≥16mg/L）。全基因组测序显示，3 株突变株中均有 ampC 基因 Y150 突变及 ampD 基因突变，其中 120030V8 仅有 ampC 基因 Y150 及 ampD 基因

突变。将 3 株突变菌株及 1 株原始菌株中的 ampC 基因克隆到 pET-28a(+) 中，并通过电穿转化到 120030XΔampC 及 120030V8ΔampC 中。肉汤稀释法测定氨曲南-阿维巴坦的 MIC 值，通过 RT-qPCR 测定 ampC 基因在各回补株中的表达量。使用分子可视化工具 Pymol 和 AutoDock 软件进行分子模拟和分子对接，显示和分析蛋白质结构的改变。

结果 回补到 120030XΔampC 的 4 株菌未恢复抗性，其中初始菌株的 MIC 从 0.25mg/L 上升到 1mg/L，其他 3 株突变菌株 MIC 值均＜16mg/L，；回补到 120030V8ΔampC 的 4 株菌均产生抗性，其中初始菌株的 MIC 从 0.25mg/L 上升到 128mg/L，其他 3 株突变菌株 MIC 恢复至初始水平。通过 RT-qPCR 发现，回补到 120030V8ΔampC 的 4 株菌的表达量是回补到 120030XΔampC 的 4 株菌的表达量的 50-100 倍左右，即 ampD 基因突变导致了 ampC 过表达。分子模拟和分子对接发现 ampC 基因 Y150 突变导致对阿维巴坦的亲和力下降。

结论 AmpC 酶的过表达及结构改变可以介导产金属 β-内酰胺酶的阴沟肠杆菌复合体对氨曲南-阿维巴坦耐药。

关键字：阴沟肠杆菌复合体；AmpC；AmpD；耐药；机制

In Vivo Divergent Evolution of Cross-resistance To New B-lactam/β-lactamase Inhibitor Combinations in Pseudomonas Aeruginosa Following Ceftazidime/avibactam Treatment

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Objective To describe and characterize the cross-resistance mechanisms to ceftazidime/avibactam, ceftolozane/tazobactam and imipenem/relebactam of a carbapenem-resistant P. aeruginosa lineage isolated from a patient receiving two courses of ceftazidime/avibactam treatment

Methods The P. aeruginosa strains were isolated from the patient before, during and after the ceftazidime/avibactam treatment. The MICs of strains were determined by broth microdilution methods. The mutant genes were identified by the WGS results. Cloning, knockout and complementation experiments were used to verify the impact of the resistance relative genes on the MICs. Reverse transcription-quantitative PCR was used to evaluate the relative gene expression of ampC and mexA. To figure out the fitness cost changes during the drug resistance evolution, growth curve tests were performed

Results The ceftazidime/avibactam resistant P. aeruginosa strains were clustered into two clades and evolved in two pathways. In both evolutionary pathways, the overexpression of ampC was crucial to ceftazidime/avibactam resistance while it was meditated by the deficiency of AmpD and DacB, respectively. The mutation of MraY and a new allele of AmpC (PDC-575) elevated resistance level of ceftazidime/avibactam in clade A, and the latter mutation also conferred resistance to ceftolozane/tazobactam. Meanwhile, overexpression and modification of MexAB-OprM efflux pump was associated with resistance to both ceftazidime/avibactam and imipenem/relebactam in clade B. In addition, the fitness costs of P. aeruginosa strains generally increased with the elevated MICs of ceftazidime/avibactam

Conclusion We demonstrated that the CRPA lineage presented divergent evolution in the cross-resistance to new β-lactam/β-lactamase inhibitor combinations, which resulted in a complex phenotype. This phenomenon poses tremendous challenge to clinical treatment and new therapeutic strategies are urgently required

关键字：P. aeruginosa，ceftazidime/avibactam，ceftolozane/tazobactam，imipenem/relebactam，cross-resistance evolution

Racking Emergence and Outbreak of Klebsiella Pneumoniae Co-producing NDM-1 and KPC-2, A KPC-2-Producing Isolate Acquired BlaNDM-1-Positive Plasmid During Sulfamethoxazole-trimethoprim Treatment

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The co-producing of two carbapenemases in carbapenem-resistant Klebsiella pneumoniae (CRKP), such as KPC and OXA-48 or KPC and NDM, complicates clinical treatment and increases mortality rates. The emergence of KPC-NDM CRKP was believed that aroused from acquiring an NDM plasmid by KPC-2-CRKP, especially under selective pressure of ceftazidime-avibactam (CZA). In this study, a CRKP-producing KPC-2 (JNP990) isolated from a patient was collected at a tertiary hospital in Shandong Province. The change from JNP990 to co-producing KPC and NDM CRKP (JNP989) occurred following sulfamethoxazole-trimethoprim (SXT) treatment, accompanied by the emergence of resistance to SXT (MIC>2/38mg/L) and CZA (dd≤14mm). Whole-genome sequencing (WGS) and S1 pulsed-field gel electrophoresis (PFGE) revealed that compared to the isolate JNP990, isolate JNP989 acquired a carried sul1 and blaNDM-1 genes IncC plasmid (NDM plasmid) spanning 197kb. NDM

plasmid could be successfully transferred into E. coli J53 at a conjugation frequency of (8.70 ± 2.47) × 10-4. The IncFII/IncR plasmid carrying the blaKPC-2 gene originally harbored in JNP990 can only be transferred in the presence of the NDM plasmid, at a conjugation frequency of (1.93 ± 0.41) × 10-5. Five strains of CRKP with the same antibiotic resistance pattern as JNP989 were also isolated from five other patients in the same hospital. Xba I PFGE and draft genome analysis revealed that the five isolated strains belong to the same clone as JNP989, with a sequence type of ST11. In patient P6, compared to the original JNP885, strains JNP887 and JNP888 separated 50 and 98 days later and lost resistance to CZA. WGS revealed the blaNDM-1-carrying fragments loss with different lengths mediated by insertion sequence 26 in two strains. Plasmid stability testing showed that the IncC plasmid was more stable than the blaNDM-1 genes in the hosts. Growth assay showed there was no significant difference in fitness cost between those dual-/unitary-carbapenemase-producing CR-KP isolates. Our study described that a KPC-producing CRKP accepted a blaNDM-1-carrying plasmid after SXT treatment evolved into KPC-NDM-CRKP and spread in hospitalized patients. This case offers an unexpected but reasonable perspective for understanding KPC-NDM-CRKP formation and suggests the severity of the current widespread resistance spread.

关键字：carbapenem-resistant Klebsiella pneumoniae; KPC; NDM; genetic linkage; sulfamethoxazole-trimethoprim; helper plasmid; resistance missing

四川地区 2019 年至 2023 年支气管肺泡灌洗液分离细菌分布及耐药性分析

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目的 了解四川地区 5 年间支气管肺泡灌洗液（BALF）分离细菌分布和细菌耐药情况，为临床抗菌药物选择提供参考

方法 按照四川省细菌耐药技术方案，参照 临床和实验室标准委员会（CLSI） 推荐的药敏试验要求采用纸片扩散法或自动化仪器法进行。利用 WHONET5.6 软件对 2019—2023 年四川省细菌耐药监测网成员单位上报 BALF 分离的细菌及药敏结果数据进行分析，同一患者相同细菌仅纳入第一株菌

结果 本次研究共纳入 26575 株细菌，其中革兰氏阴性菌占 83.2%，革兰氏阳性菌占 16.8%。常见细菌排名前 5 位的依次为肺炎克雷伯菌（19.8%）、铜绿假单胞菌（18.5%）、鲍曼不动杆菌（12.3%）、金黄色葡萄球菌（7.7%）、嗜麦芽窄食单胞菌（6.7%）。药敏结果显示，肺炎克雷伯菌对所有抗菌药物的耐药性呈逐年升高，尤其是对碳青霉烯类抗菌药物的耐药性明显高于大肠埃希菌和阴沟肠杆菌。大肠埃希氏菌对碳青霉烯类药物相对敏感，耐药率均＜5%，其次是头孢哌酮-舒巴坦、哌拉西林-他唑巴坦，耐药率＜15%。非发酵菌中铜绿假单胞菌对主要抗菌药物的耐药性逐年降低，对阿米卡星、哌拉西林-他唑巴坦、头孢哌酮-舒巴坦、头孢吡肟、头孢他啶、环丙沙星及庆大霉素的耐药性均＜20%。鲍曼不动杆菌对大部分抗菌药物的耐药性相对较高，＞50%，但是对米诺环素的耐药率从 2020 年起逐年降低，对替加环素的耐药率最低约 1%。5 年间 MRSA 的检出率分别为 25.2%，34.5%，32.2%，35.6%，30.8%，未发现对利奈唑胺，万古霉素，替考拉宁耐药的金黄色葡萄球菌。肺炎链球菌对青霉素的耐药率为 0.0%-1.8%，且青霉素耐药肺炎链球菌（PRSP）的比例从 2020 年起逐年升高

结论 四川地区 BALF 标本分原菌以革兰阴性菌为主，细菌耐药现象依然严重。针对下呼吸道感染病例，临床应当提高高质量 BALF 标本的送检率，并且重视病原菌的监测，及时了解各感染部位病原菌分布及抗菌药物耐药性可为临床经验性治疗提供依据

关键字：支气管肺泡灌洗液；下呼吸道感染；药物敏感性试验；耐药变迁

危重症监护室泛耐药鲍曼不动杆菌血流感染的危险因素及预后评价

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目的 比较泛耐药鲍曼不动杆菌（Extensively Drug Resistant Acinetobacter baumannii，XDRAB）血流感染与非泛耐药鲍曼不动杆菌（Non Extensively Drug Resistant Acinetobacter baumannii，NXDRAB）血流感染的临床特征，探讨 XDRAB 血流感染的危险因素及预后，为临床防治 XDRAB 提供科学指导。

方法 采用病例对照研究方法，回顾性分析 2013 年 1 月 1 日至 2022 年 12 月 31 日期间广东省人民医院危重症监护室鲍曼不动杆菌（Acinetobacter baumannii，ABA）血流感染 143 例患者的临床资料，包括基础疾病、临床特征、危险因素、细菌耐药情况、治疗用药及预后情况等。根据病原菌耐药情况，分为 XDRAB118 例与 NXDRAB25 例。以 ABA 血培养标本采集 14 天预后情况，将 143 例 ABA 血流感染患者分为存活组 90 例与死亡组 53 例。

结果 多因素 Logistic 回归模型分析显示，急性生理学与慢性健康状况评分II（APACHE II评分）（OR=1.163、95%CI：1.004-1.346、P<0.05）是

XDRAB 血流感染的独立危险因素，感染性休克（OR=3.462、95%CI：1.576-7.608、P<0.05）是 ABA 血流感染患者 14 天死亡的独立危险因素。143 例 ABA 血流感染患者 14 天死亡 53 例，死亡率 37.06%。XDRAB 血流感染患者 14 天死亡率显著高于 NXDRAB 血流感染患者（$\chi 2$=11.54，P<0.05）。

结论 APACHE II评分是 XDRAB 血流感染的独立危险因素，感染性休克是 ABA 血流感染患者 14 天死亡的独立危险因素，XDRAB 血流感染患者 14 天死亡率高，应加强对相关危险因素的评估，采取针对性的防控干预措施，以改善 XDRAB 血流感染患者的预后。

关键字：鲍曼不动杆菌；泛耐药；血流感染；危险因素；预后

幽门螺杆菌耐药性:2003-2023 年的文献计量学研究

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目的 幽门螺杆菌耐药是消化系统一个常见的问题，一直得到研究者们显著的关注和研究。本研究旨在分析幽门螺杆菌耐药性的研究现状和热点，并预测其未来发展方向。

方法 本研究从 Web of Science(WoS)数据库中检索 2003-2023 年发表的与幽门螺杆菌耐药相关的英文文章和综述，根据系统综述和 Meta 分析优秀报告规范即 PRISMA 声明对文献进行筛选纳入。最后使用 VOSviewer 1.6，CiteSpace 6.1 高级版和 SCImago Graphica Beta 1.0.35 等软件进行知识图谱和文献计量学分析。

结果 研究时间为 2003 年至 2023 年，共有 114 个国家的 4152 个机构的 15914 位作者撰写了 3625 篇论文，发表在 788 种期刊上，引用了 10575 种期刊的 81700 篇参考文献。Graham 是幽门螺杆菌耐药性研究领域最多产、最具影响力的作者。《幽门螺杆菌》是产出最多的期刊，《消化药理学与治疗学》是被引用文章最多的期刊。中国是最多产的国家，美国是最具影响力的国家。接着对关键词和文献的分析表明，该领域的研究热点是克拉霉素耐药性和甲硝唑耐药性。近 5 年来最热门的话题包括竞争性酸阻滞剂、铋剂、共识、肠道微生物群、富马酸伏诺拉生、生物膜形成和一线治疗等。

结论 简而言之，在过去二十年中对幽门螺杆菌的研究，耐药性的研究普遍呈上升趋势。且幽门螺杆菌对克拉霉素和甲硝唑的耐药性一直是研究的热点。而伴随疗法和新药可能是未来流行的研究方向和趋势。

关键字：幽门螺杆菌耐药，文献计量学，CiteSpace， VOSviewer

广东省某三甲医院心脏重症监护室病原菌分布及耐药性分析

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目的 分析广东省某三甲医院心脏重症监护室病原菌分布和耐药性，为明确其感染特点及合理院感防控提供依据。

方法 采用 WHONET 5.6 软件对广东省某三甲医院心脏重症监护室患者 2023 年全年送检的培养数据进行处理，分析感染患者病原菌的标本来源、分布及耐药性。

结果 2023 年某三甲医院 CCU 住院患者送检标本培养出病原菌 151 株。分析检出占前十的病原菌分布发现，呼吸道标本(包括痰、肺泡灌洗液和纤支镜冲洗液等)的检出比例最高，占 47.02% (71/151)，菌种检出比例最高的是肺炎克雷伯菌，占 17.22% (26/151)；铜绿假单胞菌、大肠埃希菌和屎肠球菌占比分别 14.17%、12.54%和 11.47%。对主要流行菌株的药敏分析发现，肺炎克雷伯菌耐药率较高；铜绿假单胞菌对大部分药物普遍敏感，但对碳青霉烯类药物的耐药率偏高大肠埃希菌较敏感，但对喹诺酮类和氨苄西林，复方新诺明耐药率较高。分析 CCU 多重耐药菌分离情况，对碳青霉烯类药物耐药的铜绿假单胞菌和鲍曼不动杆菌比例高出全院平均水平。

结论 心脏重症监护室 CCU 患者的感染以呼吸道感染最多见，血液和尿液的感染比例也很高。主要的病原菌为肺炎克雷伯菌、铜绿假单胞菌、大肠埃希菌、屎肠球菌。主要流行菌株对大部分抗菌药物的敏感性较高，但部分多重耐药菌分离率偏高，亟待加强院感防控措施。

关键字：CCU；病原菌分布；药敏特征；多重耐药

儿科重症监护室病原菌特征及药敏分析

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目的 分析儿科重症监护室患者感染病原菌分布及药敏特征，为明确其感染特点及合理防控提供

依据。

方法 采用 WHONET 5.6 软件对 2023 年某三甲医院儿科重症监护室送检的培养数据进行处理，分析感染患者病原菌的标本来源、分布及药敏特征。

结果 2023 年某三甲医院儿科重症监护室送检标本培养出病原菌 173 株。分析检出占前十的病原菌分布发现，呼吸道标本(包括痰、纤支镜冲洗液和肺泡灌洗液)的检出比例最高，占 46.82% (81/173)，菌种检出比例最高的是肺炎克雷伯菌，占 15.03% (26/173)，其次是大肠埃希菌(11.56%，20/173)，表皮葡萄球菌和金黄色葡萄球菌分别 9.83%和 8.67%。对主要流行菌株的药敏分析发现，肺炎克雷伯菌对氨苄西林/舒巴坦(74.6%)和头孢唑林(72.4%)的耐药率最高，大肠埃希菌对头孢唑林(77.1%)和头孢曲松(72.3%)的耐药率最高，金黄色葡萄球菌对青霉素 G 耐药率达到 93.8%，对苯唑西林耐药率达到 48.6%。

结论 儿科重症监护室的感染以呼吸道感染常见,主要的病原菌为肺炎克雷伯菌、大肠埃希菌和金黄色葡萄球菌，主要流行菌株对大部分抗菌药物的敏感性较高，与成人有很大的不同。

关键字：儿科重症监护室，病原菌分布，药敏特征，耐药性

广东省某院老年呼吸科病原菌特征及药敏分析

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目的 分析广东省某院老年呼吸科患者病原菌分布及药敏特征，为明确其感染特点及合理防控提供依据。

方法 采用 WHONET 5.6 软件对 2023 年广东省某院老年呼吸科送检的培养数据进行处理，分析感染患者病原菌的标本来源、分布及药敏特征。

结果 2023 年老年呼吸科送检标本培养出病原菌 165 株。分析检出占前十的病原菌分布发现，呼吸道标本(包括痰、纤支镜冲洗液和肺泡灌洗液)的检出比例最高，占 69.10%(114/165)，菌种检出比例最高的是铜绿假单胞菌，占 16.37%(27/165)，其次是肺炎克雷伯菌和金黄色葡萄球菌，均为 10.91%(18/165)。对主要流行菌株的药敏分析发现，铜绿假单胞菌对大部分药物耐药率不高，肺炎克雷伯菌对氨苄西林/舒巴坦(100%)、头孢唑啉(100%)的耐药率最高，对头孢曲松、环丙沙星、复方新诺明耐药率均为 83.3%；金黄色葡萄球菌对青霉素 G、苯唑西林、红霉素的耐药率达到 80%。

结论 老年呼吸科的感染以呼吸道感染常见，主要的病原菌为铜绿假单胞菌、肺炎克雷伯菌和金黄色葡萄球菌。主要流行菌株对大部分抗菌药物的耐药率较高，需要引起足够重视。

关键字：老年呼吸科，病原菌分布，药敏特征，耐药性

2019-2023 年四川地区腹腔分离细菌的分布及耐药性分析

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目的 对四川省细菌耐药监测网成员单位 2019—2023 年度腹腔感染标本(包括腹水、腹腔引流液)的细菌分布及耐药情况进行统计分析，为本地区临床合理应用抗菌药物提供理论依据。

方法 按照四川省细菌耐药技术方案，参照 CLSI M100 推荐的药敏试验要求，采用纸片扩散法或自动化仪器法进行。利用 WHONET5.6 软件对 5 年四川省细菌耐药监测网成员单位上报的细菌及药敏结果数据进行分析，同一患者相同细菌仅纳入第一株菌。

结果 2019-2023 年间四川地区腹腔感染标本共分离出 22204 株非重复的细菌，其中革兰阳性菌 6023 株，占 27.1%，革兰阴性菌 16181 株，占 72.9%。腹腔感染标本中最常见的细菌为大肠埃希菌（45.8%）、肺炎克雷伯菌（8.1%）、屎肠球菌（6.1%）、铜绿假单胞菌（5.8%）和粪肠球菌（3.0%）。药敏结果显示，5 年间大肠埃希菌对三代头孢菌素中头孢曲松，头孢噻肟、头孢他啶的耐药率分别为 43.2%，45.6%, 17.0%，从 2020 年起，三代头孢菌素耐药率均呈下降趋势，2019 年起，大肠埃希菌对头孢西丁耐药率从 10.4%逐年下降至 6.6%，大肠埃希菌对环丙沙星和左氧氟沙星耐药率分别为 42.5%、38.8%。肺炎克雷伯菌对头孢曲松，头孢噻肟、头孢他啶的耐药率分别为 24.2%，28.3%，17.8%，相比 2019 年略有上升趋势。两菌对碳青霉烯类抗菌药物敏感率均在 90%以上，耐药率基本稳定。铜绿假单胞菌对碳青霉烯类、喹诺酮类、头孢他啶、哌拉西林/他唑巴坦等抗菌药物 5 年平均耐药率未超过 5.0%。耐甲氧西林金黄色葡萄球菌 (MRSA)和耐甲氧西林凝固酶阴性葡萄球菌(MRCNS)的检出率分别为 33.9%和 79.2% 。耐万古霉素的屎肠球菌（Vrefm）占 0.7%，耐万古霉素的粪肠球菌(Vrefa） 占 0.1%。屎肠球菌对环丙沙星、左氧氟沙星、氨苄西林耐药率均在 80.0%

以上。

结论 四川地区以腹水为主的标本分离细菌中，阴性菌与阳性菌之比约 7:3，以大肠埃希菌、肺炎克雷伯菌、屎肠球菌、铜绿假单胞菌、粪肠球菌为主，环丙沙星、左氧氟沙星初期经验治疗大肠埃希菌或屎肠球菌引起的腹腔感染失败的风险较大，屎肠球菌相比粪肠球菌更为耐药。碳青霉烯类药物对肠杆菌目、铜绿假单胞菌任然保持较高体外抗菌活性，孢他啶/阿维巴坦、多黏菌素针对碳青霉烯类耐药的大肠埃希菌（Creco）绝大部分有效。因此，抗菌药物使用前应规范送检腹腔标本进行细菌培养，及时了解本地腹腔感染标本细菌分布及耐药监测结果，可为临床经验治疗提供用药依据，促进抗菌药物合理应用。

关键字：细菌耐药性监测，腹腔感染，腹水，细菌分布，耐药分析，定植

南充某三甲医院血培养分离耐甲氧西林金黄色葡萄球菌临床特征 及危险因素分析

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目的 了解血培养分离出耐甲氧西林金黄色葡萄球菌的患者临床特征，探究血培养分离出耐甲氧西林金黄色葡萄球 菌的危险因素。

方法 收集 2017—2022 年血培养分离出耐甲氧西林金黄色葡萄球菌的住院患者的临床病史资料和实验室数据， 分析血培养分离出耐甲氧西林金黄色葡萄球菌的独立危险因素。

结果 2017—2022 年血培养标本共分离金黄色葡萄球菌 181 株，其中耐甲氧西林金黄色葡萄球菌 49 株，总检出率 27.07%，各年检出率变化无明显趋势。分离率科室构成比前三位为肾内科 (20.41%)、骨科(10.20%)、儿科(10.20%)。患者以老年、男性为主，其感染部位以血流感染(83.67%)和肺部感染(48.98%)为主。 49 株耐甲氧西林金黄色葡萄球菌对青霉素(100%)、红霉素(87.76%)和克林霉素(73.47%)耐药率较高；132 株对甲氧西林敏感的金 黄色葡萄球菌仅对青霉素(91.67%)耐药率较高。使用头孢菌素过往史和年龄为血培养分离出耐甲氧西林金黄色葡萄球菌的独立 危险因素。

结论 血培养分离出的耐甲氧西林金黄色葡萄球菌对多种临床常用抗菌药物耐药，使用头孢菌素过往史和年龄的因 素在耐甲氧西林金黄色葡萄球菌感染中起着重要作用，临床应注意相关危险因素，合理防治。

关键字：耐药，血培养，耐甲氧西林金黄色葡萄球菌，危险因素

耐碳青霉烯肺炎克雷伯菌对多粘菌素异质性耐药的研究

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目的 耐碳青霉烯肺炎克雷伯菌（Carbapenem-resistant Klebsiella pneumoniae，CRKP）感染已成为全球范围内的重要临床问题，多粘菌素通常是治疗的最后选择。研究表明，CRKP 对多粘菌素异质性耐药的出现可能导致治疗失败。本研究通过探究 1）CRKP 对多粘菌素异质性耐药（heteroresistance，HR）的发生率、耐药亚群比例和耐药水平；2）多粘菌素对 CRKP 的体外杀菌效果，为临床上多粘菌素异质性耐药检测和多重耐药菌感染的合理治疗与防控提供初步研究依据。

方法 从四川大学华西医院感染性疾病中心感染性疾病研究室 2014.09-2018.05 保存的所有具全基因组二代测序（Whole Genome Sequence，WGS）结果的 CRKP 菌株中，选取覆盖 31 种不同 ST 型（sequence type）者 36 株。用微量肉汤稀释法（Broth microdilution，BMD）测量多粘菌素 E 对这些菌株的最低抑菌浓度（Minimal Inhibitory Concentration，MIC）。用改良群体分析法（Population Analysis Profiles，PAP）判定这些菌株是否对多粘菌素呈异质性耐药。选取一株优势克隆 ST11 型 CRKP 多粘菌素异质性耐药株 085072，对其 9 个耐药亚群进行菌落形态、MIC 值、是否异质性耐药、耐药稳定性的多样性分析。分别设置 0、0.5×MIC、1×MIC 和 2×MIC 多粘菌素 E 浓度，绘制时间-杀菌曲线，对比对 4 株多粘菌素异质性耐药和 4 株敏感菌的体外杀菌效果。

结果 BMD 显示多粘菌素 E 对 36 株 CRKP 的 MIC 为 0.5μg -2 μg/ml，均敏感。PAP 结果显示 28（77.8%）株菌表现异质性耐药（HR）。耐药亚群的 MIC 为 8 μg - >64 μg/ml，远远高于 HR 原代菌株。CRKP 085072 菌株的 9 个耐药亚群的菌落形态、MIC 值及异质性耐药及耐药稳定性均有多样性。多粘菌素 E 在 2h 内可杀死＞99%的细菌。但几乎所有细菌出现了再生长。异质性耐药菌出现再生长的时间早于敏感菌。

结论 PAP 提示 CRKP 对多粘菌素异质性耐药可能较为广泛，且耐药亚群耐药水平高，值得临床重视。耐药亚群的比例低，易被临床常用的敏感性检测方法漏检。耐药亚群也具有异质性，临床常用的分离单菌落可能难以充分全面反映一个临床标本中所含所有细菌的特点。多粘菌素作用于异质性耐

药 CRKP 时，很可能会杀死敏感亚群后，使耐药亚群大量繁殖生长致治疗失败。

关键字：耐碳青霉烯肺炎克雷伯菌；多粘菌素；异质性耐药；耐药亚群

2016-2021 年感染性心内膜炎患者病原菌分布及其变化趋势、耐药性分析

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目的 探究福建省泉州市第一医院 2016 年-2021 年期间感染性心内膜炎患者病原菌分布及其变化趋势、耐药特点，为该地区临床合理用药提供依据。

方法 选取并采用 SPSS 18.0 软件分析福建省泉州市第一医院 6 年期间 110 例感染性心内膜炎患者的阳性血培养标本的菌种鉴定结果及常见致病菌药敏结果，按时间顺序分成 A 组（2016 年 1 月-2018 年 12 月）37 例，B 组（2019 年 1 月-2021 年 12 月）73 例。

结果 A 组 37 例患者中检出病原菌 47 株，其中主要为金黄色葡萄球菌（27.66%）、咽峡炎链球菌（10.64%）、草绿色链球菌（8.51%），B 组 73 例患者中检出病原菌 96 株，其中主要为金黄色葡萄球菌（16.67%）、咽峡炎链球菌（10.42%）、血链球菌（10.42%），A 组病原菌检出率低于 B 组，两组病原菌检出率差异无统计学意义（P=0.502＞0．05）。143 株病原菌中，链球菌属（50.35%）为主要菌属，其次为葡萄球菌属（31.47%）和肠球菌属（7.69%），A、B 两组病原菌分布无统计学意义（P=0.239＞0.05）。革兰阳性菌对万古霉素、利奈唑胺无耐药性，对四环素和或红霉素耐药性强，耐药率均＞50%；大部分革兰阴性菌对哌拉西林/他唑巴坦耐药率低（9.09%），对四环素（54.55%）、氨苄西林（81.82%）耐药率高。

结论 根据该地区在病原菌分布、药敏结果的特异性，选择万古霉素、利奈唑胺而不选择四环素、红霉素作为经验性治疗感染性心内膜炎的抗菌药物较为有效，亦可以根据实际药敏结果选择合适抗菌药物进行 IE 的精准抗感染治疗。

关键字：感染性心内膜炎，病原菌，抗菌药物，耐药率

The Molecular Evolution of KPC Variants and Their Relationships with B-lactams

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Objective To explain the selection driver of KPC-Type Carbapenemases

Methods KPC phylogroups analysis were conducted according to the results of the maximum-likelihood (ML) tree obtained using the nucleotide sequences by MEGA-X software, and 31 and 8 variants in nature and artificiality, respectively, were obtained by overlap extension PCR and expressed in an isogenic context. Drug susceptibility assays were performed by a standard broth microdilution method. enzyme kinetics assays were conducted to compare the hydrolytic activities of KPCs, and molecular modeling and ITC assay were also employed to compare the interaction between AVI and different KPC variants

Results In this study, we cloned 33 clinically described KPC variants and 8 artificially created variants into the same plasmid vector, and assess their impact on β-lactam susceptibility. Strains expressing KPC-14, KPC-28, and KPC-31 exhibited increased resistance to ceftazidime and ceftazidime-avibactam while showing decreased resistance to carbapenems. Enzyme kinetics, molecular modeling, and isothermal titration calorimetry analysis revealed a diverse array of selective pressures, including, but not limited to, aztreonam and ceftriaxone, shifting the evolution of KPCs, with ceftazidime playing a central role in this process. Substitutions within the KPC hydrolytic active sites notably reduced the inhibitory effect of avibactam on KPC, resulting in enhanced hydrolysis of ceftazidime

Conclusion We first systematically analyzed the effect of amino acid mutation on the resistance of KPC enzyme and further identified ceftazidime as a driver drug of the KPC subtype outbreak. And this study also highlights avibactam may serve as an additional driving force in KPC evolution

关键字：KPCs， Phylogenetic Reconstruction，Ceftazidime/Avibactam， Evolution, Resistance

Mefloquine Can Restore The Sensitivity of Polymyxin Resistant Carbapenem-producing Enterobacterales

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Objective Due to the lack of effective treatment, carbapenem-resistant Enterobacterales (CRE) cause a serious threat to human health. In this study, we evaluate the efficacy of mefloquine in combination with multiple drugs against 94 carbapenemase-producing Enterobac-

terales (CPE) clinical isolates and 2 mcr-1-positive clinical isolates

Methods The minimum inhibitory concentrations (MICs) of mefloquine (MEF), ceftazidime-avibactam (CAZ-AVI), ceftazidime-avibactam-mefloquine (CAZ-AVI-MEF), aztreonam-avibactam (ATM-AVI), ATM-AVI-MEF, IPM, IPM-MEF, COL and COL-MEF were determined by broth microdilution method. In order to evaluate the synergistic effect of COL and MEF in vitro, the time killing test was carried out on three colistin-resistant isolates

Results Mefloquine alone showed little antibacterial activity for all the 94 clinical CPE and 2 mcr-1 positive isolates. The MIC50 values of 96 strains of MEF, CAZ-AVI, CAZ-AVI-MEF, ATM-AVI, ATM-AVI-MEF, IPM, IPM-MEF, COL and COL-MEF were 128, > 128, > 128, 0.25, 0.125, 32, 16, 0.25 and 0.0156 μg/mL, respectively; MIC90 values are > 128, > 128, > 128, 1, 0.5, 128, 64, 1 and 0.0312 μg/mL, respectively. The results showed that MEF alone had weak antibacterial activity against 94 clinically isolated CPE strains and 2 mcr-1 positive strains, MIC50 and MIC90 were 128 and > 128 μg/mL, respectively. Combined use of MEF (32 μg/mL), the MIC50 and MIC90 values of CAZ-AVI-MEF, ATM-AVI-MEF and IPM-MEF did not decrease significantly, while the MIC50 value of COL-MEF (0.25 μg/mL vs 0.0156 μg/mL) and MIC90 value (1 μg/mL vs 0.0312 μg/mL), which indicates that MEF may restore the sensitivity of 94 clinically isolated CPE strains (98.9%) and 2 mcr-1 positive strains (100%) to COL. For the time killing experiment of three COL-R isolates, MEF or COL alone had little killing effect, and its growth curve was consistent with that of the blank control group. When MEF-COL was used in combination, the bacteria could be completely killed within 4 hours, and there was no "regeneration" of NDM-5 positive Klebsiella pneumoniae within 24 hours. In vitro drug sensitivity test and time killing test showed that the combined use of MEF-COL had better effect on killing bacteria

Conclusion Our study suggested that the combination of mefloquine and colistin might be a potential alternative for the treatment of CRE and COL-R Gram-negative bacterial infections

关键字：carbapenem-resistant，Enterobacterales，mefloquine， colistin

耐碳青霉烯类弗劳地枸橼酸杆菌的耐药机制及分子分型

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目的 分析耐碳青霉烯类弗劳地枸橼酸杆菌(Carbapenem-resistant Citrobacter freundii，CRCF)的检出率、分布特点、耐药机制及分子分型，为临床治疗与防控提供理论依据。

方法 分析 2019-2023 年福建医科大学附属泉州第一医院分离 CRCF 的药敏结果，验证耐药表型，扩增耐药基因，多位点序列分型（MLST）分析同源性。

结果 共检出弗劳地枸橼酸杆菌 119 株，其中 CRCF27 株，检出率 22.7%。CRCF 主要分离自神经外科和泌尿外科；标本类型主要是中段尿。对碳青霉烯类和头孢菌素均耐药，阿米卡星的耐药率较低，替加环素及多粘菌素均敏感，其余抗生素的耐药率>50%。成功复苏的 22 株 CRCF 耐药表型均阳性，均携带耐药基因,其中单耐药基因共 17 株（77.3%，17/22）：blaNDM-1 14 株、blaKPC-22 株及 blaNDM-51 株。同时携带双耐药基因的菌株共 5 株（22.7%，5/22）：其中同时携带 blaKPC-2、blaNDM-1 有 3 株，同时携带 blaNDM-1、blaIMP 和同时携带 blaVIM、blaNDM-1 各 1 株。共检出 8 个 ST 型，主要为 ST116 及 ST352 分别有 8 株、6 株。

结论 CRCF 以多重耐药为主，主要耐药机制是携带 blaNDM-1，一部分菌株会同时携带双耐药基因，以 ST116 和 ST352 流行为主。

关键字：耐碳青霉烯类弗劳地枸橼酸杆菌；blaNDM-1；blaVIM；blaIMP；ST116；ST352

Epidemiology and in Vitro Activity of Imipenem-relebactam, Cefepime-zidebactam, Ceftolozane-tazobactam, Ceftazidime-avibactam, Ceftaroline, Plazomicin, Omadacycline and Eravacycline Against Carbapenem Resistant Klebsiella Pneumoniae

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Objective The prevalence of carbapenem resistant Klebsiella pneumoniae (CRKP) poses a great challenge on clinical treatment. The new β-lactam/β-lactactamase inhibitors, the novel tetracycline and the next-generation aminoglycoside provided novel promising therapeutic options for CPKP infections

Methods We collected the CRKP isolates at Peking University Third Hospital from 2017 to 2022. The Minimum inhibitory concentration (MIC) Test Strip method was performed to assess the MICs of imipenem–relebactam, cefepime-zidebactam, ceftolozane-tazobactam, ceftazidime–avibactam, ceftaroline, plazomicin, omadacycline and eravacycline

against CRKP isolates. Whole genome sequencing and bioinformatic analysis were performed to identify the sequence type, capsular serotypes, resistance and virulence genes

Results A total of 141 CRKP isolates were enrolled in this study. A significant number of CRKP infected patients were admitted to ICU and Emergency department (35.5% and 32.6%, respectively). Most of the CRKP strains were isolated from the sputum (47.5%), urine (24.1%), blood (11.3%) and so on. In addition, CRKP isolates mainly belonged to ST11 (106, 75.2%), which is the epidemic clone in China, with the capsular serotypes of KL64 or KL47. A great number of CRKP isolates presented with carbapenemase gene blaKPC-2 (126, 89.4%), followed by blaNDM-1 (8, 5.7%), blaOXA-48 (3, 2.1%). Notably, a significant number of CRKP had a virulence score of 4, indicating the emergence of carbapenem resistant hypervirulent Klebsiella pneumoniae (71, 50.4%). Susceptibility to imipenem–relebactam, cefepime-zidebactam, ceftolozane-tazobactam, ceftazidime–avibactam, ceftaroline, plazomicin, omadacycline and eravacycline was 72.3%, 97.9%, 3.5%, 83.0%, 0.0%, 32.6%, 53.9% and 71.6%, respectively

Conclusion Imipenem–relebactam, cefepime-zidebactam, ceftazidime–avibactam, omadacycline and eravacycline are promising antibacterial agents against CRKP infections. However, the emergence of resistance to these new agents highlights the need for enhanced surveillance and optimized treatment strategy

关键字：carbapenem resistant Klebsiella pneumoniae, imipenem–relebactam, cefepime-zidebactam, ceftazidime–avibactam, omadacycline, eravacycline

The Emergence of High-level Cefiderocol-resistant CRPA Clinical Strains Harboring BlaAFM

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Objective Carbapenem-resistant Pseudomonas aeruginosa (CRPA) bring a serious threat to global public health. Cefiderocol (CFDC), a novel siderophore cephalosporin, has unique therapeutic advantages due to its resistance to β-lactamase hydrolysis and efflux pumps. However, against the backdrop of CFDC not yet being approved for use in China, we have isolated CRPA strains with high-level resistance to CFDC (MIC > 256mg/L) from clinical patients, differing from previously reported low-level resistant strains (MIC up to 16mg/L). Through a combination of multi-omics approaches, we performed experiments to elucidate the resistance mechanisms of CRPA to CFDC

Methods The MIC values of 500 CRPA strains against CFDC were determined using the iron-deleted broth microdilution method recommended by CLSI. The antimicrobial usage history of the selected strains was recorded, and susceptibility test for other commonly used antibiotics was performed. Whole genome sequencing was performed on CFDC-resistant CRPA clinical strains to analyze their MLST typing, and cgMLST was used to analyze the homology of strains within the same sequence type. Conjugation experiments were performed on selected CFDC-resistant CRPA strains to obtain CFDC-resistant transconjugants. Susceptibility testing for various other antibiotics was performed on both CFDC-resistant CRPA clinical strains and transconjugants to determine their resistance profiles. Biofilm formation ability was assessed, and efflux pump function was verified through efflux pump inhibition experiments combined with CFDC susceptibility changes. Plasmid-eliminated strains were obtained through continuous passages, and CFDC phenotype verification was performed to assess the correlation between the resistant plasmid and CFDC resistance, as well as the stability of the resistant plasmid. Cloning of AFM and KPC was performed in Escherichia coli DH5α and Pseudomonas aeruginosa PAO1, respectively. Whole genome sequencing and analysis were performed to compare genetic mutations and gene copy number changes between resistant and sensitive strains. Transcriptome sequencing and enrichment analysis were performed to identify key pathways and genes with altered expression between strains

Results The MIC50 and MIC90 of all strains were 0.25mg/L and 0.5mg/L, respectively. According to EUCAST standards, 5 CRPA strains were resistant to CFDC, including 2 strains (ST270, carrying blaAFM-2) with high-level resistance to CFDC (MIC > 256mg/L, 0.9%) and 3 strains with low-level resistance to CFDC (MIC = 8mg/L, ST260, carrying blaAFM-2 and blaAFM-3). These strains had strong biofilm forming ability and highly stable resistant plasmids. Antimicrobial susceptibility testing of clonal strains revealed that AFM increased the CFDC MIC of DH5α and PAO1 by more than 5 times. Changes were observed in various siderophore/siderophore receptor and efflux pump genes, with higher expression levels of AFM in high-level resistant strains compared to low-level resistant strains. The copy number of blaAFM was increased by 2-3 times in high-level resistant strains. Sequence analysis showed that all CFDC-resistant PA strains carried IncP2 plasmids encoding AFM, which harbored multiple resistance genes. Mutations were observed in the blaKPC gene after induction, accompanied by a certain

level of increase in copy number. All induced strains exhibited premature termination of fptA, and the proportion of this mutation gradually increased with increasing drug concentration. Transcriptome sequencing results showed that 2498 genes were up-regulated and 1806 genes were down-regulated in the CFDC high-level resistant strain after plasmid elimination. In PAO1TET, 227 genes were up-regulated and 541 genes were down-regulated after acquiring the resistance plasmid

Conclusion We have identified the clinical emergence of CRPA strains with high-level resistance to CFDC, which carry the blaAFM-2. Clone experiments further confirm that AFM and KPC mutants can elevate the MIC value of CFDC. Additionally, experiments demonstrate that fptA is associated with the uptake of CFDC by the strains, and premature termination of its translation can lead to the development of resistance. Clinical surveillance should focus on monitoring CRPA strains carrying AFM and KPC mutants to prevent the dissemination of these β-lactamase genes through IncP2 plasmids

关键字：CRPA,Cefiderocol,blaAFM,Iron transfer system,β-lactamase

Characterization of Two Novel VIM-type Metallo-β-lactamases, VIM-84 and VIM-85, Associated with The Spread of IncP-2 Megaplasmids in Pseudomonas Aeruginosa

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Objective This study aimed to characterize two novel VIM-type metallo-β-lactamases, VIM-84 and VIM-85, from five clinical Pseudomonas aeruginosa isolates and reveal the important role of the IncP-2 type megaplasmids in the spread of antimicrobial resistance (AMR) genes

Methods Clinical isolates were whole-genome sequenced using the Illumina and Oxford Nanopore platforms. The blaVIM-24, blaVIM-84 and blaVIM-85 genes were cloned into plasmids and introduced into E. coli DH5α and Pseudomonas aeruginosa PAO1. Minimum inhibitory concentrations (MICs) were determined using the broth microdilution method. In vitro enzyme kinetics of the purified VIM variants were measured employing spectrophotometry, and the VIM protein structures were modelled using Protein Preparation Wizard

Results VIM-84 and VIM-85, two previously undescribed metallo-β-lactamases were encoded by the two genes blaVIM-84 and blaVIM-85 which showed similarity to blaVIM-24. The blaVIM-85 gene was identified in a megaplasmid, which was related to 17 megaplasmid sequences with sizes larger than 430kbp, deposited previously in Genbank. A comparative analysis of complete plasmid sequences showed highly similar backbone regions and various antimicrobial resistance (AMR) genes. A phylogenetic tree revealed that these megaplasmids, which were widely distributed globally, were vehicles for the spread of AMR genes. The antimicrobial susceptibility test of the cloning strains showed high levels of resistance to β-lactams while they remained susceptible to aztreonam. Enzymatic tests revealed that both, VIM-84 and VIM-85, exhibited higher activity in hydrolyzing β-lactams compared to other VIMvariants. A D117N mutation found in VIM-24 affected binding to the antibiotics

Conclusion VIM-84 and VIM-85 demonstrate higher β-lactamase activity compared to VIM-24. The IncP-2-type megaplasmids are geographically distributed and are likely to play an important role in the spread of VIM variants in P. aeruginosa

关键字：Pseudomonas aeruginosa, metallo-β-lactamase, VIM, megaplasmid, antimicrobial resistance

艰难拟梭菌耐药机制的研究进展

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艰难拟梭菌是一种广泛分布于人和动物肠道的革兰阳性厌氧菌，是导致医疗机构和社区感染性腹泻常见的病原体。通过粪口途径传播，引起患者腹泻、呕吐、结肠炎甚至脓毒血症，严重者引起患者死亡。数十年来，艰难拟梭菌引起感染频率和严重程度不断增加，已成为全球医疗系统重大威胁之一。艰难拟梭菌感染是患者服用抗菌药物后引起相关腹泻的常见原因，抗菌药物也是治疗艰难拟梭菌感染的主要手段。然而艰难拟梭菌对克林霉素、氨基糖苷类、大环内酯类和喹诺酮类等药物都具有广泛耐药性，而且不同耐药基因在社区和医疗机构等环境中存在的不同菌种间相互转移，伴随新耐药基因的产生与相互转移，和高毒力菌株和多重耐药菌株的出现逐渐成为艰难拟梭菌流行的重要原因。同时由于临床抗菌药物大量且不恰当使用，艰难拟梭菌耐药性正在迅速恶化，已被美国疾病控制和预防中心确定为需要紧急应对的耐药威胁之一。之前对艰难拟梭菌耐药性和耐药机制多样性的研究主要集中在喹诺酮类和大环内脂类药物，近年来针对艰难拟梭菌万古霉素和甲硝锉等药物的耐药机制也取得众多突破性研究。因此，本文针对近年来国内外艰难拟

梭菌耐药研究进行综述，为监测艰难拟梭菌耐药性发展、临床治疗和抗菌药物合理使用提供依据。

关键字：艰难拟梭菌，抗菌药物，耐药性，耐药机制

Antibacterial Effects of Indole Derivatives on Extensively Drug-Resistant Acinetobacter Baumannii

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Objective Extensive drug-resistant Acinetobacter baumannii (XDRAB) spreads globally, and there is an urgent need to reveal new mechanisms and discover new compounds. This study is based on the theory of new bacterial indole signaling systems, taking XDRAB as the research object, exploring the resistance mechanism from a new perspective, looking for indole derivatives with good antibacterial activity, and providing new ideas for the development and research of antibacterial drugs

Methods This experimental strain was derived from XDRAB isolated from the First Affiliated Hospital of Chengdu Medical College. ①. The minimum inhibitory concentration (MIC) of 22 indole derivatives was determined using the broth microdilution method.②. The crystal violet staining method was used to quantitatively determine the effect of indole derivatives on XDRAB biofilm formation. ③. The effect of indole derivatives on XDRAB motility was evaluated using the motility agar plate method. ④. The plate counting method was used to detect the effect of indole derivatives on the adhesion ability of XDRAB.⑤. The broth microdilution checkerboard method was used to determine the effect of two indole derivatives combined with antibacterial drugs (imipenem, meropenem, sulbactam/cefoperazone, tigecycline, polymyxin B) on XDRAB synergistic antibacterial effect

Results ①. Among the 22 indole derivatives, 15 compounds showed varying degrees of antibacterial activity against 6 strains of XDRAB. Among them, 5-iodoindole and 3-methylindole had the best antibacterial activity, with an MIC of 64 μg/mL. ②. The Crystal violet staining method shows that 7 compounds have different effects on XDRAB biofilm. in The inhibition rates of 5-iodoindole at 1/2 MIC and 1/4 MIC are 42.22%-92.68%; 37.78%-90.24% respectively, and the inhibition rates of 3-methylindole at 1/2 MIC and 1/4 MIC, the inhibition rates are 60.00%-89.86%; 15.56%-75.61% respectively. ③. The exercise ability measurement showed that the six compounds had different effects on XDRAB exercise ability. Among them, the inhibition rates of 5-iodoindole at 1/2 MIC and 1/4 MIC are 34.62%-51.93%; 23.37%-39.89% respectively, and 3-methylindole at 1/2 MIC and 1/4 MIC. Under the conditions, the inhibition rates were 14.29%-38.91%; and 6.19%-30.70% respectively. ④. Plate counting method showed that the seven compounds had no significant effect on the adhesion ability of XDRAB. ⑤. Synergistic antibacterial experiments show that the synergistic antibacterial results of two indole derivatives combined with five antibacterial drugs on XDRAB show varying degrees of synergistic or additive effects. Among them, the partial inhibitory concentration index of 5-iodoindole combined with imipenem, meropenem, and sulbactam/cefoperazone was 0.375-0.75; 0.375-0.75; 0.1875-0.62. 3-methylindole was combined respectively The partial inhibitory concentration index of imipenem, meropenem, sulbactam/cefoperazone is 0.125-0.625; 0.1875-0.625; 0.25-0.75

Conclusion Among the 22 indole derivatives, 15 compounds have a certain degree of antibacterial activity against XDRAB, and 7 of them have varying degrees of inhibitory effects on XDRAB biofilm and motility. The antibacterial effects of 5-iodoindole and 3-methylindole are the most obvious; the combination of imipenem, meropenem, and cefoperazone-sulbactam sodium has the best synergistic antibacterial effect. 5-iodoindole and 3-methylindole have good antibacterial activity and provide laboratory data for the development of new indole antibacterial drugs

关键字：Indole derivatives, Extensively Drug-Resistant Acinetobacter baumannii, Synergistic effect

Diversity Transfer of A New Integrative and Conjugative Element Associated with Genome Deletion and Non-conjugative Elements Mobilization in Streptococcus Agalactiae

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Objective The primary cause of macrolide resistance in Streptococci is the transfer of integrative and conjugative elements (ICEs) which carry erm(B) or mef(A). Due to the occurrence of frequent module exchanges, newly discovered ICEs tend to become more complex. To investigate the diverse evolution of ICEs responsible for the spread of macrolide resistance

Methods Thirteen clinical S. agalactiae strains carrying erm(B) or mef(A) were characterized. The

transferability of the ICEs were explored through bioinformatics analysis and conjugation transfer experiments

Results Among the thirteen isolates, erm(B) was identified in seven within ICEs characterized by the presence of unusual triple serine integrases, designated as ICESag55. The ICESag55 backbones showed similarities to ICE10750-RD2/Tn1806-like (60–80%) and the internal elements of ICESag139 and ICESag100414 (>80%); however, its transferability remains unclear. During transfer, ICESag55 integrated into three different sites (snf2, MTase-1, and Mtase-2) of the recipient SagR31, producing four types of transconjugants. When ICESag55 was integrated into two adjacent sites, ICE was excised from the malposed positions, resulting in a ~36.6 kb deletion of the ICE flanking sequences. ICESag55 also mobilized flanking non-transfer elements when integrated into Mtase-2 of prophages. Comprehensive analysis showed that the widespread diversity of complex ICEs may derive from integration of ICESag55-like ICEs into Mtase and snf2 sites within other elements

Conclusion This is the first study to demonstrate the transferability of triple serine integrase-containing ICEs. The diverse integration of ICESag55-like ICEs may result in the evolution of single ICEs as composite mobile elements and enhance genomic diversity

关键字：Macrolide resistance, Streptococci, Composite, ICEs evolution, genome diversity

中国社区发作尿路感染主要病原菌磷霉素耐药机制研究

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目的 调查中国社区发作尿路感染来源主要病原菌（大肠埃希菌和肺炎克雷伯菌）的磷霉素耐药情况及耐药机制，为中国社区发作尿路感染的合理治疗及耐药防控提供理论依据。

方法 选取 2017 年 11 月 1 日至 2019 年 8 月 31 日间中国华东及华南地区 4 个省市 19 家三级医院社区发作尿路感染来源的大肠埃希菌和肺炎克雷伯菌，琼脂稀释法测定磷霉素最低抑菌浓度（MIC），参照美国临床与实验室标准协会（CLSI）标准将 MIC ＞128mg/L 作为磷霉素耐药菌株筛选标准。全基因组第二代测序筛查已知的磷霉素耐药基因，分析耐药基因上、下游转座移动元件的结构，并对耐药菌株进行核心基因组系统发育树（cgMLST）构建及单核苷酸多态性（SNP）分析。S1 核酸酶脉冲场凝胶电泳（S1-PFGE）及 Southern blot 印迹杂交明确 fosA3 基因的定位及所在质粒大小。滤膜接合实验明确质粒对耐药性的传递作用。分子克隆及基因回补实验验证临床耐药菌中染色体介导的磷霉素耐药机制。

结果 中国社区发作尿路感染中，大肠埃希菌和肺炎克雷伯菌的磷霉素耐药率分别为 3.53%（38/1332）和 7.27%（8/110）。38 株耐药大肠埃希菌中 36 株携带 fosA3，1 株同时携带 fosA3 和 fosA7，剩余 1 株未比对到已知磷霉素耐药基因；8 株磷霉素耐药肺炎克雷伯菌均携带 fosAKP 及 fosA3。磷霉素耐药大肠埃希菌克隆高度分散，无克隆传播现象；8 株耐药肺炎克雷伯菌中 3 株菌株为同一克隆。除 3 株大肠埃希菌和 1 株肺炎克雷伯菌外，其余携带 fosA3 基因的耐药菌株 fosA3 基因均定位于质粒上，fosA3 基因所在质粒大小并无相似性，由 26.2kb 至 336.5kb 不等。22 株大肠埃希菌和 3 株肺炎克雷伯菌接合成功，接合子均可达到与供体菌相似的磷霉素耐药水平。fosA3 基因位于两个同向 IS26 之间，其上下游环境中包含磺胺类、氨基糖苷类、大环内酯类及 β-内酰胺类等抗生素耐药基因。1 株 fosA 家族基因阴性的磷霉素耐药大肠埃希菌经 SNP 分析，发现其磷霉素靶酶 MurA 发生 D76E、V214I 错义突变，将突变后的 murA 基因回补至大肠埃希菌野生株 BW25113 可介导磷霉素 MIC 值显著上升。

结论 中国社区发作尿路感染来源大肠埃希菌和肺炎克雷伯菌的磷霉素耐药率较低。携带 fosA3 基因是中国社区发作尿路感染中介导大肠埃希菌和肺炎克雷伯菌磷霉素耐药的主要机制。fosA3 基因往往定位在质粒上，可发生水平转移以促进磷霉素耐药性传播；fosA3 基因传播依赖于 IS26 等转座元件，其遗传环境中常存在多种耐药基因。靶酶 MurA 突变是临床病原菌发生磷霉素耐药的重要机制之一。

关键字：中国社区发作尿路感染，大肠埃希菌，肺炎克雷伯菌，磷霉素，fosA3，MurA

烟曲霉 af-MFS95 基因敲除株构建揭示该基因在重楼皂苷与泊沙康唑协同抗烟曲霉中的作用

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目的 重楼皂苷（Paridis Rhizoma）是中药重楼主要活性成分，对四种广泛传播的人类致病真菌具有显著抑制作用。af-MFS95（Aspergillus fumigatus major facilitator superfamily proteins，烟曲霉 MFS 转运体）基因的编码产物在烟曲霉中推定为一种 MFS 外排转运蛋白基因，可能参与真菌的氧化呼吸过程。通过敲除烟曲霉 af-MFS95 基因，构建烟曲霉 af-MFS95 基因的敲除株，揭示该基因及其编码蛋白在

重楼皂苷与泊沙康唑协同抗烟曲霉中的作用，并探索了其对烟曲霉药物敏感性和渗透压、氧化压力物质敏感性的影响。

方法 本研究采用同源重组构建出 af-MFS95 基因的敲除盒，筛选出符合的烟曲霉 af-MFS95 敲除株 Δaf-MFS95。利用纸片法和棋盘法观察该突变株与野生株 WT(ku80，pyrG+)在重楼皂角与泊沙康唑联合抗烟曲霉中的敏感性变化。利用 E-test 法检测 Δaf-MFS95 对 3 种唑类药物（泊沙康唑、伊曲康唑、伏立康唑）的敏感性。同时，观察该突变株与野生株 WT 对氧化压力(H2O2 和甲萘醌)、渗透压物质(NaCl、D-山梨醇)敏感性的变化。

结果 体外联合药物敏感性试验结果显示 Δaf-MFS95 对重楼皂角与泊沙康唑的分级抑菌浓度指数(fractional inhibitory concentration index,FICI)为 0.5，显示无相互作用，而对照组 WT 对重楼皂角与泊沙康唑的 FICI 值为 0.156，存在协同作用。纸片法结果发现重楼皂角与泊沙康唑联合对 Δaf-MFS95 的抑菌圈比对照组 WT 产生的抑菌圈直径明显变小，重楼皂角与泊沙康唑联合时对敲除株抑制作用更显著，差异有统计学意义(P<0.05)。在 E-test 实验中，结果证实 Δaf-MFS95 对泊沙康唑的敏感性明显提高。在渗透压和氧化应激的培养试验中，与野生株 WT 相比较，Δaf-MFS95 对氧化剂 H2O2、甲萘醌、NaCl 和 D-山梨醇更敏感。

结论 敲除烟曲霉 af-MFS95 基因后，其对氧化和渗透压力的敏感性增加，逆转了重楼皂角与泊沙康唑的协同作用，af-MFS95 可能是重楼皂角作用于烟曲霉的靶点。本研究丰富了重楼皂角协同唑类抗真菌的机制研究，为将来的临床应用奠定了基础。

关键字：烟曲霉；MFS 转运体；重楼皂苷；泊沙康唑

Effect of RND Efflux Pump on Virulence Factors of Acinetobacter Baumannii

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Objective In this study, Acinetobacter Baumannii AYE (multidrug-resistant standard strain) was used as the research object to investigate the effect of RND efflux pump(AdeABC, AdeFGH, AdeIJK)on the production of virulence factors

Methods ①RND efflux pump genes (adeA, adeB, adeC, adeRS, adeFGH, adeIJK) of AYE strain were knocked out by marker-free method for gene deletion, quantitative reverse transcription-polymerase chain reaction(qRT-PCR) was used to verify the gene knockout of strain efflux pump genes. ②The minimal inhibitory concentration (MIC) of 15 antibiotics for AYE,AYE △ adeA,AYE △ adeB,AYE △ adeC,AYE △ adeRS, AYE△adeFGH, andAYE△adeIJK were determined by using broth microdilution method. ③The expressions of virulence factor related genes (abaR,bfmR,csuE,bap,pgaA) were determined by qRT-PCR. ④By measuring the migration diameter of colonies on motility plates,the effect of RND efflux genes knockout on the motility ability of AYE strain was studied. ⑤The adhesion ability was detected by plate counting method. ⑥The biofilm formation ability was detected by crystal violet staining. ⑦The change of virulence was detected by Galleria mellonella

Results ①qRT-PCR results showed that RND efflux pump genes (adeA,adeB,adeC,adeRS,adeFGH,adeIJK) of AYE strain had been successfully knocked out

②The experimental results showed that the MIC of various antimicrobial agents were decreased to varying degrees, and the knockout of adeB had the most obvious effect on drug resistance.

③ qRT-PCR results showed the expression of abaR in the 6 gene knockout strains increased to varying degrees, and the increase of AYE△adeRS was the most obvious. Compared with AYE, the expression was upregulated by about 8.5 times.But bfmR, csuE, bap, and pgaA showed a downward trend, and the down adjustment of AYE△adeB was the most obvious, bfmR, csuE, bap ,and pgaA genes were downregulated by about 6.7, 37, 4.8 and 5 times, respectively.

④ Compared with AYE (7.053±0.123mm), except AYE△adeFGH (7.25±0.36mm), the motility ability of AYE △ adeA(14.74±0.67mm),AYE △ adeB(10.69±0.17mm),AYE △ adeC(14.47±0.43mm),AYE △ adeRS(16.89±0.40mm), and AYE△adeIJK (14.56±0.35mm) were increased (P < 0.001), and the AYE△adeRS were the most significant.

⑤Adhesion ability results showed that the adhesion ability of AYE strain decreased to varying degrees(P<0.001).Among them, the adhesion ability of AYE△adeB decreased most significantly, followed by AYE △ adeIJK, AYE △ adeRS, AYE △ adeC, AYE △ adeA.

⑥The results of biofilm formation ability showed that compared with AYE, the biofilm formation of gene knockout strains were reduced to varying degrees, and the reduction of biofilm of AYE△adeB was the most significant (43.90%),followed by AYE △ adeIJK (37.16%),AYE △ adeA (36.63%) , AYE △ adeC

(34.97%), AYE△adeRS (27.15%), and AYE△adeFGH (18.77%).

⑦In the Galleria mellonella infection model,compared with AYE, the virulence of AYE△adeB, AYE△adeC, AYE△adeRS , and AYE△adeFGH strains decreased, of which AYE△adeB had the most significant virulence decline, followed by AYE△adeFGH, AYE△adeC and AYE△adeRS.

Conclusion These results indicated that RND efflux pump(AdeABC,AdeFGH,AdeIJK)of multidrug-resistant Acinetobacter baumannii had significant regulatory effects on virulence factors such as motility, adhesion , and biofilm formation ability of bacteria, thus affecting drug resistance and pathogenicity of bacteria

关键字：Acinetobacter baumannii,RND efflux pump,Drug resistance,Virulence factor

绿假单胞菌（CRPA）和碳青霉烯类耐药的鲍曼不动杆菌（CRAB）检出率为分别为 9.5%和 22.1%。流感嗜血杆菌对氨苄西林耐药率为 84.0%，β 内酰胺酶阳性率为 76.1%，β 内酰胺酶阴性氨苄西林耐药的流感嗜血杆菌（BLNAR）检出率为 7.8%。未发现对头孢他啶、头孢曲松、头孢吡肟、美罗培南和亚胺培南耐药的流感嗜血杆菌。卡他莫拉菌中 β 内酰胺酶产酶株占 98.0%。

结论 多重耐药菌株在儿童中的感染形势严峻，临床分离的常见细菌对不同抗菌药物的耐药率不同，应重视儿童细菌耐药监测，积极采取措施遏制耐药细菌的传播，合理使用抗菌药物。

关键字：细菌耐药监测； 儿童； 甲氧西林耐药金黄色葡萄球菌； 碳青霉烯类耐药肠杆菌目细菌；肺炎链球菌；流感嗜血杆菌

2020—2022 年河北省某儿童医院临床分离细菌分布及耐药性监测

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目的 了解 2020-2022 年河北省儿童医院临床病原菌的分布及抗菌药物使用情况，为临床抗菌药物的正确选用提供依据。了解 2020-2022 年河北省儿童医院临床病原菌的分布及抗菌药物使用情况，为临床抗菌药物的正确选用提供依据。

方法 用纸片扩散法(K-B 法) 、梅里埃自动化仪器 VITEK 2 Compact 和 BD Phoniex 100 和 E-Test 方法检测最药物敏感性 ，结果参考美国临床和实验室标准化协会（CLSI）2022 年文件标准判断，用 WHONET 5.6 软件对本院分离细菌耐药性进行统计分析。

结果 2020-2022 年共分离 11909 株非重复临床分离菌，革兰阳性菌 5372 株，占 45.1%，革兰阴性菌 6537 株，占 54.9%。金黄色葡萄球菌中甲氧西林耐药株（MRSA）检出率为 36.8%，凝固酶阴性葡萄球菌中甲氧西林耐药株（MRCNS）检出率为 73.8%。粪肠球菌、屎肠球菌对氨苄西林的耐药率分别为 2.3%和 92.7%，高浓度庆大霉素的耐药率分别为 42.2%和 66.2%，屎肠球菌对测试抗菌药物的耐药率均明显高于粪肠球菌。肺炎链球菌中非脑脊液标本分离株中青霉素耐药肺炎链球菌（PRSP）和青霉素敏感肺炎链球菌（PSSP）分别为 2.6%和 93.6%。未发现万古霉素和利奈唑胺耐药的葡萄球菌属、肠球菌属和链球菌属。肠杆菌目中，大肠埃希菌和肺炎克雷伯菌中超广谱 β 内酰胺酶（ESBLs)表型检出率分别为 47.4%和 32.3%，碳青霉烯类耐药菌株的检出率分别为 2.4%和 24.4%。碳青霉烯类耐药的铜

耐碳青霉烯类肺炎克雷伯菌的临床特点、耐药基因及毒力分析

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目的 对我院耐碳青霉烯类肺炎克雷伯菌进行临床特点、耐药基因及毒力分析，了解其临床感染特征、危险因素及碳青霉烯高耐药和高毒力情况，为临床合理使用抗菌药物提供科学依据。

方法 收集 2020 年 6 月 1 日-2023 年 10 月 31 日于川北医学院附属医院中心 ICU、神经外科 ICU 及急诊 ICU 共 44 例患者临床标本中分离到的 CRKP 菌株。分析患者的临床表现，运用拉丝实验定义高粘滞表型，通过 PCR 技术对分离菌株进行耐药基因、毒力基因和荚膜特异性血清型检测，并对产 KPC 酶的 CRKP 进行基因测序。将 rmpA、iucA、peg-344 中至少两种毒力基因阳性定义为 hvKP。

结果 44 例 CRKP 患者主要为肺部感染，均接受侵袭性操作，脓毒症发生率 25.0%，总体治疗失败率 38.6%，44 株 CRKP 菌株均产 KPC 酶，且全部为 blaKPC-2（100%）；拉丝实验阳性 14 株（31.8%）；扩增出相关毒力基因 23 株（52.3%），其中 rmpA10 株（22.7%），iucA 16 株（36.4%），peg-344 19 株（43.2%）；扩增出荚膜特异性血清型有 5 株（11.4%），K1、K2、K5、K57 分别有 1 株（2.3%）、2 株（4.5%）、1 株（2.3%）、1 株（2.3%）。鉴定为 hvKP 有 13 株，即 CRKP 中 hv-CRKP 检出率为 29.5%。

结论 我院 CRKP 耐药机制均为产 blaKPC-2，CRKP 中毒力基因检测率高，拉丝实验阳性和高毒力荚膜血清型检出率较高，兼具碳青霉烯耐药性和高毒力的肺炎克雷伯菌已经不在少数，临床及感控部门应加强对该类菌株的监测和防控，减少医院感

染的发生，提高疗效，保障患者健康。

关键字：耐碳青霉烯类肺炎克雷伯菌，高毒力肺炎克雷伯菌，耐药基因，毒力基因，荚膜特异性血清型

上海市某三甲医院阴沟肠杆菌复合体的分布及耐药性

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目的 了解上海市某三甲医院阴沟肠杆菌复合体(ECC)临床株的分布及耐药性

方法 收集 2018 年-2020 年临床分离的 ECC 菌株。药敏试验采用微量肉汤稀释法和琼脂稀释法。PCR 检测常见碳青霉烯酶耐药基因（blaKPC、blaNDM、blaIMP、blaVIM、blaOXA-48）

结果 2018-2020 年共分离 ECC 菌株 222 株，其中 36 株分离自普外科，为全体 ECC 菌株的 16.2%；标本类型主要为痰液（41.0%）和尿液（20.3%）。药敏结果显示 ECC 菌株对 甲氧苄啶/磺胺甲噁唑、第二代、第三代头孢菌素、氨曲南和喹诺酮类药物耐药率高（31.1%-71.2%），对替加环素、阿米卡星、美西林和头孢他啶/阿维巴坦耐药率低（0.5%- 9.0%）；对美罗培南和亚胺培南的耐药率分别为 9.5%和 10.4%。对碳青霉烯类药物不敏 感的 34 株 ECC 中有 23 株对碳青霉烯类耐药，25 株对美西林敏感（占 73.5%）。对碳青 霉烯类药物不敏感的 34 株 ECC 经 PCR 检测有 21 株携带碳青霉烯酶基因（14 株 blaNDM，5 株 blaIMP 和 2 株 blaKPC），其中 15 株产金属酶的菌株对美西林敏感。2019 及 2020 年 ECC 临床分离株对亚胺培南和头孢他啶/阿维巴坦的耐药率较 2018 年显著上升（P<0.05）， 多与产 NDM 相关。对第三代头孢菌素耐药的 ECC 菌株中，对亚胺培南和美罗培南的耐 药率为 20.4%，对阿米卡星和美西林的耐药率分别为 4.9%和 8.7%；对替加环素的不敏感 率为 9.7%

结论 2019-2020 年 ECC 临床分离株对碳青霉烯类药物及头孢他啶/阿维巴坦 的耐药率上升，与细菌产金属酶相关。部分产金属酶的 ECC 菌株对美西林敏感

关键字：阴沟肠杆菌复合体，临床分布，耐药性，病原菌

中国不同谱系 MRSA 对达托霉素敏感性分析

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目的 达托霉素 （DAP） 对耐甲氧西林金黄色葡萄球菌 （MRSA） 有效。然而，MRSA 中对 DAP 的易感性降低可能导致治疗失败。我们旨在确定中国 MRSA 谱系中 DAP 最小抑制浓度（MIC）和 DAP 异抗性 （hDAP） 的分布。

方法 基于课题组之前完成的全国金黄色葡萄球菌流行病学调查，首先，通过药物敏感性检测，明确我国临床上不同克隆的 MRSA 菌株对达托霉素敏感性的差异。通过全基因组测序分析和稳定性实验，阐明达托霉素异质性耐药菌株的分子机制及稳定性。

结果 对 2015—2017 年在中国收集的 472 株临床 MRSA 分离株进行了 DAP 敏感性检测。所有分离株（n＝472）均对 DAP 敏感，但其中 35.17%（166/472）表现出高 DAP MIC（MIC >0.5 μg/mL）。与低 DAP MIC 组相比，高 DAP MIC 组含有更高万古霉素或替考拉宁 MIC 的分离株比例（>1.5 μg/mL）（19.3% vs 7.8%，P＜0.001;22.3% vs 8.2%，P＜0.001）。我们比较了通过 DAP MIC 分层的 MRSA 分离株的克隆复合物（CC）分布和临床特征。 CC5 分离株对 DAP （MIC 50＝1 μg/mL） 的敏感性低于 CC59 分离株 （MIC 50＝0.5 μg/mL，P＜0.001）。群体分析分析显示，在研究的 10 个 ST5 和 ST59 DAP 敏感 MRSA 分离株中，有 5 个表现出 hDAP。

结论 我们的研究表明，MRSA 中 DAP 耐药性和 hDAP 的增加可能会威胁到 MRSA 感染的有效性。

关键字：达托霉素;异质抗性;甲氧西林耐药金黄色葡萄球菌;mprF;walR/walK。

实验室进化的黏菌素耐药鲍曼不动杆菌的基因组及代谢特征

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目的 多重耐药鲍曼不动杆菌（multi-drug resistant Acinetobacter baumannii, MDR-AB）是医疗机构和免疫功能低下患者严重感染的常见病原菌，其可选治疗药物少，患者感染病死率高。多黏菌素类药物是治疗 MDR-AB 的最后一道防线，其临床应用近年来迅速增加。随着黏菌素使用率上升，鲍曼不动杆菌在临床上出现耐药性，大多数报告的耐药机制涉及磷脂酰乙醇胺（PETN）对脂质 A 的修饰或脂

多糖（LPS）缺失。本研究通过细菌的进化实验，比较了不同黏菌素敏感性鲍曼不动杆菌的基因组和代谢特征，旨在了解黏菌素耐药性的相关机制，揭示种群适应的耐药突变特性及生长影响。

方法 选取 12 株分离自临床的黏菌素敏感鲍曼不动杆菌（COLS），分别接种至黏菌素浓度连续增加的阳离子调节肉汤中连续传代，以获得实验室进化的黏菌素耐药鲍曼不动杆菌（COLR），并测定其最低抑菌浓度（Minimum inhibitory concentration, MIC）及生长曲线。采用全基因组测序（WGS）及 Snippy 序列比对软件分析基因突变位点。BIOLOG 微孔板用于测试细菌在单一营养物质（碳源或氮源）中的生长情况，通路分析用于阐明 COLS 和 COLR 之间的代谢物利用差异。

结果 本研究共获得 16 株可稳定遗传的黏菌素耐药株，MIC 范围为 32 μg/ml 至>128 μg/ml。与 COLS 相比，大多数 COLR 菌株表现出生长性减弱，对舒巴坦、美罗培南表现出更高的敏感性。WGS 分析鉴定出参与双组分调控系统（pmrAB）、脂质 A 生物合成（lpxAD）、脂多糖转移（lptAD）、ABC 转运蛋白（mlaD）、不动杆菌三聚体自耦转运蛋白（ata）、谷胱甘肽过氧化物酶（soxR）、脂肪酸生物合成（fabD）、钾转运 ATP 酶亚基（kdpB）和多药外排 RND 转运蛋白（adeF）等基因突变。BIOLOG 结果提示 COLR 菌株代谢物利用率普遍下调。相关通路分析显示，COLS 和 COLR 菌株在天冬氨酸代谢、脂肪酸生物合成、尿素循环、柠檬酸循环、精氨酸和脯氨酸代谢、半乳糖代谢和谷胱甘肽代谢方面存在差异。

结论 抗菌药物的过度使用可对细菌产生较强的选择性压力，诱导其产生耐药性。这项研究拓宽了我们对黏菌素耐药性机制的理解。据报道，耐药性与细菌适应性的下降有关（例如，生长较慢、抗菌药物敏感性的改变和代谢物利用率的降低）。此外，基因组和代谢表型的结果表明，鲍曼不动杆菌的黏菌素耐药性可能与膜重塑、氧化应激有关。对脂肪酸合成和氧化还原代谢途径的干预可能有助于控制黏菌素抗性菌株的传播。

关键字：鲍曼不动杆菌，黏菌素耐药性，基因组，代谢特征

外排泵基因 qacA 与 ST5 型耐甲氧西林金黄色葡萄球菌对万古霉素异质性耐药的相关性研究

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目的 万古霉素治疗耐甲氧西林金黄色葡萄球菌（MRSA）感染被广泛采用，但异质性万古霉素耐药金黄色葡萄球菌（hVISA）的出现增加了治疗失败的风险。外排泵基因 qacA 在 ST5 型 MRSA 等院内感染菌株中表达，并可能与 hVISA 的形成相关。然而，目前尚不清楚 qacA 基因是否会介导 ST5-MRSA 对万古霉素的异质性耐药。

方法 采用菌群分析-曲线下面积法（PAP-AUC）筛选 MRSA 肺炎患者的 hVISA 菌株。对所有菌株进行全基因组测序，确定分子分型，并分析 qacA 携带率、携带质粒和突变位点。透射电镜测定 5 株 qacA 阳性的 ST5 型 hVISA 菌株和 5 株 qacA 阴性的万古霉素敏感金黄色葡萄球菌（VSSA）菌株的细胞壁厚度，并使用 Snippy 软件分析与 hVISA 相关的双组分系统基因 graSR、vraSR、walKR 的单核苷酸多态性（SNP），以排除细胞壁增厚导致的 hVISA 形成。选取 1 株 qacA 阳性的 ST5 型 hVISA 和 1 株 qacA 阴性的 VSSA 菌株，在万古霉素处理 24 小时后，用液相色谱串联质谱法测定胞内外万古霉素浓度。为验证 qacA 是否介导 VSSA 形成 hVISA，将携带 qacA 的质粒电转入 qacA 阴性的 VSSA 菌株中，采用实时荧光定量 PCR（RT-qPCR）测定 qacA 基因的相对表达量。

结果 本研究纳入 128 株 MRSA 肺炎菌株，73 株确认为 hVISA 菌株。hVISA 菌株主要为 ST5 型，而 VSSA 菌株主要为 ST764 型。qacA 基因主要存在于 ST5 型，并且其中 50%的 ST5 hVISA 携带外排泵基因 qacA。透射电镜显示 hVISA 和 VSSA 菌株细胞壁厚度无显著差异，并且在双组分系统基因中未发现 hVISA 特有的 SNP。在相同万古霉素浓度下，24 小时后 hVISA 株细胞内浓度仅为 VSSA 株的 21.2%。将 qacA 基因电转入 VSSA 菌株后，PAP-AUC 筛选显示 1 株 ST5 型 VSSA 菌株表现出万古霉素异质性耐药特性，且 qacA 表达水平是未形成 hVISA 电转株的 2 倍以上。ST5-MRSA 的亚型分析中，qacA 不表达在 t002 中，仅在 t311 和 t2460 中表达。质粒分析表明，不同于 t2460 型菌株携带的 VRSAp 质粒，t311 型菌株中携带 SAP105B 质粒。此外，与 VRSAp 质粒中所携带的 qacA 基因序列相比，t311 型菌株中普遍出现了 qacA 的同一位点（V23I）突变。

结论 多药外排泵基因 qacA 与 ST5 型 MRSA 介导对万古霉素的异质性耐药相关，qacA 高表达株更有可能形成 hVISA 株。qacA 基因在 ST5 型 MRSA 中的携带和表达呈现出基于 spa 亚型的特异性。

关键字：外排泵基因，qacA，ST5 型，耐甲氧西林金黄色葡萄球菌，万古霉素，异质性耐药

抗菌药物的 PK/PD 研究与临床试验

藏族患者万古霉素血药谷浓度与疗效和肾毒性的相关性研究

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目的 探讨万古霉素血药谷浓度监测与藏族患者治疗效果、肾毒性之间的相关性，为藏族患者万古霉素个体化用药提供参考。

方法 连续纳入 2020 年 4 月至 2022 年 9 月西藏自治区人民政府驻成都办事处医院收治使用万古霉素并接受治疗药物 监测的藏族患者，根据谷浓度监测结果进行分组，分别比较感染治疗效果和肾毒性发生风险。

结果 共纳入 88 例患者，其中有 治疗效果评价结果的病例 88 例，有肾毒性评价结果的病例 81 例。单因素和多因素分析结果均提示在藏族患者中，谷浓度是否 低于 10 mg·L–1 对于感染治疗效果的影响无统计学意义，而谷浓度是否高于 20 mg·L–1 对于肾毒性发生风险的影响也无统计学意义。

结论 当前常用的万古霉素血药谷浓度范围（10～20 mg·L-1 ）可能并不适于藏族人群的血药浓度监测，仍需开展该人群 的群体药动学研究以进一步探寻适合的万古霉素血药谷浓度监测范围。

关键字：万古霉素，藏族，血药谷浓度，治疗效果，肾毒性

The Efficacy of Polymyxin B Combined with Cefepime-avibactam Against The Biofilm of Polymyxin B-resistant Pseudomonas Aeruginosa and Klebsiella Pneumoniae in An in Vitro and in Vivo Model

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Biofilms, which often form on medical devices implanted in critically ill patients, can lead to treatment failure due to their resistance to antibiotics. Cefepime-avibactam (CFP-AVI) when used with polymyxin B (PMB), has shown potent activity against Pseudomonas aeruginosa and Klebsiella pneumoniae in vitro. However, there is a lack of data on its efficacy in biofilm-associated infections. This study aimed to evaluate the synergistic activity of PMB combined with CFP-AVI against the biofilms of PMB-resistant Gram-negative bacteria, using both an in vivo Galleria mellonella infection model and an in vitro biofilm pharmacokinetic/pharmacodynamic (PK/PD) model. Eight PMB-resistant strains known for strong biofilm formation were selected. Combination treatment with CFP-AVI and PMB improved larvae survival rate by 6.67% to 33.33% compared to CFP-AVI monotherapy after 7 days. In the PK/PD biofilm model, which simulates human drug exposures, the combination of PMB monotherapy (2.5 mg/kg load, 1.5 mg/kg q12h, 2-h infusion) and CFP-AVI (2g q8h, 2-h infusion) demonstrated bactericidal activity against all strains at 72 h (Δlog10 cfu/mL = -5.345 to -3.243). These findings suggest that the combination of PMB and CFP-AVI could be an effective therapeutic strategy to treat biofilm infections in clinical practice.

关键字：biofilm; polymyxin B-resistant; polymyxin B; pharmacokinetic/pharmacodynamic; in vivo.

HPLC 法测定人血浆中泊沙康唑药物浓度及其临床应用

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目的 建立一种简单、准确、可靠的 HPLC 方法来测定人血浆中泊沙康唑药物浓度的方法，并将其应用于临床，为制定泊沙康唑个体化用药方案提供参考。

方法 用乙腈沉淀蛋白法处理血浆样品，内标选用伊曲康唑。采用 HPLC 法结合紫外分光检测器，使用 Agela Technologies C18 (250 mm × 4.6 mm,5μm) 色谱柱，在流动相为乙腈-水(60:40)、柱温为 25℃、流速为 0.8 mL·min-1 、检测波长为 261 nm 条件下检测泊沙康唑的血药浓度，进行方法学验证，并将其应用于临床。

结果 泊沙康唑与内标及血浆中其他杂质分离良好，在 0.5～16 mg·L-1 内有良好线性关系，标准曲线为 Y = 0.501 1X－0.107 2(R2 = 0.999 9)； 0.5、4、8 mg·L-1 3 个浓度的质控样品的日内和日间精密度 RSD＜7% 。不同储存条件下稳定性良好，RSD 值均小于 10%。平均提取回收率为 96.7%。测定了 14 例血液病患者的泊沙康唑稳态谷浓度，12 名患者相同剂型的泊沙康唑（肠溶胶囊）与服药剂量（300mg, qd)下测得的浓度范围为 0.4~6.05mg·L-1，2 名患者服用泊沙康唑（口服混悬液）在服药剂量（200mg, tid)下测得的浓度分别为 0.42 和 0.64mg·L-

1，结果显示在相同剂型和剂量下，不同患者的血药浓度范围存在较大个体差异。

结论 该方法操作简单，高效、准确、特异性强，适用于临床预防或治疗侵袭性真菌感染时使用泊沙康唑患者的血药浓度监测，为实现泊沙康唑的个性化治疗提供参考。有助于制定更有效的个体化治疗方案。

关键字：泊沙康唑；治疗药物监测；HPLC；血药浓度；个体化用药

抗菌药物管理与院感防控

Effectiveness of A Pharmacist-led Hospital Antimicrobial Stewardship in A Chinese Tertiary Hospital

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Objective Antimicrobial resistance has become a global concern . Antibiotics are becoming increasingly ineffective, leading to increased difficulty in treating infections, causing death, and imposing significant costs to national economies and healthcare systems. The AMS strategy is internationally recognized as a key strategy for addressing the global threat of escalating bacterial resistance . The term "AMS" was first used in 1996 to refer to organized antimicrobial management. The implementation of the AMS strategy is relatively common in American hospitals. Pharmacists in the working group are more focused on the prospective audit with intervention and feedback (PAIF) and pre-authorization of antibiotics . In previous studies of AMS in China, the AMS working group consists of many departments, such as the medical department, infection department, clinical pharmacists. Clinical pharmacists, as members of the AMS working group, are often the only reviewers of medical orders when doctors prescribe. They are the consultants who provide a reference for clinicians' decision-making, or reviewers of prescriptions after patients are discharged from the hospital. Although the overall utilization rate of antibiotics, or the per capita consumption amount, decreased, the effect of the administrative intervention led by the director or the medical department in the AMS working group cannot be ruled out, nor can it be ruled out that the decrease in drug cost is the primary cause . In the context of the participation disparity between domestic and foreign pharmacists in AMS work, what needs to be discussed is how clinical pharmacists, as members of the AMS working group in China, can play a greater role in the reduction of bacterial drug resistance and achieve more detailed and comprehensive management

Methods Beginning in 2017, a clinical pharmacist-led hospital antimicrobial stewardship was initiated in a Chinese tertiary hospital. Pharmacists participated in all aspects of antibacterial drug management. Clinical pharmacists managed antibiotic use according to the relevant regulations of the State, such as the Prescription Management Measures, the Clinical Application Management Measures of Antibiotics, and the Notice of the National Health Commission on Further Strengthening the Management of Antimicrobials to Curb Drug Resistance. They optimized the management system of antibiotics; refined the responsibilities of the department; established the assessment system; participated in the

management of drug selection and elimination, in-depth clinical training, and supervision; and standardized the use of antibiotics before, during, and after treatment. From January to December 2017, clinical pharmacists led the responsibilities of members of the antibacterial drugs working group and formulated a standard antibacterial drug management process. To fully exploit the subjective initiative of clinical pharmacists, we developed a series of management plans focusing on clinical pharmacists: 1. regularly perused the antibiotics supply list and submitted adjustment suggestions to the antibiotics working group; 2. participated (together with the discipline inspection office) in the temporary procurement procedure of antibiotics to completely grasp the suitability of this procedure; 3. used the information management system to statistically analyze monthly antibiotic use and monitor antibiotic use in departments by physicians, in order to identify the causes of excessive combined antibiotic use (while verifying the permission-seeking protocols of information system personnel and the authorization process of the medical department to find problems and develop timely rectification); 4. participated in joint outpatient and inpatient treatment (services included consultation and discussion with physicians, ward rounds, and anti-infection treatment planning); 5. participated in the maintenance of the pre-prescription review system to prevent unreasonable use of antibiotics by physicians; 6. ensure the physician received online and offline training on the rational use of antibiotics either as a single department or all hospital departments; 7. established the responsibility indicators of antibacterial drug assessment of AUD in each department, and conducted monthly and annual assessments (departments were penalized for unreasonably exceeding the standard); 8. compiled irrational prescriptions dispensed throughout the hospital using a grid management system and provided advice, comments, and feedback to the clinic department; 9. participated in the monthly surveillance of drug-resistant pathogens and provided guidance for the inspection of antibiotics before use; 10. participated in the review of clinical pathways for single diseases and the irrational use of anti-infection drugs for community-acquired pneumonia and chronic obstructive pulmonary disease; 11. participated in the data maintenance of the hospital information systems to ensure their standardization.. This retrospective study included the pre-intervention (2013-2016) and post-intervention (2018-2021) stages. Antibiotic use was evaluated by antibiotic use rate (AUR), the combination antibiotic use rate, and the pathogen detection rate prior to antibiotic administration, and the antibiotic use density (AUD) was calculated

Results The results demonstrated that the implementation of the AMS program was associated with a reduction in antibiotic use. The AUR of outpatients declined by 6.69% (P<0.05). The combination antibiotic use rate of inpatients lowered by 5.67% (P<0.05) and the AUD declined appreciably (P<0.05). Conversely, the pathogen detection rate to antibiotic administration increased by 18.68% (P<0.05)

Conclusion These results revealed significant correlations between antibiotic standard use and the pharmacist-led AMS. Implementing proper management strategies and reducing unnecessary antibacterial drug use may be an effective measure to reduce the spread of resistant bacteria, which should be confirmed by further studies

关键字：Pharmacist-led antimicrobial stewardship,antibiotic resistance,excessive combined

某肺癌高发地三级医院抗真菌注射剂临床应用情况及合理性分析

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目的 对安庆市某三级医院2023年6月至2023年 12 月住院患者抗真菌注射剂的临床使用情况进行分析，并且根据临床应用情况分析药物使用的合理性。

方法 采用回顾性调查法，利用电子病历系统收集我院 2023 年 6 月至 12 月年龄>16 岁的住院患者且至少使用过 1 次抗真菌注射剂，对药物使用合理性进行分析评价。

结果 2023 年 6 月至 12 月该院抗真菌注射剂使用品种数量及消耗金额同时增长；氟康唑氯化钠注射液的应用数量最多，销售金额及用药频度（DDDs）排序均占首位。抗真菌注射剂使用中存在的不合理用药现象主要在治疗用药时未给予负荷剂量、给药频率和联合用药不合理等。

结论 该院抗真菌注射剂存在着一定的不合理使用现象，应进一步加强处方点评制度的实施，降低医院抗真菌注射剂应用的不合理性，保障患者的合理用药，不断提高抗菌药物的临床合理应用水平，以确保临床用药更加经济、安全、有效。

关键字：抗真菌注射剂；住院患者；合理性；评价分析；三级医院

伏立康唑原研与仿制药的有效性、安全性及经济性评价

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目的 比较国家第四批集采中选药品伏立康唑

片剂与非中选原研药在有效性、安全性和经济性的差异，为伏立康唑中选药品提供真实世界依据。

方法 回顾性收集广西医科大学第一附属医院 2019 年 1 月至 2023 年 6 月使用伏立康唑中选药品或原研药治疗真菌感染的患者信息。采用 1:1 有放回的最近邻匹配进行倾向性得分匹配。通过临床疗效、微生物清除率和影像学综合评估疗效，以累计有效率和特殊人群分层分析评价有效性；使用不良反应发生率及累计不良反应发生率评价安全性；采用最小成本法和药品的用药频度、日均费用评估经济性。

结果 有 436 例患者符合排纳标准，经匹配后，两组各有 190 例。在疗效上，伏立康唑中选药品和原研药有效率为 62.63%和 59.47%，P=0.528。在不同真菌菌种感染、基础疾病、肝肾功能受损以及老年人这些常见特殊人群中两组的疗效相当（P＞0.05）；在安全性方面，中选药品不良反应发生率为 13.68%，原研药 7.89%，P=0.069；经济性方面，中选药品平均住院总费用 4636.26 元，原研药 8613.2 元，P＜0.001。中选药品在集采实施后年用药频度上升 87.3%，日均费用下降 59.03%，并且经集采后一年为本院节省 60.2 万元。

结论 伏立康唑中选药品在治疗真菌感染的有效性和安全性方面与原研药相似，并且具有更大的经济优势。

关键字：国家药品集中采购；伏立康唑；倾向性得分匹配；真实世界

Impacts of Pharmacist-led Multifaceted Antimicrobial Stewardship on Antibiotic Use and Clinical Outcomes in Urology Department of A Tertiary Hospital in Guangzhou, China: An Interrupted Time Series Study

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Objective Despite several studies demonstrating the success of pharmacist-led antimicrobial stewardship programs (ASPs) in intensive care units (ICUs) and emergency department (ED) settings, limited research has explored their effectiveness in urology. Our study aims to explore whether the interventions of clinical Pharmacist-led multifaceted ASP reduced the use of antibiotics without worsening patient clinical outcomes, to determine the effectiveness of the intervention in urology and to provide a scientific basis for the application of the intervention in urology using interrupted time series (ITS) analysis

Methods This study was conducted in the urology department of a 3,956-bed academic teaching hospital located in Guangzhou, China. The department consists of two wards with approximately 100 beds and served a total of 14,995 discharged patients during the study period from April 2019 to March 2023, with a total of 44,551 antibiotic prescriptions issued. In this study, any discharged patient who was readmitted during the study period was considered as a new patient. The inclusion criteria comprised all patients who received at least one antibiotic prescription at the Department of Urology between April 2019 and March 2023. Patients were excluded if they did not use any antibiotics or if data were missing. Out of the total number of patients who were prescribed antibiotics during the study period (12,755), 11 patients only received antofloxacin, which is not classified in the AWaRe classification system or under J01 antibiotics. Additionally, 268 patients had missing data, resulting in the final inclusion of 12,476 patients

The pharmacist-led multifaceted ASPs included: (1) Frequent physician training: Train physicians on the rational use of antibiotics, including providing training and assessment sessions, as well as facilitating regular communication among healthcare professionals; (2) Medication consultation: One-on-one medication guidance and education should be provided to patients who require it, especially elderly patients, as well as clinicians; (3) Regular review of medical orders: The temporary and standing orders of each patient were regularly reviewed to advise physicians on improving prescriptions for problematic cases. And we pay special attention to the selection, indications and treatment course of antibiotics in perioperative patients; (4) Monthly indicator feedback: At the end of every month, the antibiotic usage in the urology department was analyzed statistically. Feedback related to antimicrobial management indicators for performance evaluation in the department was provided; (5) Consultation and case discussions: Active participation in consultations regarding complicated infection cases in the field of urology.

The outcomes included antibiotic use (antimicrobial consumption in urology, average antimicrobial cost, average the total cost of hospitalization, percentage of antimicrobial drug cost) and clinical outcome (average LOS). The data was analyzed using interrupted time series analysis (ITSA). The ITS analysis adopted segmented linear regression (SLR), and the SLR model for each indicator was described as follows:

$$Yt = \beta0+\beta1\times time+\beta2\times intervention+\beta3\times post\text{-}time +\beta41\times covid19\_1+ \beta42\times covid19\_2+ \varepsilon$$

where Yt represents each indicator; time is a continuous time variable, assigning 1-48 in this study; intervention is a binary variable assigned a value of 0 before intervention and 1 after intervention; post-time is a time variable that calculates the number of months after the intervention (for the time before intervention, post-time=0, and after intervention, post-time is assigned a

value of 1 to 24 in this study); COVID-19 is a dummy variable indicating the pre-COVID-19 period (April 2019 to December 2019, coded 0), COVID-19 period (January 2020 to March 2020, coded 1), and post-COVID-19 (coded 2); ε is a random variable; β0 is the baseline level of the indicators when time = 0; β1 is the baseline trend before intervention; β2 represents changes in the levels of indicators during the intervention; β3 is the trend change after the intervention. β41 is the level change during the COVID-19 period, and β42 is the level change post-COVID-19.

Results Following the implementation of ASPs, we observed an immediate decrease in total antibiotic consumption (β = -36.24 DOT/100PD, P < 0.001) and Antibiotic use rate (β = -7.87 %, P = 0.002). But the trend change of total antibiotic consumption and AUR were not significant

For ATC classification, (1) Second-generation-cephalosporins: the intervention resulted in a significant immediate decrease in consumption (β2 = -15.18 DOT/100PD, P < 0.001) but a no significant positive change in slope (β3 = -0.40 DOT/100PD per month, P = 0.18); (2) Third-generation-cephalosporins: there was a significant decrease in level of consumption (β2 = -6.16 DOT/100PD, P = 0.002), and a significant increase in trend by 0.82 DOT/100PD per month was observed (P < 0.001) after the intervention; (3) Carbapenems: we observed a significant decrease in level (β2 = -1.91 DOT/100PD, P = 0.03), but a no significant change in trend (β3 = -0.13 DOT/100PD per month, P = 0.20); (4) Fluoroquinolones: there was a significant decrease in level (β2 = -12.70 DOT/100PD, P < 0.001), and a significant change in trend (β3 = -0.42 DOT/100PD per month, P = 0.01); (5) Other antibacterials: change in level were -1.99 DOT/100PD (P = 0.001) and change in trend were -0.10 DOT/100PD per month (P = 0.18); For the Other Beta-lactam antibacterials, the level change and trend change were not statistically significant after intervention.

For the WHO AWaRe categories, The intervention resulted in a significant immediate decrease in Watch category antibiotics consumption (β2 = -34.96 DOT/100PD, P < 0.001) but no significant change in slope (β3 = 0.04 DOT/100PD per month, P = 0.93). However, the intervention resulted in level change and trend change in Access category antibiotics consumption were no significant.

There were no differences observed in mortality rate before and after the intervention, and no significant short-term or long-term effects were found on length of hospital stay (LOS) using ITSA. However, there was a significant short-term effect on average antibiotic cost (β2 = -446.83 RMB, P = 0.004).

Conclusion This study presents significant evidence from an interrupted time series intervention study in urology. The implementation of pharmacist-led multifaceted ASPs was found to be associated with a significant reduction in antibiotic use, particularly for second-generation cephalosporins, fluoroquinolones and Watch category antibiotics, as well as a decrease in antibiotic cost. Importantly, this reduction was achieved without any increase in length of stay (LOS) or mortality. These findings suggest that promoting this beneficial intervention in other clinical settings is highly promising and that hospital administrators should pay attention to the important role played by clinical pharmacists in antimicrobial stewardship

关键字：antimicrobial stewardship, pharmacist, urology, antibiotic use,clinical outcomes

人工智能在医院感染领域中应用的文献计量学分析

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目的 采用文献计量学分析人工智能在医院感染领域中应用的研究热点及发展趋势，为进一步开展相关研究提供参考。

方法 基于 Web of Science 数据库中有关人工智能与医院感染的文献检索结果，使用 CiteSpace6.2.R6 软件和 VOSviewer 1.6.19 软件绘制科研合作网络、关键词等知识图谱，进行文献计量学分析。

结果 共纳入文献 305 篇，早期文献发表数量与被引频次长期维持在很低的水平；2018 年后，二者均呈现逐年上升趋势。这些文献来自 50 个国家/地区，文献发表数量最高的国家为美国。文献发表数量最多的科研机构为哈佛大学，文献发表数量最高的学者是来自南卡罗来纳州医科大学的 Heather L. Evans 教授。人工智能在医院感染领域中应用的研究主要集中在医院感染监测模型和人工智能算法的优化方面。

结论 人工智能在医院感染领域的相关研究已迈入新阶段。我国在这一领域的学术成果较世界先进水平仍有差距，未来可针对热点方向进行更深入的研究。

关键字：医院感染；人工智能；文献计量分析；CiteSpace

Colistin Methanesulfonate Is Efficacious and Safe for The Management of Serious Infections in Hematological Diseases Patients: A Retrospective Study in China

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Objectives Serious infection is a significant contributor of increased mortality in hematological diseases patients. This study aims to analyze the efficacy and safety of colistimethate sodium (CMS) in the treatment of serious infections in Chinese patients with hematological diseases

Methods We performed a retrospective study of hematological diseases patients who were diagnosed as serious infection and treated with CMS between November 2021 and July 2023 in the First Affiliated Hospital of Soochow University in Jiangsu. Demographics, clinical presentation, causative organism, clinical outcomes and adverse events (AEs) were recorded. The univariate analysis of clinical efficacy and renal insufficiency was conducted

Results Of 190 hematological patients, clinical cure was seen in 72.11% of patients, bacteriological eradication rate was 71.05% and 28-day all-cause mortality was 13.68%. The median length of ICU and hospital stays was 13.5 and 32.5 days. AEs were reported in 30 patients, including 27 (14.21%) renal insufficiency, 1 (0.53%) circumoral numbness, 1 (0.53%) pruritus cutanea and 1 (0.53%) rashes. Univariate analysis showed a significant correlation between clinical failure and age, past medical history, APACHE II score, Charslon comorbidity index, SOFA score at initial infection, transplantation, septic shock, mechanical ventilation, vasoactive drugs, and bloodstream infection ($P < 0.05$). Aplastic anemia (AA) was the only predictor of renal insufficiency in hematological diseases patients

Conclusion Our results confirmed that in Chinese patients with hematological diseases, CMS was effective in treating serious infections while maintaining an acceptable toxicity profile, providing strong clinical evidence of the application of CMS in patients

关键字：Colistin methanesulfonate; Hematological diseases patients; serious infection; efficacy; safety

The Impact of Three Carbapenems at A Single-day Dose on Intestinal Colonization Resistance Against Carbapenem-resistant Klebsiella Pneumoniae

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Gut microbiota play a crucial role in providing colonization resistance against multi-drug resistant organisms including carbapenem-resistant Klebsiella pneumoniae (CRKP). However, the impact of different carbapenems on intestinal colonization resistance against CRKP remains poorly understood. In this study, we aimed to investigate the effects of three commonly used carbapenems (meropenem, imipenem and ertapenem) administered at single-day doses, which are typically employed in emergency departments for managing infected patient, on CRKP gut colonization. We conducted experiments in mice by intravenously administering each carbapenem using human-simulated one-day regimens. The composition of the gut microbiota was analyzed using 16S rRNA amplicon sequencing before and after carbapenem administration. Our results revealed that all three carbapenems, when administered at a single-day dose significantly altered the abundance and diversity of the gut microbiota, leading to compromised colonization resistance against CRKP. Notably, the ertapenem and imipenem groups showed an increase in Allobaculum, Bifidobacterium, Enterobacteriaceae, while the meropenem and imipenem groups exhibited a decrease in Ruminococcaceae, S24-7, and Akkermania. Additionally, the Shannon index exhibited a negative correlation with both the number of days of CRKP colonization CFUs and the duration of bacteria shedding. Furthermore, the count of CRKP in mice after ertapenem administration on the first day and the duration of CRKP shedding were significantly lower compared to meropenem and imipenem. Predictive metabolic pathway analysis demonstrated that the three carbapenems similarly affected a range of metabolic pathways of gut microflora, including carbohydrate metabolism and vitamin B. Our findings emphasize that ertapenem, with its relatively narrow spectrum minimizes perturbations of the gut microbiota and has a relatively less impact on gut colonization resistance against CRKP.

关键字：carbapenem, intestinal microbiota, colonization resistance, CRKP, 16S rRNA

某三级医院美罗培南集采前后使用分析及报量体会

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目的 通过分析某三级医院美罗培南集采前后使用数据，评估集采政策对该药临床应用的影响，提高后续抗菌药物集采采购量的测算精准度。

方法 临床药师对该院美罗培南集采前后（2022 年 1-11 月 vs. 2023 年 1-11 月）的使用数据进行分析，比较集采前后使用数量、用药总金额、使

用强度、DDDc、患者该药平均次均费用等，评估集采政策对美罗培南临床使用的影响。

结果 美罗培南纳入集中采购后，使用数量约为当初集采报量（以 2021 年医院采购量为基数）的 70 倍；较集采前用量增长 235.86%，用药金额较前下降 79.91%；使用强度为集采前的 2.4 倍（0.17 vs. 0.41）；患者日均费用（DDDc）下降 88.53%；患者该药次均费用大幅下降 92.42%（5396.41 元 vs. 409 元）。

结论 1.美罗培南集采后，极大减轻了患者的经济负担，节约了国家医保基金的使用。2.该院美罗培南集采后实际使用量远大于集采报量，且较集采前用量也有大幅上升，分析其原因可能为：①对采购时间不足一年的新进品种，药剂部门未根据网采平台反馈的采购数量进行年度用量换算；②从报量完成到执行集采合同有较长时间，期间医院科室业务调整、新增病种、收治患者病情严重程度发生变化；③医疗机构对顺利完成集采任务及特殊使用级抗菌药物滥用存在担忧。3.优化集采药品报量方法①报量前，应关注新进院品种，对采购周期不足一年的品种进行年度换算预测；②应结合医院发展计划、病种变化及同类药物影响等进行仔细测算，提高报量准确性；③临床药师可提升抗菌药物管理的参与度，通过科室宣教、处方审核/点评、用药干预等方式促进集采抗菌药物（尤其是特殊使用级）的合理使用。

关键字：抗菌药物，美罗培南，集中带量采购，采购量测算

医用材料改良与念珠菌生物膜防治进展综述

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目的 由于念珠菌是人体内正常菌群的组成部分，因此可机会性附着在植入体内的材料上形成生物膜；同时病原菌也可能通过医务人员的操作，在植入前或植入医用材料过程中污染材料，进而形成生物膜，并引发继发的真菌感染。念珠菌血流感染致死率高，其中 70.0%与生物膜相关。目前已知的影响念珠菌生物膜在医用材料上形成能力的因素中，念珠菌自身的生物因素阐释较为详细，而材料性质因素（材料自身的物理、化学性质）和植入体内的环境因素（材料植入位置的人体环境）的相关研究较少。为此，本文综述了材料性质与植入环境对念珠菌形成生物膜能力的影响及医用材料的改进等方面的研究成果与进展。

方法 材料自身的性质如表面粗糙度、疏水性、气孔率、化学成分和电荷数等直接影响念珠菌在其表面的粘附作用及形成生物膜的能力。此外，患者医疗的需求决定了不同身体部位所需使用的医疗器械种类与材料性质，进而因相应植入环境中的微生态因素（包括念珠菌与其他微生物的种类分布与丰度）与宿主因素（体液环境中的生物大分子及材料表面修饰层性质），影响念珠菌生物膜在医用材料表面的形成可能性与能力。

结果 通过医用材料的改进，包括使用抗菌药物及其他活性分子功能化处理，以及高分子、纳米材料等新材料的改进与应用，可提升医用材料的抗念珠菌生物膜形成性能。

结论 材料自身的物化性质与植入环境是影响念珠菌生物膜形成的重要因素，通过使用抗真菌药物和其他抗真菌活性分子功能化材料，和对材料本身进行改进及应用新的抗真菌材料，可以抑制念珠菌生物膜形成，降低患者医疗负担，并改善临床结局。本文特别综述了通过改进医用材料防治念珠菌生物膜的研究进展，为植入物相关念珠菌病提供了新的思路与方法。

关键字：念珠菌生物膜，侵袭性真菌感染，医用材料

Microsatellite Markers for Genotyping of Kodamaea Ohmeri: Demonstrating Outbreaks Based on A Multicenter Surveillance Study in China

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Objective Kodamaea ohmeri, an emerging human pathogen, caused both sporadic and nosocomial infections among immunocompromised people with high mortality. However, there is limited research on the molecular epidemiology of K. ohmeri.

Methods A total of fifty microsatellite loci were designed based on K. ohmeri type strain NRRL Y-1932 and three loci were finally selected for microsatellite analysis. Non-duplicated K. ohmeri isolates and strains of other species were collected across China as a part of CHIF-NET program for sensitivity and specificity verification. Antifungal susceptibility was determined using Sensititre YeastOne TM YO10

Results The three loci (P10, P11 and P26), with a cumulative discriminatory power of 0.98, exhibited a

prospective specificity and reproducibility in the PCR of 92 K. ohmeri strains from different hospitals. A total of 54 microsatellite types (MT) were identified and most of them distributed sporadically. However, six strains of MT12 clustered in HZ hospital and were isolated in the same department within two months, indicating a potential outbreak. Of seven isolates exhibited MIC values of >8 mg/L for fluconazole, three isolates from LR hospital shared the same genotype of MT44

Conclusion Herein, we established a set of microsatellite loci for K. ohmeri, as a rapid and specific tool for genotyping K. ohmeri, and identified several potential clusters. This study will help us better understand the molecular epidemiology of the emerging pathogen K. ohmeri.

关键字：Microsatellite, Kodamaea ohmeri, Outbreaks

基于构建药物浓度监测 CDSS 系统提高住院患者抗菌药物浓度采集正确率

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目的 从临床护士视角出发，在品管圈护理质量改进活动背景下，应用基于 CDSS 系统构建的基于患者个体情况、治疗医嘱以及抗菌药物组的抗菌药物血药浓度监测标本采集 CDSS 系统提高住院患者抗菌药物浓度采集正确率的效果，为改进临床护理质量，规范抗菌药物浓度血标本采集流程，提高采集正确率提供借鉴。

方法 在把握科室现状的基础上，以品管圈护理质量改进活动为背景，以提高住院患者抗菌药物浓度采集正确率为主要目标，分析住院患者抗菌药物浓度采集正确率低下的原因，以循证护理思想为核心，根据实际情况归纳最佳证据，制定抗菌药物浓度血标本采集流程和考核标准、联合临床决策系统(CDSS)对抗菌药物浓度血标本采集时间落实标准化并进一步实施。 采用前后对照方法，于活动开展前、后收集本科室住院患者抗菌药物浓度血标本采集和送检情况作为研究对象。统计品管圈活动实施前后患者的抗菌药物浓度标本采集正确率情况。

结果 实施基于循证护理理念的改进措施后，抗菌药物浓度采集正确率由 60.5%提高至 93%（P＜0.05）。

结论 品管圈活动提高了抗菌药物浓度采集正确率；CDSS 系统的开发，解决了护理人员因相关药理知识缺乏导致采血时间节点不正确这一难题，提高了临床护理质量，为后续解决类似护理质量问题提供了新的解决方法和思路。

关键字：抗菌药物浓度监测；品管圈；临床决策系统；住院患者

运用 AMS 和多元干预策略整体提升全市各级医疗机构抗菌药物合理应用水平

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目的 国家自颁布关于加强抗菌药物合理使用的文件以来，二级医院和基层乡镇医院滥用抗菌药物的问题仍然非常突出。如何提高临床抗菌药物合理使用水平方面还未形成一套切实可行的运行模式。本研究通过运用 AMS（抗菌药物科学管理体系）和多元干预策略来整体提升全市各级医疗机构抗菌药物合理应用水平。

方法 一、粤北人民医院组建起本院的 AMS 团队：1.建立由院领导作为总责任人的本院 AMS 团队和 MDT 核心团队，发布抗菌药物管理制度。2.医务处及质控科，临床科室，药学部，院感科，信息科，微生物科等明确各自责任。3.组建抗疑难感染的多学科联合会诊的 MDT 核心团队，包括临床抗感染专家、临床药学专家和微生物检验专家、影像学专家等，每月开展会诊活动，起到引领作用。二、在完成院级 AMS 团队建设的基础上，我院牵头组建市级 AMS 专家组和 MDT 团队，邀请了广州呼吸健康研究院抗感染专家团队等，对全市二级以上医疗机构的抗菌药物 MDT 团队进行系统培训和技术指导，加强抗菌药物监测网和细菌耐药监测网建设。三、经过调研，市 AMS 专家团队针对各级医院存在问题拟定具体的帮扶工作计划，定期开展日常管理和指导工作。四、具体的多元干预措施：1.行政发文要求；2.编写面向基层的简明培训教材并开展培训；3.推行处方点评；4.开发嵌入医嘱系统的抗菌药物合理应用辅助软件；5.开发应用微信软件；6.定期督查。

结果 1.经过 AMS 实践，粤北人民医院的各项抗菌药物使用指标均持续向好。2019～2021 年，医院的住院患者抗菌药物使用率从 44.43%下降至 34.01%，使用强度（DDDs）从 40.0 左右降低至 37.5 左右，门、急诊患者处方使用率从 21.74%下降至 10.64%，I类切口手术预防性抗菌药物使用率从 28.43%下降至 24.89%，抗菌药物使用金额占比从 15.01%下降至 9.42%，明显优于全国同类医院的平均水平。全市二级以上医院的监测数据同样向好。2.运用 AMS 和多元干预策略的基层医院的急性呼吸道感染患者抗菌药物平均处方率从从 70%以上下降至 25%左右；而未进行多元干预的对照组的比例仍

在 50%以上。目前，我院各项监测数据在国考中均取得满分。

结论 我院作为省级区域医疗中心，承担引领责任和义务，在全国率先组建市级 AMS 领导团队和临床抗疑难感染的 MDT 技术团队，运用 AMS 和多元干预策略，积极主动帮扶基层医院，提升基层医生的抗菌药物合理应用水平，显著降低处方抗菌药物使用率。建立起整个区域内各级医疗机构上下联动、协调一致，共同提升抗菌药物合理应用水平、遏制细菌耐药的区域合作模式，取得显著成效，保障了医疗质量，造福整个地区的患者。

关键字：AMS，多元干预，全市医疗机构，抗菌药物合理应用，

Clinical and Economic Evaluation of Blood Culture Whole Process Optimization in Critically Ill Adult Patients with Positive Blood Cultures

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Objective Optimizing blood culture processing is important to ensure bloodstream infections are accurately diagnosed while minimizing adverse events caused by antibiotic abuse

Methods We evaluated the impact of optimized blood culture processes on antibiotic use, clinical outcomes and economics in intensive care unit (ICU) patients with positive blood cultures. From March 2020 to October 2021, our microbiology laboratory implemented a series of improvement measures, including the clinical utility of Fastidious Antimicrobial Neutralization (FAN® PLUS) bottles for the BacT/Alert Virtuo blood culture system, optimization of bottles reception, graded reports and an upgraded Laboratory Information System. A total of 122 ICU patients were included in the pre-optimization group from March 2019 to February 2020, while 179 ICU patients were included in the post-optimization group from November 2021 to October 2022

Results Compared with the pre-optimization group, the average reporting time of identification and antimicrobial sensitivity was reduced by 16.72h in the optimized group. The time from admission to targeted antibiotic therapy within 24 h after receiving both the Gram-stain report and the final report were both significantly less in the post-optimization group compared to the pre-optimization group. The average hospitalization time was reduced by 6.49 days, the average antimicrobial drug cost lowered by $1,720.85 and the average hospitalization cost by $9,514.17 in the post-optimization group

Conclusion Optimizing blood culture processing was associated with a significantly increased positive detection rate, a remarkable reduction in the hospital length of stay and in hospital costs for patients in the ICU with bloodstream infections

关键字：bloodstream infections; blood culture; emergency department; process optimization; economic anlaysis

云南省某院 2022-2023 年 CRKP 耐药性及碳青霉烯酶基因分析

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目的 分析昆明医科大学第一附属医院 2022 年 8 月-2023 年 8 月碳青霉烯类耐药肺炎克雷伯菌（carbapenem resistant Klebsiella pneumoniae，CRKP）的耐药性及碳青霉烯酶基因的分布情况，为临床治疗提供指导依据，并为后续研究中耐药基因的变迁提供溯源资料。

方法 收集昆明医科大学第一附属医院 2022 年 8 月-2023 年 8 月临床分离的 CRE 菌株，采用 K-B（Kirby-Bauer）法及 VITEK-2 Compact 微生物鉴定药敏系统进行药敏分析，PCR 方法检测耐药基因，药敏结果参照美国临床及实验室标准化协会（CLSI）M100 第 33 版标准判读，统计分析应用 WHONET 5.6 软件进行。

结果 2022 年 8 月-2023 年 8 月我院共分离 CRE232 株，其中 CRKP 分离率为 90.10%（209/232），主要分离自重症监护病房，占 60.29%（136/209），其次为神经外科及呼吸内科，分别占 8.61%（18/209）、8.13%（17/209）；主要标本来源为痰液 37.80%（79/209）、血液及无菌体液 19.14%（40/209）、直肠拭子 15.31%（32/209）、尿液 10.04%（21/209）、肺泡灌洗液 9.09%（19/209）；分离的 CRKP 菌株对氨苄西林、头孢西丁、阿莫西林-克拉维酸 100%耐药，对美罗培南、厄他培南及亚胺培南的耐药率分别为 99.04%、99.04%、96.17%，对替加环素、头孢他啶/阿维巴坦、粘菌素（多粘菌素 B）、复方新诺明、阿米卡星、庆大霉素的耐药率分别为 0.55%、6.63%、8.28%、76.92%、78.47%、85.17%；检出的耐药基因分布为 blaKPC77.99%（163/209）、blaOXA-48 8.61%（18/209）、blaNDM6.22%（13/209）、blaIMP0.96%（2/209）、同时携带 blaKPC 及 blaNDM0.48%（1/209）、同时携带 blaKPC 及 blaOXA-480.48%（1/209），本研究中未检出 blaVIM，共有 8（5.26%，11/209）株 CRKP 未检出本研究所检测的耐药基因。

结论 本研究中分离的 CRKP 所携带的耐药基因以 blaKPC、blaOXA-48 为主，目前 CRKP 对临床常用抗生素的耐药情况不容乐观，应积极采取预防措施控制 CRKP 的传播，并寻求新型治疗方法以应对 CRKP 的感染。

关键字：碳青霉烯酶； 肺炎克雷伯菌； 耐药基因； 耐药性

肛拭子主动筛查降低神外重症监护病房碳青霉烯类抗菌药物耐药的肠杆菌目细菌（CRE）院内感染

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目的 对我院神外重症监护病房（NICU）患者采用肛拭子主动筛查，分析主动筛查降低碳青霉烯类抗菌药物耐药肠杆菌目细菌（CRE）医院内感染中的作用。

方法 选取 2021 年 7 月 1 日—2022 年 6 月 30 日所有入住某院 NICU 的 323 名患者，2021 年度未进行主动筛查的患者为对照组；2022 年度进行肛拭子主动筛查的患者为干预组。运用 Pearson 卡方检验等统计学比较两组患者 CRE 的感染情况，分析患者肛拭子 CRE 主动筛查及阳性患者的相对隔离对控制 CRE 院内感染的作用。

结果 NICU 肛拭子主动筛查的病原菌主要为肺炎克雷伯菌（91.8%），其主要 CRE 酶型为 KPC-2；其次为大肠埃希菌（8.2%），其主要 CRE 酶型为 NDM-1。对照组共 162 例患者，CRE 感染率 8.6%，干预组共 162 例患者，CRE 感染发病率 3.1%；两组比较差异有统计学意义（卡方值=4.471，P=0.034 < 0.05），同时发现与不进行主动筛查相比，神外重症病房住院患者采取主动筛查并隔离措施，可以使 CRE 的感染的风险下降为原来的 33.9%（95%CI 0.119-0.964）。

结论 肛拭子主动筛查可以尽早识别 CRE 携带者和对阳性患者的相对隔离措施，可有效降低 NICU 患者 CRE 感染风险。

关键字：CRE， 院内感染， 主动筛查

Epidemiological Characteristics and Antimicrobial Resistance Change of Carbapenem-resistant Klebsiella Pneumoniae and Acinetobacter Baumannii During The COVID-19 Pandemic: An Interrupted Time Series Analysis in A Large Teaching Hospital

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Objective To investigate the epidemiological characteristics and resistance change of carbapenem-resistant organisms (CROs) before and after the COVID-19 outbreak to provide evidence for precise prevention and control measures against hospital-acquired infections during the pandemic

[Method]

The distribution characteristics of CROs (i.e., carbapenem-resistant Klebsiella pneumoniae and Acinetobacter baumannii) were analyzed by collecting the results of the antibiotic susceptibility tests of diagnostic isolates from all patients. Using interrupted time series analysis, we applied Poisson and linear segmented regression models to evaluate the effects of COVID-19 on the numbers and drug resistance of CROs. We also conducted the stratified analysis using the Cochran-Mantel-Haenszel test.

Results The resistance rate of carbapenem-resistant Acinetobacter baumannii (CRAB) was 38.73% higher after the COVID-19 outbreak compared to before ($p < 0.05$). In addition, the long-term effect indicated that the prevalence of CRAB had a decreasing trend ($p < 0.05$). However, the overall resistance rate of Klebsiella pneumoniae did not significantly change after the COVID-19 outbreak. Stratified analysis revealed that the carbapenem-resistant Klebsiella pneumoniae (CRKP) rate increased in females (OR = 1.98, $p < 0.05$), those over 65 years old (OR = 1.49, $p < 0.05$), those with sputum samples (OR = 1.40, $p < 0.05$) and those in the neurology group (OR = 2.14, $p < 0.05$)

Conclusion The COVID-19 pandemic has affected the change in nosocomial infections and resistance rates in CROs, highlighting the need for hospitals to closely monitor CROs, especially in high-risk populations and clinical departments. It is possible that lower adherence to infection control in crowded wards and staffing shortages may have contributed to this trend during the COVID-19 pandemic, which warrants further research

关键字：antimicrobial resistance, multidrug-resistant organisms, nosocomial infection, COVID-19, interrupted time series

Comparison of Fitness Cost and Global Transcriptome Profile of Hypervirulent Klebsiella Pneumoniae ST23 Acquired Different Carbapenemase-encoding Plasmids

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pital of Anhui Medical University, Hefei, Anhui Province, People's Republic of China;

Objective To investigate the effects of carbapenemase-encoding plasmid acquisition on the fitness cost and global transcriptome profile of hypervirulent Klebsiella pneumoniae (hvKP)

Methods We compared the transcriptome profile, related fitness cost, and bacterial virulence of hvKP after acquiring a carbapenem plasmid

Results The plasmid stability of both carbapenem-resistant hvKPs (CR-hvKPs) decreased to varying degrees. Further, competitive index values indicated significant fitness defects in CR-hvKPs compared with hvKP. Moreover, the growth rate, and capsule and biofilm production decreased significantly in CR-hvKPs compared with hvKP. The transcriptome analysis revealed a dramatically different expression of 222 and 148 genes in KP54798-pAKPC-2 (128 upregulated and 94 downregulated genes) and KP54798-pANDM-1 (97 upregulated and 51 downregulated genes), respectively. The expression of genes involved in carbohydrate transport and metabolism, enzyme biosynthesis, and amino acid transport and metabolism increased, whereas that of genes related to capsule biosynthesis and virulence factors significantly reduced

Conclusion When hvKP acquired the carbapenemase-encoding resistance plasmid, the expression of genes involved in carbohydrate metabolism, antibiotic resistance, related fitness cost, and virulence decreased significantly. Moreover, the expression of genes involved in bacterial capsular polysaccharide production decreased, leading to a decrease in bacterial virulence. The blaKPC-2-carrying hvKP isolate exhibited a more significant decrease in bacterial capsular polysaccharide production, bacterial virulence factors, and fitness cost than the blaNDM-1-carrying hvKP isolate

关键字：Hypervirulent K. pneumoniae, carbapenemase-encoding plasmids, transcriptome, fitness cost, virulence

A Single Hospitalized Patient Hub Mediating Interspecies Transfer and Clone Spread of Mcr-1 Resistance

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Objective Infections caused by colistin resistant bacteria have very limited treatment options and high patient mortality, mcr-1deteriorates colistin resistance globally. It is urgent need to prevent its transmission in the clinical settings. The value of transmission and spread of mcr-1 from a single specific patient needs to be clarified

Methods In this study, a long-term hospitalized patient (hereinafter referred to as Z) were continuously sampled to investigate the occurrence and spread of mcr-1 resistance in Enterobacterales. Meanwhile, clinical isolates of other hospitalized patients in the same ward during Z's hospitalization were collected for comparative analysis. The transmission of mcr-1 in patients and spread in the wards was observed and confirmed by plasmid conjugation test and comparative genomics analysis

Results From February 2016 to March 2019, a total of 37 mcr-1 positive strains (Escherichia coli, n = 27; Klebsiella aerogenes, n = 9; Klebsiella. quasivariicola, n = 1) were isolated from clinical specimens (sputum, n = 11; urine, n = 24; faeces, n = 2) of patient Z. All of E. coli and K. aerogenes were ST2599 and ST56, respectively. The patient Z acquired first hospital lung infection at 29 days after admission. Sputum culture confirmed the first mcr-1 positive K. aerogenes, and three days later, E. coli and K.quasivariicola with mcr-1 were isolated from the patient faeces. All the three isolates were resistant to colistin, and carried an IncI2 ~66 kb plasmid encoding mcr-1, with sequence identity as 100% each other. Plasmid conjugations successfully transferred the plasmids from the three species to E.coli EC600 and stably maintained in the recipient , which suggested interspecies transmission of the plasmid. The plasmid has a powerful system, the stbAB operon, that can maintain plasmid replication and segregation. Moreover, patients repeatedly treated with cefoperazone-sulbactam during hospitalization might promote the selection and maintenance of resistant plasmid carrying both mcr-1and blaCTX-M-199 in E. coli. One of nine mcr-1 positive strains from other patients was E. coli ST2599 (isolated on December 10, 2018) carrying the same plasmid as that of patient Z, which indicated clonal transmission of mcr-1 positive bacteria in the ward

Conclusion A single inpatient can be either a mcr-1 hub to mediate resistance plasmids transmission between different species or a origination for the clonal spread of colistin-resistant bacteria, which realize the quick dissemination of resistance. It is necessary to strengthen the screening of mcr-1 positive strains and take control actions

关键字：IncI2; MCR-1; single patient; Enterobacterales；transmission

重症科室微生物耐药性防控策略研究进展

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目的 梳理总结国内外重症科室微生物耐药性防控策略，指导我国重症科室更好地进行微生物耐药性预防与管理。

方法 通过文献研究法、内容分析法等方法对国内外重症科室微生物耐药性防控策略进行研究，总结已有微生物耐药性防控的策略、特点及实施内容。

结果 当前实施成效显著的重症科室微生物耐药性防控策略包括规范 ICU 抗生素使用、利用临床监测指标指导临床诊疗、多学科协作推进抗生素管理计划、提高感染控制措施的依从性以及关注重点人群，加强耐药菌筛查等。

结论 重症科室作为医院耐药细菌感染预防控制的重要枢纽，更应采取积极有效的感染防控措施，做好监测预警、感染控制、评价监督等全链条防控工作，减少重症科室耐药细菌的产生和传播。

关键字：重症科室；微生物耐药性；防控策略

碳青霉烯类药物临床应用合理性及干预措施效果分析

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目的 根据全国抗菌药物应用监测网数据分析及反馈，2019 年来天津碳青霉烯类药物使用强度显著高于全国平均水平。为进一步规范碳青霉烯类抗菌药物临床应用管理，提高碳青霉烯类抗菌药物临床应用水平，本研究分析总结天津市碳青霉烯类药物临床应用合理性及干预措施效果 。

方法 本研究分析天津市 85 家 2019 年至 2022 年碳青霉烯类抗菌药物临床应用监测数据，根据上报数据汇总近三年机构各类碳青霉烯类抗菌药物使用强度情况，2022 年通过开展重点单位碳青霉烯类抗菌药物应整用专项点评、抗菌药物合理应用专项督导、培训学习、相关病例点评、定期反馈改进结果、追踪组织数据上报、特殊级抗菌药物会诊专家考核、行政管理培训等作为干预措施强化特殊使用级抗菌药物管理。

结果 整体而言天津市涉及碳青霉烯类药物使用的医疗机构数量逐年增加，近 3 年碳青霉烯类药物使用强度呈上升趋势，2021 年碳青霉烯类药物使用强度较 2019 年增幅为 54.6%，其中厄他培南使用强度增幅为 101.1%，美罗培南使用强度增幅为 44.7%，其中美罗培南使用强度增加为二级及以下医疗机构碳青霉烯类使用强度显著增加的主要因素。各医疗机构专项病例自评用药合理性平均 67.8%。通过系列干预措施，2022 年天津市碳青霉烯类抗菌药物使用强度 3.65 DDDs，较 2021 年 4.03 DDDs 下降 10%。

结论 天津市 2022 年通过多举措、多种形式干预措施提升碳青霉烯类抗菌药物应用合理性，遏制细菌耐药，进一步提升医务人员规范诊治细菌真菌感染及抗微生物药物合理应用水平。抗菌药物应用管理是一项持续的工作，应进一步加强医疗机构的抗菌药物管理、加强医务人员的培训与学习，促进我市抗菌药物应用水平整体提升。

关键字：抗菌药物，管理，碳青霉烯，抗菌药物使用强度

Development of Implementation Facilitation Strategies To Promote Etiological Submission Prior To Antibiotic Treatment Using The CFIR-ERIC Strategy Matching Tool

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Objective Enhancing the etiological submission rate before antibiotics treatment has been designated as one of the Ten National Medical Quality and Safety Improvement Goals of China. Despite the implementation of national activities, the persistently low submission rate and limited attention from healthcare professionals remain prevalent issues in Chinese medical institutions. Furthermore, there is a notable absence of robust facilitation strategies designed to promote the successful integration and long-term sustainability of pertinent policies and guidelines within clinical practice. This study aimed to: 1) explore the factors contributing to the variance of etiological submission rates before antibiotic treatment among hospitals, and 2) develop implementation strategies aimed at fostering etiological submission before antibiotic treatment accordingly

Methods This study used a qualitative study design and was conducted in June 2023. Eleven interviewees representing different healthcare professionals, including doctors, nurses, pharmacists, clinical laboratory technicians, and staff from hospital infection management departments, were invited from pioneer hospitals (n=6) participating in the Etiological Submission Rate Improvement Project of Guangdong province and non-pioneer hospitals (n=5). The interviewees were queried

about their experiences with etiological submission before antibiotic treatment, covering aspects such as knowledge and performance, perceived necessities, initiated policies or activities, and encountered difficulties. The interviews were recorded, transcribed, and analyzed using a deductive approach to identify facilitators and barriers related to etiological submission, following the framework of the Consolidated Framework for Implementation Research (CFIR). A cross-case comparison method was employed to evaluate the valence and strength of all identified constructs across different cases and a "construct-evaluation" matrix was created to identify constructs exhibiting significant differences across cases. The CFIR-ERIC (Expert Recommendations for Implementing Change) strategy matching tool will be applied to generate a list of strategies that are believed to be potentially effective in dealing with the barriers

Results Seven principal constructs (barriers) contributing to the variance in the rate of etiological submission before antibiotic treatment are identified, mainly related to the domain of characteristics of individuals (i.e., knowledge & beliefs about the intervention), implementation process (i.e., reflecting and evaluating, executing, and planning), and the domain of inner setting (i.e., structural characteristics, available resources, and goals and feedback). Utilizing the CFIR-ERIC strategy matching tool, the first-level strategies (e.g., a single strategy that ≥50% of experts believe can effectively deal with implementation barriers) designed to address implementation barriers effectively are: access new funding (78%), develop a formal implementation blueprint (73%), audit and provide feedback (61%), develop and implement tools for quality monitoring (60%), conduct educational meetings (56%), and conduct a local needs assessment (50%)

Conclusion Barriers to the etiological submission before antimicrobial treatment still exist in the aspects of individuals, inner settings, and the implementation process. Further implementation trials are needed to evaluate whether the strategies generated by the CFIR-ERIC strategy matching tool could promote etiological submission practice before antibiotic treatment

关键字：Etiological submission before antibiotic treatment, Antimicrobial stewardship, Implementation science

Promoting Nurse Involvement in Hospital Antimicrobial Stewardship: A Realist Review

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Objective Antimicrobial Stewardship (AMS) is a collaborative intervention strategy aimed at promoting the selection of optimal antimicrobial regimens to improve and measure the appropriate use of antimicrobials, thereby facilitating rational use of antimicrobials, improving patient outcomes, and curbing the widespread transmission of microbial resistance. In recent years, the critical role of nurses within the AMS multidisciplinary teams has increasingly gained widespread attention and recognition. However, the complex mechanisms by which specific contexts and strategies promote the involvement of nurses in hospital antimicrobial management are not yet precise. This review aims to uncover and analyze the mechanisms and contextual factors facilitating nurse involvement in hospital AMS program interventions

Methods This study adhered strictly to the implementation method of a realist review based on the Normalization Process Theory, generating preliminary program theories through an extensive literature review and perspectives of relevant stakeholders. Systematic searches were conducted in PubMed, Medline, EMBASE, CINAHL, Web of Science, Cochrane Library, CNKI, and Wangfang. Final Context-Mechanism-Outcome (CMO) configurations were determined through thematic coding to validate the last program theories. This study is registered on the PROSPERO platform(CRD42024500647)

Results A total of 3655 articles were retrieved, with 57 studies ultimately included for synthesis analysis. Seven key CMO configurations were developed, clarifying the interplay between context, mechanism, and outcome: (1) Recognition of the indispensable role of nurses within AMS multidisciplinary teams at organizational culture and practice levels; (2) Enhancing positive perceptions and attitudes of clinical stakeholders towards the expansion of nurses' roles in AMS practices; (3) Mobilizing nurses to enhance their capability in AMS-related practices; (4) Overcoming barriers to nurse involvement in AMS practices within the hospital setting; (5) Promoting a collaborative and motivational practice environment; (6) Strengthening the impact of nurses on clinical decision-making in AMS; (7) Emphasizing continuous quality improvement and feedback on effects

Conclusion This realist review has culminated in a program theory that promotes nurse involvement in hospital AMS, highlighting the complex and dynamic mechanisms that facilitate or impede nurse involvement in AMS. It is anticipated that evidence-based strategies will promote extensive nurse participation in AMS practices through multiple mechanisms, enhancing the effectiveness of hospital AMS programs and, consequently, improving AMS efficiency and patient care quality in the hospital environment

关键字：Antimicrobial Stewardship，Realist Review, Nurse

Characterization of Antibiotic Prescription and Analysis of Influencing Factors in Pediatric Emergency Department

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Objective Antibiotics are commonly prescribed for children in hospital, especially emergency department. Having access to data from emergency departments on antibiotic prescription and understanding the factors that influence antibiotic prescription in this setting is essential for the optimization of antimriobial prescriptions which is a key point of antimirobial stewardship. This survey aimed to collect key information for children attending emergency department, frequency of antimrobial prescription, and influencing factors on it

Methods A retrospective, observational study was done at emergency departments of Shenzhen Children's hospital including children aged younger than 18 years who visited the emergency department between Jan 1, 2020, and Dec 31, 2020. Data were prospectively including general characteristics of the patient, clinical signs and symptoms, ancillary examination results, diagnosis, types and dosages of antibiotics if used. Visit time and title of the attending doctor are also included. In the descriptive analysis, we evaluated the proportion of antibiotics prescribed in different diagnosis. And we used a multilevel logistic regression model to calculate the influence of patient-level determinants, diagnostic assessment, and specific hospital determinants on antibiotic prescription in more detail

Results Overall 2100 patients were admitted on the days of survey carried out, of which 562 patients (26.8%; 562/2100) received at least one antibiotic prescription. The three most common indications for antibiotic prescribing were supurative tonsilitis(100%), tonsilitis(66.67%), sepsis(55.56%), pneumonia(53.57%) and diarrhea(39.53%). Of the 562 antibiotic prescriptions for children, the top five classes of antibacterial agents prescribed for children were second-generation cephalosporins (229, 40.75%), third-generation cephalosporins(158, 28.11%), macrolides (85, 15.12%), first-generation cephalosporins(61, 10.85%) and penicilin lactam-beta lactamase inhibitors (22, 3.91%). Hyperthermia (OR=8.0, 95% CI (1.21-52.85)), wet rales(OR=5.29, 95% CI (2.61-10.71)), elevated blood leukocyte level(OR=4.69, 95% CI (2.61-10.71)), elevated C-reactive protein (OR=11.36, 95% CI (7.89-16.35)) were positively associated with emergency antimicrobial use. Associate physicians (OR=1.18, 95% CI (0.53-2.61)) did not decrease antimicrobial utilization compared with residents. Visit at midnight(OR=0.61, 95% CI (0.40-0.92)) were negatively associated with antimicrobial use

Conclusion Respiratory tract infections are the most common type of infection with highest antibiotic prescription in paediatric emergency department. On patient characteristics, higher body temperature and mucous bloody stool were associated with an increased likelihood of antibiotic prescription. Other significant predictors were wet rales audible in lungs and high blood concentrations of leucocyte, neutrophil ratio or C-reactive protein. At hospital level, there was little difference in the impact of attending physicians and associate physicians on antimicrobial use. Forenight shifts had little effect on antibiotic use while midnight shift was associated with reduced antimicrobial use

关键字：Antimicrobial drug；Peadiatric；Emergency department；Influencing factor

中国抗真菌药物应用现状及目录优化思考

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目的 随着广谱抗生素、皮质类固醇激素、免疫抑制剂的大量使用，免疫低下或缺陷人群的增加，器官及骨髓移植、侵入性操作的广泛开展，导致侵袭性真菌感染发病率不断上升。一项旨在探索经验性抗真菌治疗与 ICU 患者死亡率之间关系的真实世界研究纳入了 1981 例入住 ICU 的侵袭性真菌感染（IFI）患者，其中 714 例患者采用了经验性抗真菌治疗，Cox 回归分析结果显示，尽早地开始抗真菌治疗（经验性抗真菌治疗）可使进入 ICU 的 IFI 患者的 28 天死亡率的降低 43%（$p<0.001$），早期有效抗真菌治疗可以改善患者预后。目前，医疗机构抗菌药目录中限定的 5 种抗真菌药能否满足临床需要，日益受到临床关注。本文旨在为临床合理使用抗菌药物以及恰当的抗真菌药物目录遴选提供参考依据。

方法 本文总结临床常见各类抗真菌药物的药理特征及适应症，探讨全身用抗真菌药物优化方案。

结果 本文总结我国抗真菌药的适应证和临床应用现状，通过药物可及性分析，可以了解到常见抗真菌药物不同特点决定了药物间不可相互替代。目前三级医院抗真菌品种多为 8 种，且相似度较高。

结论 深部真菌感染越来越严重地危害人类的健康与生命安全。当前，三级医院面临抗真菌药物品种限制，不能满足临床需求，医疗机构应当定期（1-2 年）调整抗菌药物供应目录品种结构。具有相似或者相同药理学特征的抗真菌药物不宜同时列入供应目录（如米卡芬净与卡泊芬净同属棘白菌素类抗真菌药物； AmB、L-AmB 与 ABCD 属于两性霉素 B 的不同制剂），根据真菌病病种特点选择是否将伊曲康唑纳入供应目录。医疗机构确因临床工作需要，当深部抗真菌类药物超过 5 个品种时，需要及早启动“备案”，简化临采流程，以保证尽快启动抗真

菌治疗。鉴于目前三级医疗机构普遍存在品种数受限、不能满足临床需求的现状，建议适当放宽抗真菌药物品种数限制。临床医师应充分遵从指南，正确选择抗真菌药物，以改善患者预后、降低病死率，医疗机构也应重视临床工作反馈，及时调整抗菌药物品种目录。

关键字：抗菌药物；侵袭性真菌感染；品种目录

临床药师在基层医院抗菌药物科学化管理模式中的作用

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目的 随着药品集采工作常态化、制度化开展，抗菌治疗费用明显下降的同时，抗菌药物的临床应用管理开始面临新的问题和挑战。抗菌药物大量使用引起的耐药问题，已成为全社会的严重威胁。从2022年起，我院采取抗菌药物科学化管理模式，从被动点评模式转为主动干预模式，持续改进抗菌药物应用管理，保障患者用药安全有效。该实验为了探究邛崃市医疗中心医院临床药师参与抗菌药物科学化管理后医院抗菌药物合理应用的情况，为后续科学、规范化管理医院提供依据。

方法 2022年1月至2023年12月，随机抽取我院应用抗菌药物治疗的住院患者120例为研究对象。随机数字表法分为对照组和观察组，观察组实施临床药师参与抗菌药物科学化管理模式，对照组采用常规管理模式。对比两组患者在住期间抗菌药物的联合应用情况、抗菌药物不合理应用情况、抗菌药物不良反应情况和治疗情况及管理效果。

结果 在临床药师参与的抗菌药物科学化管理模式下，观察组的抗菌药物联合应用率、抗菌药物不合理应用情况（主要体现在无指针使用抗菌药物，遴选的抗菌药物品种不适宜，联合用药不适宜，抗菌药物用法用量不适宜，用药疗程过长等方面）、抗菌药物不良反应发生率以及患者抗菌药物的管理效果方面（包括人均药物费用、人均抗菌药物费用、患者平均住院时间及抗菌药物费用占比）均低于对照组，且差异有统计学意义（$P<0.05$）。

结论 临床药师参与到抗菌药物科学化管理中，可有效减少抗菌药物联合应用率与抗菌药物不合理应用情况，提高抗菌药物的应用安全性，值得临床推广普及。同时采用抗菌药物科学化管理后可以避免抗菌药物滥用，对规范化诊疗、提升医疗质量具有积极作用。

关键字：临床药师，抗菌药物科学化管理模式，基层医院

县级医院急性胰腺炎患者抗菌药物应用分析

张红*
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目的 通过回顾性分析急性胰腺炎患者抗菌药物应用情况以及临床疗效，旨在为AP患者合理使用抗菌药物提供临床依据。

方法 本文收集2020.04~2023.03乐至县人民医院消化内科住院部收治的309例急性胰腺炎病人，统计抗菌药物使用时间、种类、临床转归等数据，分析抗菌药物应用情况以及临床疗效。

结果 本次研究患者的抗菌药物平均使用天数为5.78 d，患者平均住院周期为6.22 d，抗菌药物使用率为96.9%，其中有1.6%的两种抗菌药物联合使用，运用 SPASS 软件对病人的住院结局和抗菌药物的用药时间进行比较，并没有显著性差异（$P>0.05$）。

结论 目前，在AP患者的治疗过程中，除液体复苏、抑制胰酶活性、胃肠减压等治疗措施以外，抗菌药物的使用频率较高，存在不合理用药，其主因是由于临床医生对患者的病情评价并不全面，缺乏对抗菌药物和停药时间的判断，因此，很有可能会出现细菌耐药性，同时也会增加药物的副作用，并且从总体来看抗菌药物使用增加或者抗菌时间增加对AP转归不是决定性因素，因此，需要对医生进行教育和培训，以促使其合理用药。

关键字：急性胰腺炎，抗菌药物，应用分析

新行标下某三甲医院软式内镜和终末漂洗用水质量状况

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目的 了解上海某三甲医院软式内镜清洗消毒效果和内镜终末漂洗用水质量，为提高软式内镜清洗消毒质量和预防软式内镜相关的感染提供指导。

方法 回顾性收集2018年-2022年常态监测的软式内镜和终末漂洗用水微生物检测结果，分析不同类型软式内镜和不同来源终末漂洗用水合格情况，以及不合格标本中的常见微生物种类。

结果 五年间共采集软式内镜标本834份，终末漂洗用水515份，两者的总合格率分别为96.8%和73.2%。鼻咽喉镜和气管镜合格率均为100%，消化内镜合格率为95.7%；鼻咽喉内镜中心、呼吸内镜中心和消化内镜中心来源的终末漂洗用水合格率分别为52.6%、73.0%和77.3%；机器来源、手工清洗

槽水龙头来源和灌流管接口来源的终末漂洗用水合格率分别为 74.9%、80.2%和 65.9%，卡方检验显示，差异具有统计学意义（P<0.05）。消化内镜检出的常见致病菌前四位分别为大肠埃希菌（27.6%）、肺炎克雷伯菌（20.7%）、铜绿假单胞菌（13.8%）和分支杆菌属（13.8%）。

结论 终末漂洗用水质量和内镜清洗消毒质量仍有待于提高，特别应重视对手工清洗槽灌流管口来源终末漂洗用水的监测并提高其质量。提高消毒质量预防软式内镜引起的致病菌传播，降低患者感染风险。

关键字：软式内镜， 终末漂洗用水， 消毒，微生物监测， 感染

院内感染防控与护理的研究进展

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医院是病人密集的场所，医院环境最容易被病原微生物污染，从而为疾病的传播提供发生条件，促进医院感染的发生。如今院内感染已成为全球主要的公共卫生问题，严重影响医疗保健质量与安全，WHO 指出，10%发展中国家和 7%发达国家的患者一生中至少会发生一次医院感染。在我国，护理专业约占医院感染控制人员总数的 70%。因此，了解传染源及预防措施，提升护理人员在院内感染控制上的专业素养，是控制院内感染的重要手段。本文阐述了院内感染的背景、常见院内感染传播途径、常见传染源、院内感染预防措施、院内感染管控措施和院内感染管控措施的效果评估。院内感染防控是医疗机构保障患者安全的重要环节。为了有效防控院内感染，医疗机构需要采取一系列综合性措施。首先，强化手卫生是防控院内感染的基础，医务人员应定期进行手部清洁和消毒，以减少病原体传播的风险。其次，医疗机构需要加强医疗设备的清洁和消毒工作，确保医疗设备的安全性。此外，规范使用抗生素和合理使用激素也是防控院内感染的重要措施，避免滥用抗生素导致耐药菌株的产生。并根据我国进行院内感染防控的不足与难点，从护理人员为主导的医院感染模式的方向上提出展望。旨在为国内学者在院内感染与护理的研究上提供参考与借鉴。

关键字：院内感染，护理，院感防控

其他微生物及其感染

奈玛特韦/利托那韦疑似诱导严重血小板减少症 1 例

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目的 为奈玛特韦/利托那韦片（Paxlovid）疑似诱导严重血小板减少症的临床诊疗提供思路。

方法 对患者使用 Paxlovid 后出现血小板减少症的诊断和治疗过程进行分析。一名 79 岁中国女性，诊断为 I 型呼吸衰竭、重症肺炎、COVID-19、脓毒性休克，在奈玛特韦/利托那韦（Paxlovid）的抗逆转录病毒治疗中出现血小板减少症。患者血小板计数从 102×10^9/L 降至 6×10^9/L，即使在停用抗菌药物美罗培南和万古霉素后，血小板计数仍持续低水平。因此，Paxlovid 作为我们的首要怀疑对象。

结果 停用 Paxlovid 后（共使用 9 日），患者的血小板计数逐渐上升，第 7 天患者上升至 111×10^9/L，但该患者最终因重症肺炎导致的脓毒症休 克死亡。

结论 说明书及国内外文献均未提及 Paxlovid 可导致血小板减少症的发生，这可能与 Paxlovid 上市时间较短，信息不足有关，本案例为临床医生在 Paxlovid 治疗中可能出现的严重血小板减少症提供了新的参考。

关键字：COVID-19；奈玛特韦/利托那韦；血小板减少症

先诺特韦/利托那韦在新型冠状病毒感染治疗中的疗效观察

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目的 探讨治疗新型冠状病毒感染的国产自主研发药-先诺特韦/利托那韦在真实世界中的疗效和不良反应。

方法 回顾性选取 2023 年 5 月 2 日至 2023 年 9 月 26 日在天津市人民医院感染免疫科诊断为新型冠状病毒感染并应用先诺特韦/利托那韦治疗的成年患者，观察患者用药后的疗效及不良反应发生情况。

结果 本研究共纳入 22 例患者，平均年龄（74.9±12.9）岁，其中女性 9 例（40.9%），男性 13 例（59.1%），未接种新冠疫苗 4 例（18.2%），患者治疗前主要症状为发热、咽干咽痛、咳嗽咳痰、喘

息、恶心呕吐、乏力、晕厥、头痛、肌肉酸痛，其中咳嗽咳痰在治疗后好转率 94.4%，余症状消失率 100%，先诺特韦/利托那韦针对临床症状有效率 100%；化验室指标中快速 C 反应蛋白在药物治疗后下降（P＜0.05），淋巴细胞绝对值计数、血小板计数在药物治疗后升高（P＜0.05），结果均具有统计学差异；共有 10 例患者发生药物不良反应（46.2%），包括白细胞减少、肝功能异常、腹泻、反酸、手部皮疹和肌肉酸痛，无严重不良反应发生。

结论 对于新型冠状病毒感染的成年患者，应用先诺特韦/利托那韦可有效缓解患者的临床症状，减轻炎症反应，不良反应较轻。

关键字：先诺特韦/利托那韦，新型冠状病毒感染，真实世界研究，

罕见成人 X 连锁无丙种球蛋白血症患者接种新冠病毒疫苗的风险分析与药学监护实践

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目的 X 连锁无丙种球蛋白血症是一种罕见的原发性免疫缺陷病，该类患者接种新型冠状病毒疫苗的风险目前尚无相关报道。本文旨在探讨 X 连锁无丙种球蛋白血症患者接种新型冠状病毒疫苗的风险与可行性，为该类患者接种新冠疫苗提供参考价值。

方法 临床药师通过前期参与 X 连锁无丙种球蛋白血症患者的治疗，中期查阅文献资料分析该患者接种新冠疫苗的安全性和可行性并指导其进行新冠疫苗的接种，后期对该患者进行用药监护并密切观察该患者接种后的反应，并对患者接种新冠病毒疫苗的生活指导，全过程指导和观察患者用药与接种情况。

结果 在临床药师的药学监护和密切观察下，该患者接种疫苗后无严重不良反应，与其他常规用药无明显冲突。

结论 X 连锁无丙种球蛋白血症患者在自身感染得到控制且无禁忌症时接种灭活新冠病毒疫苗具有一定安全性，为该类患者接种新冠病毒疫苗提供了参考价值。

关键字：X 连锁无丙种球蛋白血症，新冠病毒疫苗，疫苗接种，药学监护

临床药师参与 1 例鹦鹉热衣原体重症肺炎治疗

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目的 为鹦鹉热衣原体致重症肺炎的诊疗提供一定的诊疗思路，同时为合理用药提供理论依据。

方法 回顾性分析遂宁市中心医院收治的 1 例鹦鹉热衣原体感染的重症肺炎患者的抗感染治疗经过。患者入院前外院治疗时间长达 20 天，入院时给予气管插管呼吸机辅助呼吸、糖皮质激素抗炎、经验性给予哌拉西林他唑巴坦抗感染，效果欠佳，同时送检肺泡灌洗液 mNGS 检测，入院第 3 日 mNGS 提示鹦鹉热衣原体（序列数 47677），临床药师针对病原学特点，查阅文献，并结合危重症患者病情特点，建议更换为盐酸多西环素片联合注射用阿奇霉素的个体化治疗方案，医师采纳。

结果 口服多西环素联合静脉阿奇霉素治疗鹦鹉热衣原体致重症感染效果明显，患者病情好转转出 ICU。出院后随访 4 周痊愈。

结论 临床药师全程参与鹦鹉热衣原体重症肺炎的抗感染治疗，为临床提供合理用药建议，保障患者合理用药安全。

关键字：鹦鹉热衣原体；重症肺炎；mNGS；合理用药；临床药师

上呼吸道定植金黄色葡萄球菌及其超抗原与哮喘关联性的 Meta 分析

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目的 探讨上呼吸道定植金黄色葡萄球菌及其超抗原与哮喘发病的关系。

方法 以“Staphylococcus aureus enterotoxins”、“superantigen”和“asthma”为关键词对 PubMed、Web of Science、Embase 以及 Cochrane Library 数据库进行检索，收集从建库至 2023 年 4 月公开发表的相关研究。采用 Newcastle-Ottawa Scale 量表对纳入文献的质量进行严格评价，按照 Meta 分析的要求提取并整理数据，用 Revman5.3 和 Stata12.0 软件对最终纳入的文献进行统计分析、异质性检验、敏感性分析和亚组分析等。

结果 共纳入 26 项研究。Meta 分析结果显示，上呼吸道定植金黄色葡萄球菌与哮喘患病率显著相关[OR=1.58,95%CI(1.26,3.27),P<0.05]，存在统计学差异；病例组金黄色葡萄球菌超抗原阳性率较对照组高[OR=3.12,95%CI(2.54,3.91) ,P<0.05]，存在统计学差异。

结论 上呼吸道定植金黄色葡萄球菌与哮喘存

在正相关性，金黄色葡萄球菌超抗原可能参与哮喘发病。

关键字：金黄色葡萄球菌，定植，超抗原，哮喘，Meta 分析

3 例布鲁氏杆菌感染合并脊柱炎的病例报道

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目的 探讨布鲁氏杆菌感染合并脊柱炎的临床特征、诊治方法及预后。

方法 对我院 2023 年收治的 3 例布鲁氏杆菌感染合并脊柱炎的病例进行报道。结合国内外指南、专家共识以及同期病例进行分析讨论，同时对这一类患者的临床特征、诊治方法及预后进行总结归纳。

结果 3 例患者的发病年龄均为 50-55 岁，均为不明原因腰痛伴间断发热就诊，其中 2 名患者为售卖羊肉的商贩。结合患者的流行病学接触史、临床表现和实验室检查结果、影像学检查结果等综合判断为布鲁氏杆菌感染合并脊柱炎。根据《布鲁病菌诊疗专家共识》予以一线治疗方案：多西环素+利福平+头孢曲松。经过 20 天左右的住院治疗后 2 名男性患者好转出院，出院后继续口服多西环素+利福平，1 名女性患者因合并严重肝功能不全转上级医院治疗。

结论 布鲁氏菌病是一种动物源性感染疾病，临床表现主要包括病情轻重不一的发热、多汗、关节痛和肝、脾、淋巴结肿大等等。其并发症可累及 1 个或多个局灶部位，骨关节病是最常见的，占比高达 70%。综合患者的流行病学资料、临床表现和辅助检查可做出诊断。治疗原则为早期、联合、足量、足疗程用药，必要时延长疗程，以防止复发及慢性化。治疗过程中注意监测血常规、肝肾功能等。

关键字：布鲁氏杆菌；脊柱炎

肿瘤专科医院多重耐药菌感染危险因素分析及列线图预测模型构建

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目的 探讨肿瘤专科医院多重耐药菌感染的危险因素，构建肿瘤患者多重耐药菌感染的风险预测模型。

方法 回顾性调查分析 2019 年 11 月-2023 年 1 月某肿瘤专科医院收诊的 476 例患者病例资料，分析肿瘤患者多重耐药菌感染分布特点及耐药性，单因素及多因素 Logistic 回归分析多重耐药菌感染的危险因素。将筛选所得的危险因素，采用 R 语言构建肿瘤患者多重耐药菌感染的预测风险列线图模型，并评估该模型的预测效果。

结果 单因素分析结果显示，年龄、长期卧床、糖尿病史、联用抗生素数量、抗生素使用时长、气管插管/切开、中心静脉置管、导尿管留置与多重耐药菌（MDRO）感染显著相关（P<0.05）。感染组的年龄、抗生素使用时长显著大于未感染组（P<0.05）。感染组长期卧床、联用抗生素种类≥2、有糖尿病的患者比例显著增高（P<0.05）。感染组的气管插管/切开、中心静脉置管、导尿管留置的人数比例明显更高（P<0.05）。Logistic 多因素分析结果显示，年龄、抗生素使用时长、中心静脉置管为肿瘤专科住院患者 MDRO 感染的独立危险因素（P<0.05）。基于回归结果构建列线图预测模型，该模型 C 指数为 0.8541(95%CI:0.8032-0.8876)。模型采用 Hosmer-Lemeshow 检验($\chi2$=14.27，P=0.0749＞0.05)，提示模型具有较好的区分度和拟合优度。校正曲线趋近于理想曲线。DCA 决策曲线显示高风险阈值在 0.16~1.00 时，使用该预测模型可使患者获益。另收集 2022 年 12 月-2023 年 12 月于该院住院的 100 例患者作为研究对象进行模型外部验证，其中实际有 34 例患者感染 MDRO，模型判断为 28 例，误判 6 例，灵敏度为 82.35%；实际未感染 MDRO 患者有 76 例，模型判断为 65 例，误判 11 例，特异度为 85.53%，模型总正确率为 93.00%。

结论 年龄、抗菌药物使用时长、中心静脉置管情况是肿瘤专科医院住院患者感染 MDRO 的独立危险因素。本研究构建的列线图预测模型，可较准确预测 MDRO 感染风险，有助于临床早期识别高风险病例，及时采取干预措施，减少感染的发生，可作为评估工具在临床推广应用。

关键字：肿瘤专科，多重耐药菌，危险因素，预测模型，线列图

鱼刺致星座链球菌肝脓肿

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本文为一例罕见的个案报道

病例摘要如下：患者中年女性，44 岁，主因“间断发热伴腹痛 10 天”入住我院感染内科。患者 10 天前受凉后出现发热，体温约 37.5℃，伴腹胀便秘，恶心呕吐，自行口服达喜后缓解。7 天前无明显诱因再次出现发热，体温最高 39.0℃，伴畏寒、寒颤，

伴咳嗽，干咳，就诊于外院完善胸部 CT 及腹部核磁提示右肺下叶微小实性结节、肝脓肿，予莫西沙星及克林霉素抗感染治疗 3 天后症状未见好转，予泰能抗感染治疗 1 天收入院。既往体健。

入院考虑诊断为细菌性肝脓肿，于超声引导下行肝脓肿穿刺引流，引流液为白色脓性，后引流液为血性，复查超声示被肝右叶包膜下少许包裹性积液，患者仍高热，体温 40℃，伴畏寒寒战，继续予泰能抗感染治疗，3 天后引流液减少拔出引流管，患者体温不下降，此时引流液培养报警提示阳性球菌，加用万古霉素抗感染治疗，患者体温较前下降，波动于 37-38℃，入院后 1 周复查腹部 CT 肝区可见条形高密度影， CT 重建可见异物穿过十二指肠至肝内，再次询问病史，患者发病前 1 周有进食鲈鱼史，考虑肝内条形高密度影为鱼刺可能性大，后引流液培养示星座链球菌，将抗生素更换为舒普深联合替加环素抗感染治疗，患者体温逐渐正常。入院后第三周转至普外科行腹腔镜下异物取出术，术中可见鱼刺穿过十二指肠进入肝内，行十二指肠修补术，并取出鱼刺，复查腹部 CT 肝脓肿较前明显吸收。术后顺利康复，予口服头孢克洛加米诺环素出院。

在亚洲，肝脓肿最常见致病菌为肺炎克雷伯菌，其次为大肠埃希菌，肠球菌。星座链球菌是米勒链球菌菌属，通常为条件致病菌，大部分脓肿位于口腔颌面部，而星座链球菌引起的肝脓肿较罕见。既往文献发现新英格兰曾经报道鱼刺诱发了星座链球菌菌血症，该患者以菌血症发病，后期发现肝内小脓肿，在抗感染治疗后，患者体温正常，脓肿吸收，但是医生们认为星座链球菌菌血症并不是无缘由的，在反复对比患者多次腹部 CT 后，终于在胰头部发现了一个条状高密度异物，考虑鱼刺，并进行手术最终取出异物。通过这些病例提示我们，临床情况千变万化，发现检查结果和常见情况不同后，我们目前的治疗往往不是终点，它可能只是疾病的一个过程，需要我们临床医生进一步追寻它的起点和终点，这也是这个病例给我们的启示。

关键字：肝脓肿，星座链球菌，肠穿孔

A Large-scale Surveillance Revealed That KPC Variants Mediated Ceftazidime-avibactam Resistance in Clinically Isolated Klebsiella Pneumoniae

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To effectively monitor the resistance rate and gain a deeper understanding of the resistance mechanisms behind the ceftazidime-avibactam (CZA) usage in clinical, we conducted an over two-year surveillance focusing on the opportunistic pathogen Klebsiella pneumoniae in a teaching hospital. A total of 4641 clinically isolated K. pneumoniae isolates were screened to find the CZA resistant strains by antimicrobial susceptibility testing. And the comprehensive analyses including homology analysis, conjugation experiments, clone assay, and whole genomic sequencing (WGS) were performed on screened CZA resistant strains. Totally we isolated four CZA-resistant K. pneumoniae(CZA-R-Kp) strains from four patients and three of them have accepted CZA treatment during their hospitalization, accounting 4% for resistance development rate of K. pneumoniae under CZA stress. All of CZA-resistant isolates were found to possess variants of blaKPC-2. The identified mutations included blaKPC-33, blaKPC-86, and a novel variant designated as blaKPC-129, all of which were located in the Ω loop, as detected by WGS and plasmid transfer experiments. These mutations were found to affect the amino acid sequence and spatial structure of the enzyme's active center, consequently impacting KPC carbapenemase activity. This study underscores the importance of active surveillance to monitor the emergence of resistance to CZA, which highlights the need for ongoing research to develop effective strategies for combatting antimicrobial resistance. Understanding the mechanisms behind resistance is crucial in maintaining the efficacy of CZA, a vital tool in the battle against multidrug-resistant infections.

关键字：Klebsiella pneumoniae, ceftazidime-avibactam, clinical induced resistance, gene mutation, omega loop

Molecular Epidemiology of Nontuberculous Mycobacteria in Quanzhou, Southeast China

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Objective This study aimed to investigate the molecular epidemiological characteristics and genotype distribution of non-tuberculous mycobacteria (NTM) in Quanzhou(Southeast China), providing a basis for exploring the transmission mechanism and prevention of NTM

Methods The study retrospectively analyzed the culture results of suspected tuberculosis specimens from major hospitals and CDC microbiology laboratories in Quanzhou from 2020 to 2022, and randomly selected

some strains identified as NTM by immunochromatographic assay for further sequencing and typing

Results A total of 8,337 clinical suspected tuberculosis specimens were subjected to liquid culture (BACTEC MGIT 960), of which 3,409 (40.9%) were identified as mycobacteria. Among them, 2,559 (75.1%) were identified as Mycobacterium tuberculosis complex (MTBC), and 850 (24.9%) were identified as NTM (77.7% were slow-growing and 22.3% were rapid-growing). The study found that NTM cases occurred throughout the year in Quanzhou, with a relatively high incidence in autumn; the age of patients was mainly concentrated in the 60-69 age group, and males were predominant; there were more cases in the coastal areas with warm and humid climate, such as Huian, Nanan, and Jinjiang, while there were fewer cases in mountainous areas such as Dehua, Yongchun, and Anxi. A total of 296 NTM isolates were successfully sequenced and typed, mainly including 189 strains (63.9%) of Mycobacterium avium complex and 53 strains (17.9%) of Mycobacterium abscessus complex

Conclusion Due to the diverse species of NTM and regional characteristics, it is necessary to conduct rapid identification and appropriate drug susceptibility testing of strains to lay a foundation for better diagnosis and treatment

关键字：NTM; Epidemiology; Genotype

临床药师参与一例肺部感染合并骨组织真菌播散性感染患者诊治的药学实践

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目的 为肺结核合并骨组织播散性马尔尼菲篮状菌(talaromycosismarneffei,TM)感染患者的诊疗提供精准、个体化治疗。

方法 临床药师全程参与此例患者的诊疗，提供药物治疗方案选择、药学监护、用药干预、药物相互作用、治疗药物监测和不良反应监护等药学服务。

结果 患者诊断为肺结核合并马尔尼菲蓝状菌感染后，予异烟肼 0.3g PO qd、利福平 0.45g PO qd、吡嗪酰胺 1.5g PO qd、乙胺丁醇 0.75g PO qd 四联抗结核治疗方案基础上联合两性霉素 B 胆固醇硫酸酯复合物 150mg IVD qd 治疗 10 天后，患者出现低钾血症，K+ 2.89mmol/L，临床药师考虑低钾血症很可能是两性霉素 B 胆固醇硫酸酯复合物引起的不良反应。临床药师通过自主研发的医嘱用药干预系统进行药学干预，建议补钾治疗，3 天后患者血钾恢复正常。经过强化诱导治疗后患者症状好转，予出院带药伊曲康唑康唑 200mg PO bid。由于利福平可明显降低伊曲康唑血药浓度，故建议患者定期复查伊曲康唑血药浓度，并随访 8 个月。伊曲康唑的血药浓度均在目标治疗范围内且无明显不良反应发生，复查胸部 CT 示肺结核好转，临床症状明显改善，治疗有效。

结论 结论 临床药师参与临床疾病诊疗工作，可实现多学科协作诊疗新模式，共同为患者制定精准、个体化的治疗方案，提升药物治疗效果，降低不良反应发生，促进临床合理用药。此外，减少患者医疗经济负担，提升患者就医满意度。

关键字：肺结核、马尔尼菲蓝状菌；两性霉素 B；伊曲康唑

肝硬化患者合并嗜水气单胞菌血流及皮肤软组织感染：病例报道

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患者，女性，61 岁，农民，主因“皮肤、巩膜黄染 3 月，发热伴关节肿痛 1 月”入院。患者 3 个月前曾因“口服中药（具体不详）24 天”，乏力、纳差，发现皮肤、巩膜黄染于当地医院考虑“药物性肝炎伴胆汁淤积”，给予保肝、退黄等治疗，肝功能改善后出院，继续口服保肝药。1 月前因黄疸加重再次于当地医院住院治疗，期间患者双侧踝关节肿痛、发热，体温最高 39.0°C，伴寒战，血培养见嗜水气单胞菌，粪培养见白色念珠菌，血 G 试验 139.88pg/m，白介素-6、降钙素原升高，给予“氟康唑、美罗培南”抗感染治疗后体温逐渐降至正常，左侧踝关节肿痛好转，右侧双侧踝关节仍有肿痛，MRI 示右侧胫腓骨下段、距骨、跟骨及舟骨骨髓水肿，右踝关节少量积液，关节周围软组织肿胀，骨科会诊后考虑“反应性关节炎”，给予“塞来昔布联合地塞米松”治疗后未见明显缓解。患者逐渐出现谵妄，晨起明显，血氨升高，遂转我院。门诊以“肝硬化失代偿期 肝性脑病？软组织感染？”收住入院，患者神志清楚，偶有谵妄，精神欠佳，食纳差，睡眠尚可。既往有“乙肝”病史，外院乙肝五项示 HBsAb、HBeAb、HBcAb 阳性，HBV-DNA＜100IU/ml。查体：cT36.6°C，P72 次/分，R20 次 / 分，Bp155/80mmHg。神志清，精神欠佳，皮肤、巩膜轻度黄染，未见肝掌及蜘蛛痣，扑翼样震颤阴性。腹部平坦，腹软、无压痛、反跳痛及肌紧张，肝脾肋下未及，肝区叩击痛、墨菲氏征阴性，移动性浊音阳性，右侧踝关节明显肿胀，表面呈暗红色，皮温略升高，无明显压痛。给予完善右踝关节积液穿刺抽液，右踝软组织切开引流，腹腔穿刺引流、支气管镜等检查，对踝关节穿刺液、肺泡灌洗液、痰液、粪便等标本分别行细菌、真菌培养，行肺泡灌洗液病

原微生物 NGS 检测。最终明确诊断为：1. 肝炎后肝硬化失代偿期 慢加急性肝衰竭 肝性脑病 自发性腹膜炎 腹腔积液 低蛋白血症；2.脓毒症（嗜水气单胞菌）；3.右踝皮肤软组织感染（嗜水气单胞菌）；4 真菌性肺炎；5.弥漫性血管内凝血；6.股静脉血栓形成；7.右侧小腿肌间静脉血栓形成。给予保肝、纠正低白蛋白血症、改善凝血等综合治疗，住院初给予左氧氟沙星经验性抗感染治疗。待微生物培养结果回报后，结合药敏结果及患者病情先后给予美罗培南、头孢他啶治疗嗜水气单胞菌。患者合并真菌性肺炎，给予伏立康唑治疗。后因出现自发性细菌性腹膜炎调整为利奈唑胺联合美罗培南、伏立康唑治疗。曾出现下肢静脉血栓，置入滤器预防肺栓塞。最终患者病情明显好转，出院后口服头孢克肟、伏立康唑治疗，择期取出滤器。 经治疗后，患者体温正常，右侧踝关节肿痛消失，停用头孢克肟及伏立康唑后病情无反复。

关键字：嗜水气单胞菌，血流感染，皮肤软组织感染，慢加急性肝功能衰竭，肝硬化，深静脉血栓

侵蚀艾肯菌引起化脓性腮腺炎

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患者青年女性，因左侧耳前肿胀 1+周，疼痛 3 天入院。以左侧急性化脓性腮腺炎收入本院。入院专科查体：张口轻度受限，咽喉部粘膜稍充血，未见明显的肿胀，皮温稍升高，皮完整，未见明显的红肿、破溃、压痛，质硬，未触及明显波动感，左耳耳廓无明显充血肿胀。彩超提示左侧腮腺前后径约 23mm，实质回声欠均匀，内可见多个最大约 14*5.8mm 的弱回声结节，其边界清楚，形态规则，其上可见点状血流信号。WBC11.38*10^9/L，中性粒细胞数 72.8%，CRP25.25mg/L。CT 提示左侧腮腺稍肿胀，密度欠均匀，其内可见结节状稍高密度影，大者约 2.0*1.7mm。患者急诊入院后予以头孢唑啉 1.0g 静滴 q12h 抗感染，地塞米松 10mg 静滴 qd 消炎，氯诺昔康 8mg 静滴 qd 抗炎止痛等对症处理。后因左侧腮腺炎区域一直触及硬性肿块且不能消除，复查彩超，考虑脓肿形成可能，穿刺抽出脓肿分泌物，行细菌涂片及培养，且局麻下行脓肿切开引流术。

将分泌物接种于哥伦比亚血平板、巧克力平板、麦康凯平板，放置于 35°C 5% CO2 培养箱进行孵育培养。24 h 后,血平板上可见针尖大小的不透明菌落,麦康凯平板和巧克力平板上均无生长;继续培养至 48h 后,血平板上可见扁平、中央凸起的草帽状菌落,将菌落转纯至哥伦比亚血琼脂平板，孵育 48h 后见与之前相同的菌落生长，采用 Phoenix M50 全自动药敏鉴定系统对该菌进行鉴定，鉴定为侵蚀艾肯菌，鉴定率 99.99%。参照 CLSI M45-A3 文件中的药敏方案，以及 《热病：桑福德抗微生物治疗指南（第 44 版）》，侵蚀艾肯菌的首选药敏为阿莫西林-克拉维酸，次选 TMP-SMX、氟喹诺酮类。

侵蚀艾肯菌是人类粘膜表面的正常菌群之一，是一种条件致病菌。当人体免疫功能降低、抵抗力下降或者粘膜防御功能被破坏的时候，该菌会引发感染，比如腮腺炎、肺炎、心内膜炎、鼻窦炎、软组织炎、手术后的感染，该菌可以分离于上呼吸道标本、生殖道标本以及泌尿道标本中，在人咬伤标本中也比较常见。近年来，国内外文献报道此菌可引起成人、儿童颈部脓肿，其感染可发生在有菌部位，也可发生在无菌部位，Sheng 等曾对 1993 至 1998 年 6 年间 43 例侵蚀艾肯菌感染病例进行回顾分析，该次回顾是关于侵蚀艾肯菌相关感染的一宗大型报道，其中以头颈部感染居多，也有口鼻咽部感染、颈深部感染、甲状腺感染等；除此之外，还有肺胸膜、腹腔、骨关节、骨盆、皮肤、心内膜等其他部位的感染；其感染的特点均为化脓性炎症或者伴有脓肿形成，其中感染严重的患者可伴有持续高热，炎症指标升高以及血沉加快等；其中 5 例患者最终死亡，4 例直接归因于该菌感染。

关键字：侵蚀艾肯菌，腮腺炎

支原体肺炎患者 T 淋巴细胞亚群和 NK 细胞水平的变化及其意义

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目的 研究 T 淋巴细胞亚群及 NK 细胞水平变化对支原体肺炎患者的临床预测及诊断意义。

方法 选取 2022 年 3 月至 2023 年 3 月期间到我院接受的治疗的支原体肺炎患者 20 例作为研究组，另选择同一时间段到我院接受健康检查提示咽喉部有中度充血的鼓膜炎患者 20 例作为对照组，将经健康检查后 20 例无异常人员作为健康组，分别观察研究组、对照组与健康组人员间 T 淋巴细胞亚群及 NK 细胞水平的差异，以此判定其诊断价值；并采用 ROC 曲线观察三组人员各项指标变化情况，以此判断以上指标对支原体肺炎的预测价值。

结果 研究组与健康组的各指标差异以及对照组与健康组各指标的差异均具有统计学意义（P 均＜0.05），经 ROC 曲线检验后结果显示以上指标水平变化与患者病情发展趋势呈正相关（P 均＜0.05）。

结论 T 淋巴细胞亚群是人体中检测其细胞免疫功能是否存在异常的重要指标，当患者体内出现明显的免疫功能异常及炎症反应时其 T 细胞水平会

产生明显变化，或提示患者存在免疫缺陷疾病或恶性肿瘤；而 NK 细胞是人体内天然的免疫细胞，对机体的免疫功能也有调节作用，若 NK 细胞水平出现异常则提示患者可能存在免疫功能紊乱，可能会出现一些感染性疾病及其他炎症反应。T 淋巴细胞亚群和 NK 细胞水平对支原体肺炎具有十分重要的评价功能，同时有助于判断支原体肺炎的发展趋势。监测以上各项指标可对其病情作出初步判断，对患者预后有着积极影响。

关键字：支原体肺炎；T 淋巴细胞亚群；NK 细胞；指标变化；临床价值

采用脉冲场凝胶电泳技术分析儿科重症监护病房患者碳青霉烯耐药微生物肠道定植和继发院内感染的危险因素

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目的 研究碳青霉烯耐药微生物肠道定植与院内感染的关系，为探索有效干预措施来预防 CRO 的感染和传播提供依据。

方法 本研究在实施主动筛查的基础上，分析儿童 CRO 定植及继发院内感染的危险因素。我们采用脉冲场凝胶电泳（PFGE）的方法来验证同一患者肠道定植的菌株是否与继发院感分离得到的临床标本菌株同源。

结果 2021 年 1 月 1 日至 2022 年 9 月 31 日，我院儿科重症监护病房（PICU）共纳入 1069 名患儿，其中 77 例 CRO 肠道定植，定植率为 7.2%。所有存在 CRO 肠道定植的儿童中，15 例继发同一类别 CRO 菌株所致临床感染，并可通过 PFGE 证实为同源菌株。潜在的神经肌肉疾病和住院时长是 CRO 肠道定植的独立危险因素。存在 CRO 肠道定植的儿童中，碳青霉烯类抗生素的使用和住院时长是继发院内 CRO 感染的独立危险因素。

结论 同一患儿的 CRO 定植菌株与后续发生临床感染所分离得到的菌株可被证实为同一来源，引起临床感染的病原高度可能来源于此前肠道定植的 CRO 菌株。

关键字：碳青霉烯耐药微生物，定植，主动筛查

宏基因组测序联合常规结核分枝杆菌检测对于结核病诊断的价值

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目的 肺结核是由结核分枝杆菌引起的一种慢性传染病，主要在呼吸道传播。结核分枝杆菌可以侵犯许多器官，包括肺、骨、胸膜，肺结核是最常见的肺部受累形式。据世界卫生组织统计，2021 年全世界约有 1060 万人患有结核病，其中约有 160 万人死亡。此外，与 HIV 阳性或耐药结核病感染相结合的病例死亡率更高。因此，无论是肺内还是肺外结核，早期精准检测结核分枝杆菌对于诊断结核感染至关重要。

方法 目前，结核病感染诊断的金标准主要依靠影像学和病原学证据。然而，由于样本质量和操作人员的差异，结核分枝杆菌涂片的特异性和敏感性较低。同时，培养方法耗时长，不能及时给出明确的诊断。随着宏基因组测序（mNGS）在临床上的推广和应用，mNGS 对疾病的诊断具有重要意义，尤其是在常规检测方法无法发现病原体的情况下。因此，我们首次将所有常规结核病检测方法与 mNGS 进行了比较和讨论，以期为临床提供更为优质的检测组合。

结果 通过比较 150 例同时做了以下检测的病例：TB-IGRA、TB-IgG、TB-DNA、Xpert、结核分枝杆菌培养、抗酸杆菌涂片、宏基因组测序。我们可以发现对于其他结果阴性或者由于宿主个体原因导致的假阴性结果的情况下，mNGS 方法依然能检测出病原体。

结论 通过回顾性分析 150 例经过宏基因组测序、分子生物学和免疫学方法确诊结核分枝杆菌感染的病例。我们发现 mNGS 可以作为肺内和肺外结核病感染的重要补充检测方法。

关键字：宏基因组测序、结核分枝杆菌、诊断、脑脊液、支气管灌洗液、组织、肺内、肺外

其他

Immune Dysregulation in SARS-CoV-2 Patients Coinfected with Mycobacterium Tuberculosis (Mtb) Or HIV in China

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Objective SARS-CoV-2 infections usually cause immune dysregulation in the human body. Studies of immunological changes resulting from coinfections with Mycobacterium tuberculosis (Mtb) or HIV are limited. We aim to compare the clinical and immunological characteristics between Delta infected patients and coinfections with Mtb or HIV

Methods We conducted a retrospective study focusing on patients with COVID-19. A total of 550 patients infected with SARS-CoV-2 were enrolled in our study and categorized into four groups based on the presence of coinfections; 166 Delta-infected patients, among whom 103 patients had no coinfections, 52 who were coinfected with Mtb, 11 who were coinfected with HIV, and 384 Omicron-infected patients. By collecting data on epidemiologic information, laboratory findings, treatments, and clinical outcomes, we analyzed and compared clinical and immunological characteristics. Because more than half of the patients in the Delta group were vaccinated, we analyzed subgroups of unvaccinated patients, as were the pediatric patients

Results In the Delta group, the most common symptoms at admission were fever (36 [35%]), cough (26 [25%], and expectoration (16 [16%]), which was consistent with the symptoms of the other three groups. Compared with those in the Delta group, the median white blood cell (4.10 [3.20-5.40] and 3.57 [2.58-5.46]), CD4+ T-cell (382.5 [290.5-511.8] and 246 [56-540]) and B-cell counts (108.0 [74.0-165.75] and 136 [98-153]) were lower in the Mtb group and the HIV group. Except for those in the Omicron group, more than half of the patients in the three groups had abnormal chest CT findings. Among the three groups, there were no significant differences in any of the cytokines. Compared with those in the Delta group, the disease duration (50 [26.5-96.5] and 55 [40-73]) and LOS (45.0 [22.0-91.5]and 51 [40-71]) were longer in the Mtb group and the HIV group. For unvaccinated Delta-infected patients, in the Mtb and HIV groups, the number of B cells (104 [78.0-174.8] and 136 [98-153]) and CD4+ T cells (411 [239.5-522.3] and 246 [56-540]) was lower than that in the Delta group, with no significant difference in the LOS or disease duration. In the Mtb group, three (6%) patients presented with a disease duration greater than four months and had decreased lymphocyte and IL17A counts, possibly due to double infections in the lungs caused by SARS-CoV-2 and M. tuberculosis. In the Omicron group, 61% of the pediatric patients (under 18 years old) were diagnosed with more mild symptoms. D-dimer levels were significantly greater in the Delta group (4.02 ± 10.87) than in the Omicron group (0.04 [0.01-0.09]). The LOS and disease duration were longer in the Delta group than in the Omicron group

Conclusion We found that SARS-CoV-2 patients coinfected with Mtb or HIV exhibited a longer disease duration and longer LOS, with a decrease in B cells and CD4+ T cells, suggesting that these cells are related to immune function. Changes in cytokine levels suggest that coinfection with Mtb or HIV does not result in dysregulation of the immune response. Importantly, we discovered a chronic course of coinfection involving more than four months of Mtb and SARS-CoV-2 infection

关键字：SARS-CoV-2, Delta variant, Mycobacterium tuberculosis (Mtb), HIV, Omicron variant

In Vitro PCR Verifcation That Lysozyme Inhibits Nucleic Acid Replication and Transcription

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Objective Lysozymes are a class of naturally occurring alkaline enzymes, also known as muramidase or N-acetylmuramoylhydrolase, that occur in all living organisms and viruses.Studies have shown that lysozyme has antibacterial, antiviral, antifungal, anti-inflammatory, anticancer, immune regulation and other activities.Lysozyme can kill bacteria by its enzymatic activity or through a mechanism involving its cationic nature, which can facilitate electrostatic interactions with the viral capsid, the negatively charged parts of nucleic acids, and polymerase, so binding to nucleic acids may be another biological function of lysozyme.However, most studies focus on the pharmacodynamic effects of lysozyme, with only hypotheses and inferences about the specific mechanisms.In this study, PCR was used as a research tool to detect whether lysozyme and its metabolites have inhibitory effects on the replication and transcription of nucleic acids in PCR and to provide a theoretical basis for further explaining the pharmacological effects of lysozyme, such as antibacterial, antiviral, anticancer, and immune regulation

Methods Constructing lentiviral (EmGfp), Bacillus colony (Amp) and rat liver (Grp78) genes template. To investigate the dose-effect relationship of lysozyme on the RT–PCR system of EmGfp, Amp and Grp78 genes, lysozyme was added to each PCR system at the corresponding working concentration. The products obtained through PCR were compared using gel electrophoresis. By semiquantitative analysis, with intensity measured using ImageJ, observing the inhibitory effect of lysozyme on DNA replication, transcription and reverse transcription in vitro. To verify whether the degraded regions of lysozyme can inhibit nucleic acid replication and screen the active site of lysozyme, HepG2 cell lysate, gastric juice, liver, rabbit jejunum, ileum, colon lavage fluid and fecal filtrate etc., were used to digest lysozyme, then, PCR was used as a research tool to detect the effects of lysozyme on the replication and transcription of nucleic acids after treatment in different ways

Results lysozyme had a potent and reproducible dose-dependent inhibitory effect on DNA replication, transcription and reverse transcription in vitro.The replication and transcription of the three genes showed sensitivity to low concentrations of lysozyme, while almost 10-fold levels of lysozyme could obviously inhibit the reverse transcription reaction. Consistent with the above results, the mixture of cell lysate and lysozyme inhibited DNA replication, transcription and reverse transcription in a dose-dependent manner in vitro, however, the cell culture supernatant obtained from HepG2 cells cocultured with lysozyme did not show changes in DNA replication, transcription or reverse transcription. Artificial gastric juice and rabbit liver tissue lysate-treated lysozyme inhibit the PCR process in vitro. Rabbit jejunum lavage fluid treatment somewhat enhances the inhibitory effect of lysozyme on replication, transcription and reverse transcription of EmGfp, Amp and Grp78 DNA, however, rabbit ileum, colon lavage fluid and fecal filtrate -treated lysozyme had no effect on EmGfp, Amp and Grp78 DNA replication, transcription or reverse transcription in vitro

Conclusion Our study expands the utility of PCR as a screening platform and tool for molecular biology. Lysozyme and its hydrolysate can enter cells and inhibit PCR to varying degrees in vitro. After lysozyme is degraded by gastric acid and bile acid, its ability to inhibit nucleic acid replication and transcription is greatly improved compared with that of complete lysozyme. At the same time, there was no significant difference in the inhibition in the three selected templates, but the inhibition varied widely among different systems of the same template, so we speculated that the inhibition of lysozyme may be related through binding to polymerase

关键字：Lysozyme; antibacterial; antiviral; polymerases; PCR

Integrated Analysis of Microbiome and Host Transcriptome Unveils Correlations between Lung Microbiota and Host Immune in Bronchoalveolar Lavage Fluid of Pneumocystis Pneumonia Patients

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Objective Studies have indicated that the lung microbiota of patients with pulmonary diseases is disrupted and impacts the immunity. Pneumocystis pneumonia (PCP), a severe opportunistic pulmonary infection, is predominately attributed to host immune status. Little is known about the microbiological and immune landscape of the lungs in these patients. We aimed to explore the interaction between the lung microbiota and host immunity in PCP through multi-omics analysis

Methods We selected patients admitted to Beijing Youan Hospital, Capital Medical University, from January 1, 2022 to August 31, 2022 and underwent bronchoscopy. Participants were divided into PCP and non-PCP group. We investigated the lung microbiome (via 16S rRNA sequencing) and host immune (via RNA-seq) in adult PCP patients and non-PCP individuals through bronchoalveolar lavage fluid (BALF). For transcriptome data, we assessed differential gene analysis, GO enrichment and KEGG enrichment, etc. of the two groups. We also explored the top 10 relative abundance and differential species composition of the microbiome. The linear discriminant analysis (LDA) effect size (LEfSe) was performed to identify the significantly abundant taxa (phylum to genera) of bacteria among the different groups (LDA score > 2, $P < 0.05$).Then we constructed a diagnostic model using differential microbiota and genes by machine learning. Using linear regression method, calculated the correlation between the OUT abundance of differential species and the expression levels of immune related differential genes in two groups based on the Person correlation coefficient. The significance of each OUT-gene pair was determined by a p value <0.05

Results The study enrolled 58 patients, including 19 with PCP and 39 without. The microbiota data showed a low alpha diversity of lung microbiota in PCP patients. At the level of phylum, patients with PCP displayed the microbiota signature in the lung characterized by the declined abundance of Actinobacteriota, Bacteroidota, Fusobacteriota and Campilobacterota, and the elevated abundance of Firmicutes and Patescibacteria compared to non-PCP samples. The predicted function of these differentially abundant microbiota primarily influenced immunity and metabolism. Transcriptome data analysis showed that compared with non-PCP patients, the PCP group had 3433 DEGs, of which 1103

genes were upregulated. These genes were mainly associated with immunity, inflammatory response as well as cell growth and death. Moreover, the Gene Set Enrichment Analysis (GSEA) revealed a down-regulation of the MAPK signaling pathway. The microbial marker of Firmicutes along with MAPK10, IRAK4, PGF, and FGF22 indicated a potential to predict the onset of PCP (AUC = 0.88, 0.76-0.99). The correlation analysis of the MAPK signaling pathway-related DEGs and the OTU abundance of the differential microorganisms at the level of phylum showed that the Firmicutes was negatively correlated with these DEGs

Conclusion In addition to characterizing lung microbiota and host immunity, our study indicated that the Firmicutes may negatively regulate the MAPK signaling pathway. Five indicators, including Firmicutes, MAPK10, IRAK4, PGF, and FGF22, had potential value in distinguishing PCP and non-PCP. This knowledge may pave the way for novel therapeutic strategies targeting the lung microbiota to enhance host immune defenses and improve outcomes in PCP patients

关键字：lung microbiota; host immunity; Firmicutes; MAPK signaling pathway; pneumocystis pneumonia

特发性多中心型 Castleman 病合并继发性骨髓纤维化 1 例

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目的 探讨特发性多中心型 Castleman 病（iMCD）合并继发性骨髓纤维化的诊断学特征。

方法 回顾性分析 2023 年 1 月广东省人民医院收治的 1 例 iMCD 合并继发性骨髓纤维化患者的临床资料，实验室、影像学、病理学、骨髓活检结果和诊疗情况并结合最新文献复习，以提高对 iMCD 合并继发性骨髓纤维化的认识。

结果 女性患者，38 岁，患者双侧腋窝及右侧锁骨下窝多发增大淋巴结。临床表现为发热，水肿和乏力。该患者右颈淋巴结病理结果符合浆细胞型 Castleman 病，HHV8 阴性。骨髓活检结果显示骨髓纤维化。随后患者行 8 次司妥昔单抗针（萨温珂）+TCD 方案化疗，炎症指标、低蛋白血症和骨髓造血功能均有所改善。

结论 及早完善实验室、影像、病理、骨髓活检等检查有助于对 Castleman 病合并骨髓纤维化的早期诊断和分型，司妥昔单抗的早期、全程、规范使用有助于改善病情。

关键字：Castleman 病；特发性；多中心 ；骨髓纤维化；司妥昔单抗

HIV 感染儿童营养现状及评估方法研究进展

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营养不良是人类免疫缺陷病毒（Human Immunodeficiency Virus, HIV）感染儿童常见且加速疾病进展的因素。近期的研究对 HIV 感染儿童营养不良的流行病学有了更深入的认识。目前，儿科传染病学中尚无标准化的营养状况评估方法。完整的营养评估包括人体测量、身体成分测量、生化检查、临床和饮食评估等。本文就 HIV 感染儿童营养不良的现状及营养评估方法进行综述，以期为医务人员提出提供营养管理的科学信息。

One of the main conditions that children infected with Human Immunodeficiency Virus (HIV) frequently experience is malnutrition, which has a major role in hastening the development of HIV-related illnesses. Recent studies have shed light on the epidemiology of malnutrition in children living with HIV. There is not yet a standardized technique for evaluating nutritional status in Pediatric Infectious Diseases. A comprehensive nutritional assessment includes anthropometric measurements, body composition analysis, biochemical tests, clinical evaluations, and dietary assessments. In an effort to give medical practitioners scientific knowledge for nutrition management, this paper reviews nutritional evaluation techniques as well as the current status of malnutrition in children with HIV.

关键字：艾滋病病毒，儿童，营养不良，营养评估，营养影响症状

The Effect and Mechanism of Pseudomonas Aeruginosa on The Function of Pulmonary Vascular Endothelial Cells

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Objective To investigate the impact of Pseudomonas aeruginosa (PA) infection on the function of pulmonary vascular endothelial cells, and explore the possible mechanism of its exacerbation of lung inflammation in mice

Methods Human pulmonary vascular endothelial cells (HULEC-5a) were infected with PAO1 strain

for two hours, the mRNA expression of autophagy-related gene 5 (ATG5), 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3 (PFKFB3) and calcium adhesion protein 5 (CDH5) was detected by reverse transcription real-time fluorescent quantitative PCR (RT-qPCR). The protein expression levels of ATG5, PFKFB3 and vascular endothelial calcium adhesion protein (VE-cadherin) were detected by immunofluorescence. After knocking down ATG5 and PFKFB3 respectively using small interfering RNA (siRNA), RT-qPCR was used to detect the mRNA expression of ATG5, PFKFB3 and CDH5, and the protein expression levels of PFKFB3 and VE-cadherin were detected by immunofluorescence. In addition, lactate detection kit was used to detect the level of lactate in the cells. After infecting mice with PAO1 strain, lung inflammation was assessed through histopathological section staining. Confocal microscopy was used to capture and analyze fluorescence-labeled PFKFB3 and VE-cadherin in endothelial cells

Results Compared with the control group, after PAO1 infection of HULEC-5a cells, the expression of PFKFB3 mRNA and protein in the cells increased ($P=0.025$,and $P<0.0001$),the expression of CDH5 mRNA decreased ($P=0.023$), and the continuity of VE-cadherin protein was disrupted and its expression decreased ($P<0.0001$). Additionally, intracellular lactate content was significantly elevated ($P = 0.017$). Comparing with PAO1 infection of HULEC-5a cells, knocking down PFKFB3 led to an increase in CDH5 mRNA ($P=0.043$), and intracellular lactate levels ($P=0.047$), as well as restore the continuity of VE-cadherin after PAO1 infection; knocking down ATG5 led to an increase in PFKFB3 mRNA ($P=0.013$) and protein expression levels ($P=0.003$) as well as intracellular lactate levels ($P=0.015$), while significantly decrease the expression of CDH5 mRNA ($P=0.02$) and VE-cadherin protein ($P=0.001$) after PAO1 infection. The H&E-staining results showed obvious red blood cell leakage, inflammatory cell infiltration, alveolar septal widening, and partial detachment of vascular endothelial cells in the alveoli of PA-infected mice. Immunofluorescence staining showed increased expression of PFKFB3 and decreased fluorescence signal of VE-cadherin in endothelial cells of infected mice compared to normal mice

Conclusion PA may regulate the PFKFB3 pathway through AGT5, disrupting the function of lung vascular endothelial cells, thereby exacerbating the inflammatory response in the lungs of mice

关键字：Pseudomonas aeruginosa, pulmonary vascular endothelial cell, 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3, autophagy-related gene 5, infection

A Case of Atypical Adult Wiskott-Aldrich Syndrome

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WAS is characterized by the disruption of the actin cytoskeleton in immune cells due to mutations in the causative gene located on the X chromosome's short arm (Xp11.22-p11.23) [1]. The clinical spectrum of WAS is well documented, with typical manifestations including immunodeficiency, thrombocytopenia, and eczema [2]. Over 200 variants of the WAS gene have been identified, leading to a wide range of clinical presentations [3-5]. For WAS patients under 5 years old, allogeneic hematopoietic stem cell transplantation (HSCT) has demonstrated high efficacy, with a survival rate exceeding 90% [6]. However, without timely intervention, the majority of patients succumb to the condition before reaching 20 years of age [7].

Our case report highlights an atypical WAS patient who presented with renal dysfunction, recurrent skin abscesses, and proctitis, without thrombocytopenia and eczema. The diagnosis of WAS was not made until the age of 30, missing the optimal treatment window.

Before the age of 16, the patient enjoyed good health. At 16, the diagnosis of chronic glomerulonephritis, renal hypertension, and renal failure led to three years of peritoneal dialysis before transitioning to hemodialysis. At 24, bilateral osteoporosis, secondary hyperparathyroidism, and parathyroid hyperplasia necessitated a parathyroidectomy with autotransplantation. At 26, the patient experienced constipation, rectal bleeding, and was diagnosed with proctitis. Recurrent skin abscesses appeared at the age of 22, affecting the face, axilla, and groin areas, and by the age of 28, these abscesses had spread to the waist and lower extremities (Fig. 1). Multiple bacterial cultures from lower extremity skin abscesses identified Proteus mirabilis, with limited response to various antibacterial treatments.

Laboratory findings indicated a normal platelet count but a low platelet-to-large-platelet ratio and decreased mean platelet volume. Tests for HIV, hepatitis B, and hepatitis C were negative. Immunoglobulin A (IgA) levels were significantly elevated. Additionally, cell immunology revealed reduced CD3, CD4, and CD8 counts.

Whole-exome sequencing confirmed a novel hemizygous pathogenic variant in WAS (NM_000377.3), specifically exon 2 (c.135G>A; p.Thr45=), corroborated by Sanger sequencing. His mother also carries the gene, but family history revealed no similar cases.

To contribute to a deeper comprehension of WAS in adults, we systematically reviewed clinical presentations in adult WAS patients. Our PUBMED search, us-

ing 'wiskott-aldrich syndrome [MeSH Terms],' identified 1584 articles. After rigorous manual screening for case reports of adult WAS patients aged over 18, we selected 32 articles reporting a total of 38 cases of adult WAS (Table 1).

These cases displayed varying clinical features, emphasizing the diversity of WAS presentations. Our aim is to raise awareness among healthcare professionals, encourage genetic testing, and expedite early diagnosis and treatment.

关键字：Adult Wiskott-Aldrich Syndrome; Renal impairment; Proctitis

Microbial Community of Municipal Drinking Water in Hangzhou Using Metagenomic Sequencing

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Objective While traditional culture-dependent methods can effectively detect certain microorganisms, the comprehensive composition of the municipal drinking water (DW) microbiome, including bacteria, archaea, and viruses, remains unknown. Metagenomic sequencing has opened the door to accurately determine and analyze the entire microbial community of DW, providing a comprehensive understanding of DW species diversity, especially in the context of public health concerns during the COVID-19 era

Methods culture-dependent methods and metagenomic sequencing

Results In this study, we found that most of the culturable bacteria and some fecal indicator bacteria, such as Escherichia coli and Pseudomonas aeruginosa, were non-culturable using culture-dependent methods in all samples. However, metagenomic analysis showed that the predominant bacterial species in the DW samples belonged to the phyla Proteobacteria and Planctomycetes. Notably, the genus Methylobacterium was the most abundant in all water samples, followed by Sphingomonas, Gemmata, and Azospirilum. While low levels of virulence-associated factors, such as the Esx-5 type VII secretion system (T7SS) and DevR/S, were detected, only the erythromycin resistance gene erm(X), an rRNA methyltransferase, was identified at low abundance in one sample. Hosts corresponding to virulence and resistance genes were identified in some samples, including Mycobacterium spp. Archaeal DNA (Euryarchaeota, Crenarchaeota) was found in trace amounts in some DW samples. Viruses such as rotavirus, coxsackievirus, human enterovirus, and SARS-CoV-2 were negative in all DW samples using colloidal gold and real-time reverse transcription polymerase chain reaction (RT–PCR) methods. However, DNA encoding a new order of reverse-transcribing viruses (Ortervirales) and Herpesvirales was found in some DW samples. The metabolic pathways of the entire microbial community involve cell–cell communication and signal secretion, contributing to cooperation between different microbial populations in the water

Conclusion This study provides insight into the microbial community and metabolic process of DW in Hangzhou, China, utilizing both culture-dependent methods and metagenomic sequencing combined with bioinformatics tools during the COVID-19 pandemic era

关键字：Microbial communities, Drinking water, Metagenomic analyses, Functional genes, Virus

通过肠道微生物共培养技术挖掘木犀草素和藏红花素相关的阿尔兹海默症患者治疗靶点的研究

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背景 肠道细菌和 AD 患者大脑之间存在双向交流的证据日益增多并得到了广泛认可。中药单体木犀草素和藏红花素被认为可以改善肠道菌群、改善神经退行性疾病患者的认知功能。然而 AD 患者疾病表型多样，缺乏中药单体对疾病症状改善的基础研究。

方法 于厦门大学附属第一医院收集 67 例 AD 患者的粪便标本。将粪便标本分别于木犀草素和藏红花素进行共培养。并对所有标本（n=403）进行 DNA 提取和 16S rRNA V4 区段测序。比较分析 AD 患者肠道菌群对木犀草素和藏红花素响应的独特性。

结果 木犀草素对肠球菌属、肠杆菌属、耶尔森氏菌属、埃希菌属具有靶向抑制作用，此外木犀草素对 AD 患者肠道菌群中双歧杆菌属、梭状芽胞杆菌具有靶向上调作用。藏红花素对耶尔森氏菌属、埃希菌属具有靶向抑制作用，对阿克曼菌属相对丰度具有上调作用。所有 67 例 AD 志愿者的粪便菌群可以根据主要微生物门分成 3 型、厚壁菌门型、放线菌门型和疣微菌门型。3 种表型人群对两种中药单体的响应水平不一致，表现出了人群特异性。

结论 通过对中药单体的响应水平，可以将 AD 患者的肠道菌群进行分组。后续有望通过靶向肠道菌群达到精准治疗 AD 的目的。

关键字：AD，共培养，肠道微生物组

从药学角度对硫酸黏菌素的临床应用评价与分析

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目的 从药学角度分析和评价我院住院患者硫酸黏菌素的临床应用情况，以期为该药的合理使用及方案优化提供参考。

方法 采用回顾性研究方法，调取 2021 年 1 月~2023 年 12 月间我院使用注射用硫酸黏菌素治疗的住院患者的电子病历，采集患者的一般信息、感染分布、用药情况、实验室指标、病原学检验、影像学检查、不良反应等资料，结合说明书、指南、共识和文献，评价和分析我院临床应用硫酸黏菌素的合理性。

结果 共纳入住院患者 236 例，以肺部感染为主（93.6%）；所有患者都进行了病原学检查，碳青霉烯类耐药鲍曼不动杆菌（33.44%）检出率最高；184 例（77.97%）患者采用单独静脉输注给药，40 例患者采用静脉输注联合雾化吸入给药，12 例患者采用单独雾化给药；200 例（84.75%）患者静脉给药维持剂量为 50 万 U，2 次/天；122 例（51.7%）患者用药疗程少于 10 天，68 例患者为 10~14 天，46 例超过 14 天。194 例（82.2%）患者联用了其他抗革兰氏阴性菌药物；临床主要存在用法用量不适宜（11.02%）、用药疗程不足或过长（52.97%）、联合用药不适宜（33.47%）等不合理现象。236 例患者使用硫酸黏菌素治疗的临床有效率为 45.98%，28 例（11.86%）患者用药期间发生了急性肾损伤。

结论 硫酸黏菌素在重症感染患者中的临床合理应用有待进一步探讨和规范，临床药师有必要参与到此类患者的治疗过程中，结合指南/共识给与医师个体化的治疗建议，同时加强药学监护，密切关注不良反应的发生。

关键字：硫酸黏菌素；合理用药；急性肾损伤；用药评价

惠普尔病表现为肺受累的 1 例病例及其文献分析

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目的 惠普尔养障体属于革兰阳性菌，是引起惠普尔病的病原体。本文通过探讨惠普尔病肺受累的临床特点及其诊治，为临床提供参考。

方法 报道一例肺部占位、背痛患者诊断为惠普尔养障体引起的肺炎的病例，并通过检索 1980-2022 年国内外报道的惠普尔病表现为肺受累、不涉及胃肠道症状的病例的相关文章进行综合分析。

结果 综合文献报道及我院共 13 例患者的一般情况、症状、检查及治疗等情况。惠普尔病肺受累常出现在中年男性，可能早于胃肠道症状而独立出现，并且有异常影像学表现，通过 PAS 染色、PCR、宏基因组二代测序等方法确认病原体后，经过抗感染治疗一般效果良好。

结论 临床遇到相似临床表现病例时应疑诊这一罕见病，积极寻找活检及病原学证据，及时明确诊断并进行针对性治疗。

关键字：惠普尔病 惠普尔养障体 肺受累

应用品管圈提高手术室物体表面污染物清除率

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目的 探讨品管圈（QCC）对提高手术室物体表面污染物清除率、降低手术部位感染（SSI）发病率的效果。

方法 应用 QCC 管理模式对手术室物体表面清洁消毒质量实施监督管理，2020 年 10-11 月为改善前期，2020 年 12 月-2021 年 3 月为改善后期，并持续监测至 2021 年 9 月，借助荧光标记设备和微生物培养两种方法，找出物体表面污染物清除率低的原因，通过改进洁具、完善制度流程、优化培训模式三大对策，对比 QCC 改善前后物体表面污染物清除率及 SSI 发病率的差异。

结果 手术室物体表面污染物清除率由改善前的 52.26%提高至改善后的 88.02%；工作人员知识考核合格率从 46.82%提高至 90.29%；SSI 发病率从 0.18%下降至 0.07%；差异均有统计学意义（均 $p<0.05$）；2021 年 4-9 月 SSI 发病率为 0.06%，手术室物体表面污染清除率分别为 89.24%、90.80%、91.67%、92.53%、93.40%、94.10%，改善效果维持良好。

结论 应用 QCC 进行持续质量改进，可有效提高手术室物体表面污染物清除率及不同岗位工作人员环境清洁消毒知识掌握合格率，保障手术室清洁质量有助于降低 SSI 发病率，同时圈员能力得到提升，值得推广应用。

关键字：品管圈；手术室；物体表面；污染物；清除率；手术部位感染

一线核苷（酸）类似物对慢性乙型肝炎患者血脂的影响

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目的 评估一线抗病毒药恩替卡韦（ETV）、富马酸替诺福韦二吡呋酯（TDF）和富马酸丙酚替诺福韦（TAF）对于慢性乙型肝炎患者血脂的影响。

方法 采用回顾性队列研究，纳入2022-2023年重庆医科大学附属第一医院感染科门诊就诊的年龄大于18岁的慢性乙型肝炎患者。将患者分为未用药组、ETV组、TDF组和TAF组，比较四组患者血脂水平；根据指南标准将血脂分层，并进行多元有序logistics回归分析影响血脂分层的危险因素。

结果 共333例慢性乙型肝炎患者纳入研究，未用药组114例、ETV组134例、TDF组37例、TAF组48例。四组患者的性别、BMI、体重、相关疾病（糖尿病、高血压、高脂血症、脂肪肝、肝硬化、肝细胞癌）患病比例、肝脏生化学、肾小球滤过率、甲胎蛋白差异无统计意义（P＞0.05）。与其余几组相比，TAF组年龄较大（P＜0.05）。与未用药组相比，TDF组血脂更低（TC：3.91mmol/L vs.4.57mmol/L, P＜0.001；HDL-C：1.08mmol/L vs.1.28mmol/L, P=0.002；LDL-C：2.32mmol/L vs.2.83mmol/L, P＜0.001；非HDL-C：2.78mmol/L vs.3.30mmol/L, P=0.004）、血糖更低（5.39mmol/L vs.5.63mmol/L, P=0.014）、ASCVD高危人群占比更低（0%vs.12.3%, P=0.025）。ETV、TAF的血糖、血脂、ASCVD高危人群占比与未用药组差异无统计学意义（P＞0.05）。随访发现，与正常血脂相比，基线为高脂血症的患者在TDF治疗后TC、非HDL-C下降更明显（P＜0.05）。多元有序logistics回归分析发现使用TDF与LDL-C分层增加（OR=0.123, 95%CI：0.023-0.328, P＜0.001）和非HDL-C分层增加（OR=0.231, 95%CI：0.080-0.670, P＜0.01）负相关。

结论 TDF可能导致CHB患者血脂降低，相较于基线血脂正常者，有高脂血症并且未使用降脂药物的患者在使用TDF后血脂下降更明显。而ETV、TAF对CHB患者血脂没有明显影响。合并ASCVD高危风险的CHB患者在选用一线抗病毒药物时应该考虑ETV、TDF、TAF对血脂的影响。

关键字：慢性乙型肝炎，恩替卡韦，富马酸替诺福韦二吡呋酯，富马酸丙酚替诺福韦，血脂

棘白菌素类抗真菌药不良反应文献分析

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目的 了解棘白菌素抗真菌药致药品不良反应类型及特点，为临床合理使用棘白菌素类抗真菌药提供参考和依据。

方法 通过文献检索，收集《中国期刊全文数据库》、Pubmed等中英文数据库2000年—2022年6月棘白菌素类抗真菌致不良反应相关文献，剔除不符合要求的文献，进行归类整理与分析。

结果 共检索到文献114篇，报道卡泊芬净、米卡芬净、阿尼芬净所致药物不良反应共2 870例。其中，报道卡泊芬净所致药物不良反应1 407例；米卡芬净所致药物不良反应734例；阿尼芬净所致药物不良反应729例。以引起消化系统、全身性反应、皮肤及附件不良反应多见。

结论 临床注意合理选用棘白菌素抗真菌药，应尽可能避免或减少药物不良反应的发生，从而保障患者用药安全有效。

关键字：抗真菌药，棘白菌素，药物不良反应，合理用药，文献分析；，

Infections Associated with Inhaled Corticosteroids and Intranasal Corticosteroids: A Pharmacovigilance Analysis Based on The FAERS Database

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Objective Long term use of Inhaling Corticosteroids (ICS) and intranasal corticosteroids (INCs) will increase the risk of various infections. This study conducted a pharmacovigilance analysis based on the FDA Adverse Event Reporting System (FAERS) database to compare the differences in infection adverse events between beclomethasone, fluticasone, budesonide, ciclesonide, mometasone, and triamcinolone acetonide

Methods We used proportional imbalance analysis to evaluate the correlation between ICS and INCs and infection events. The data was extracted from the FAERS database from April 2015 to September 2023. Further analysis was conducted on the clinical characteristics, site of infection, and pathogenic bacteria of ICS and INCs infection adverse events (AEs). We used number of reports (N), the reporting ods ratio (ROR), and $\chi 2$ (chi square) to creat bubble charts to display the top 5 adverse events in terms of infection risk intensity for each ICS and INCs

Results We analyzed a total of 21837 reports of

infection AEs related to ICS and INCs, with an average age of 62.12 years. Among them, 61.14% of infection reports were related to female. Stratified analysis from the site of infection showed that about one-third of infections reported by fluticasone, budesonide, ciclesonide, and mometasone were lower respiratory tract infections, over 40% of infections reported by triamcinolone acetonide were in the eyes, and oral infections caused by beclomethasone were most (7.39%). Stratified analysis based on pathogen showed that the highest proportion of fungal and viral infections were caused by beclomethasone (21.15% and 19.2%, respectively), while mycobacterial infections were caused by budesonide and ciclesonide (3.29% and 2.03%, respectively). The reported proportion of infections caused by glycopyrronium/indacatrol/mometasone (12.76%) was significantly higher than the other compound ICS. Bubble plots have been created to show the top 5 strong signals of infection caused by various ICS and INCs. The ICS group had more fungal infections, oral candidiasis, oral infections, pneumonia, tracheitis, etc., while the INCs group had more eye symptoms, rhinitis, sinusitis, nasopharyngitis, etc

Conclusion Women who use ICS and INCs were more prone to infection events. Compared to budesonide, fluticasone seemed to have a higher risk of pneumonia and oral candidiasis. Mometasone might lead to more upper respiratory tract infections. The risk of oral infection was higher with beclomethasone. Fungal and viral infections were more common in beclomethasone, while mycobacterial infections in ciclesonide and budesonide. The use of ICS might lead to more airway and fungal infections, while INCs lead to more nasal and eye infections. Improving the standardization of patient device operation and deep mouthwash after using ICS were very important for preventing infections caused by ICS and INCs

关键字：data mining, FAERS, ICS, INCs, pharmacovigilance, infections

Lung Abscesses, Hepatic Abscesses, and Infective Endocarditis Due To Hypermucoviscous Hypervirulent Klebsiella Pneumonia (HvKP)

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Background Multi-organ infections caused by highly virulent Klebsiella pneumonia(hvKp) have a high mortality rate and poor prognosis and should be taken seriously. Infective endocarditis (IE) caused by Klebsiella pneumonia (KP) is rare, and we report a case of invasive liver abscess syndrome (IKLAS) combined with lung abscess and infective endocarditis caused by highly virulent Klebsiella pneumonia

Case presentation The patient was a 54-year-old woman, a farmer, with a previous history of diabetes mellitus, who presented with "recurrent fever and cough for 11 days", Abdominal computed tomography (CT) revealed a liver abscess, Chest CT suggestive of left apical lung abscess and pleural effusion, and cardiac ultrasound suggestive of an aortic valve vegetations. Bacterial culture results of the liver abscess puncture fluid confirmed the diagnosis of Klebsiella pneumonia, which was sensitive to various antibacterial drugs. The string test was positive. The patient's condition improved after drainage of the liver abscess and anti-infective treatment. the lesion was significantly absorbed at 1-month follow-up.

Conclusion IKLAS caused by hvKp predisposes to multiple site infections. IE is rare, and clinicians should be aware of screening for occult lesions in patients with suspected IKLAS

关键字：Keywords: invasive liver abscess syndrome; highly virulent Klebsiella pneumonia; Infective endocarditis; lung abscess; Case report.

Distinctive Features and Prognostic Utility of Neutrophil in Patients with Klebsiella Pneumoniae Infection: Observational Data From Large ICU Database

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Background Neutrophil plays a pivotal role in the management of Klebsiella pneumoniae infection. Delineate the clinical characteristics and prognostic utility of neutrophil in severe patients with K. pneumoniae infection are crucial for clinical management and prognostic assessment

Methods K. pneumoniae patients with different infection sites were enrolled from Medical Information Mart for Intensive Care IV and eICU Collaborative Research Database. Temporal variations of neutrophil counts within 30 days of clinical onset were examined using locally weighted scatterplot smoothing curves. Logistic regression analysis was performed to assess the relationship between neutrophil counts and hospital mortality

Results A total of 1,705 patients caused by K. pneumonia were included in the study. Patients with respiratory infections exhibited higher levels of neutrophils compare to those with bloodstream infection. The non-survivor group had higher neutrophil levels than the survivor group within the 30 days of hospitalization period.

Neutrophils counts peaked at admission and 1-2 weeks later. There was a 'U'-shaped relationship between neutrophil counts and hospital mortality

Conclusions Neutrophils in K. pneumoniae patients with different infection sites have distinctive features and dynamic clinical trajectories. The close monitoring of severe patients infected with K. pneumoniae upon admission and during the first 1-2 weeks after admission is of utmost importance, particularly for patients with a neutrophil count exceeding 8.0×109/L

关键字：Klebsiella pneumoniae; neutrophil; infection; Medical Information Mart for Intensive Care (MIMIC); eICU Collaborative Research Database (eICU-CRD)

行机械通气脓毒症患者 28 天死亡风险预测模型构建

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目的 探究影响行机械通气脓毒症患者 28d 死亡的危险因素并构建风险预测模型。

方法 选择 2019 年 2 月至 2021 年 2 月我院收治的 102 例行机械通气的脓毒症患者作为研究对象,根据随访 28d 患者的生存情况,分为存活组(61 例)和死亡组(41 例)。比较两组患者的一般资料和实验室检查指标,多因素 Logislic 回归分析影响患者 28 d 死亡的因素,构建风险评分模型并评价其预测效能。

结果 死亡组血管活性药物应用患者比例、APACHE II评分、血清 SCr 水平明显高于存活组,PLT、FT 、TT,水平明显低于存活组(P<0.05);血管活性药物应用、APACHE II评分增加、PLT、FTT,、T,水平下降、SCr 水平升高是导致行机械通气脓毒症患者 28d 死亡的危险因素(P<0.05);将上述危险因素纳入风险评分模型,分别赋予 36、49、25、27、33、45、38 分的权重,将总分<72 分定义为中危组,>72 分且≤185 分定义为高危组，>185 分定义为极高危组;风险评分模型的 ROC 曲线下面积、灵敏度、特异度分别为 0876(95%CI0.843~0.909,P<0.001)、93.42%、87.45%,区分度较好,校准曲线及生存曲线提示模型预测的准确性较好。

结论 分析影响行机械通气脓毒症患者 28d死亡的危险因素并构建风险评分模型,有利于临床上早期识别高危人群,指导医护人员采取个体化的治疗和护理方案,对降低患者死亡率有重要意义。

关键字：机械通气;脓毒症;死亡;危险因素;风险评分模型

酸性氧化电位水与邻苯二甲醛溶液对多重耐药纤维支气管镜的消毒效果

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目的 比较酸性氧化电位水和邻苯二甲醛(OPA)溶液对纤支镜的消毒效果。

方法 采用回顾性分析，选取 2021 年 1-6 月和 2021 年 7-12 月医院重症医学科带有人工气道并行纤支镜检查的多重耐药菌患者为研究对象，随机分为对照组(124 例)和观察组(113 例)。对照组以酸性氧化电位水为消毒液，观察组以邻苯二甲醛溶液为消毒液，比较两组纤支镜内腔和外表菌落采样、多重耐药菌检出率。

结果 观察组纤支镜内腔菌落合格率(100%)高于对照组(98.5%);观察组外表菌落合格率(100%)高于对照组(98.8%)，差异均有统计学意义(P<0.05);观察组多重耐药菌检出率(3.0%)低于对照组(15.6%)差异有统计学意义(P<0.05)。

结论 应用邻二甲醛溶液对多重耐药纤维支气管镜消毒可有效降低细菌及多重耐药菌检出率，具有良好的消毒效果。

关键字：酸性氧化电位水;邻苯二甲醛;多重耐药菌;纤维支气管镜

某三级综合医院 2021 年-2023 年病原菌分布、耐药性特征及防控策略分析

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目的 回顾性研究某三级综合医院 2021 年-2023 年常见病原菌分布、构成比及多重耐药检出率、常用抗菌药耐药性特征，分析通过加强多学科协作，落实集束化的防控措施，进一步遏制耐药菌上升趋势,为临床安全用药提供用药依据。

方法 采用质谱分析仪鉴定临床送检的细菌培养标本，依据美国临床和实验室标准协会（ CLSI ）抗菌药物的药物敏感性试验执行标准判定检测结果，应用 WHONET 5.6 软件统计分析。

结果 共收到送检标本 130655 份，主要来源于血液（40.12%）、痰液（31.37%）、分泌物（14.47%）等；分离出病原菌 19768 株，主要病原菌以革兰氏阴性菌为主，其中革兰氏阳性菌 7681 株，占 38.86%；革兰氏阴性菌 12087 株，占 61.14%；在革兰氏阴性菌中，排前 3 位的分别为大肠埃希菌（15.85%）、肺炎克雷伯菌（13.23%）、铜绿假单胞菌（7.51%）；革兰阳性菌中，排前 3 位的分别为金黄色葡萄球菌

（10.62%)、肺炎链球菌（3.16%)、屎肠球菌（2.04%）；药物敏感性试验结果显示:未检出耐万古霉素屎肠球菌、耐万古霉素粪肠球菌；金黄色葡萄球菌、肺炎链球菌、屎肠球菌等革兰阳性菌对利奈唑胺、万古霉素、替加环素均未产生耐药性；大部分革兰阴性菌对碳青霉烯类抗菌药物敏感，但鲍曼不动杆菌对常见抗菌药物耐药水平普遍较高。从 2021 年-2023 年多重耐药检出率趋势图可以看到耐药菌检出率、院内感染率均呈下降趋势，特别是碳青霉烯耐药肺炎克雷伯菌检出率从 2022 年的 25.80%下降至 11.58%，降幅明显。分析数据下降的原因来源于加强多学科协作，落实院、科两级督导，重视集束化的感染防控措施。

结论 临床重视患者的病原学检查、多重耐药菌监测，进一步加强抗微生物药物的使用管理；掌握采集标本的正确时机与报告解读，熟悉院内病原微生物流行趋势及常用抗菌药物的耐药性, 根据细菌药敏结果，综合患者病情，预防性或目的性的选择抗菌药物。不断加强医疗机构内感染预防与控制，坚持预防为主的策略，将院内感染防控与抗微生物药物临床应用管理统筹推进，加大对感染防控工作的投入力度，制定耐药微生物感染的循证防控措施，遏制耐药菌的产生，才能有效降低多重耐药菌的检出率、医院感染的发生率。

关键字：病原菌分布，耐药性分析，多学科协作，防控策略分析，落实集束化防控措施

Effect of Prophylactic Unfractionated Heparin Anticoagulant Therapy on In-hospital Mortality in Patients with Cirrhosis and Sepsis.

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Objective It is not clear whether prophylactic anticoagulation with unfractionated heparin (UFH) has an effect on the outcomes of patients with cirrhosis and sepsis, since coagulopathy in patients with cirrhosis can lead to a tendency to bleed

Methods Data on patients with cirrhosis and sepsis were extracted from the MIMIC-IV database, and these patients were categorized into UFH group (received subcutaneous UFH for at least 5 days) and the control group (used UFH for less than 5 days or not at all).The primary outcome of this study was in-hospital mortality. Secondary outcomes were 30-day mortality, the lengths of the ICU and hospital stays. Various statistical methods including propensity score matching (PSM), treatment weighted inverse probability (IPTW), multivariate logistic regression and Cox proportional risk model were used to evaluate the effect of prophylactic UFH on the outcome of patients with cirrhosis and sepsis

Results The study included 1515 patients with cirrhosis and sepsis. Patients who received prophylactic UFH anticoagulation had a 45.50% lower risk of in-hospital mortality (odds ratio [OR] = 0.545, 95% confidence interval [CI]=0.391–0.761, p<0.001). The results of the PSM (OR=0.712, 95% CI=0.536–0.945, p=0.019) and IPTW (OR=0.567, 95% CI=0.396–0.806, p<0.001) models demonstrated a significant beneficial effect of prophylactic UFH use on in-hospital mortality among patients in the ICU

Prophylactic use of UFH also reduced 30-day mortality (hazard ratio [HR] =0.533, 95%CI=0.420-0.676, p<0.001). Subgroup analysis showed that prophylactic use of UFH reduced in-hospital mortality in males and patients with high Model for End-Stage Liver Disease (MELD) score (>20) and high sofa scores (≥9) and overlapping symptoms of decompensated cirrhosis.

Conclusion Prophylactic use with UFH had a positive effect on in-hospital mortality in patients with cirrhosis and sepsis. This positive effect also seen in more severely ill patients or in those with decompensated cirrhosis without concomitant esophageal variceal bleeding

关键字：Sepsis; Cirrhosis; Unfractionated heparin; Prophylactic anticoagulation; In-hospital mortality.

肺泡灌洗液 PCT 检测在诊断肺结核合并细菌性肺炎临床应用价值研究

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目的 检测肺结核患者肺泡灌洗液（bronchoalveolar lavage fluid，BALF）、降钙素原（procalcitonin，PCT）、血清 PCT、全血白细胞计数（white blood cell count）及中性粒细胞百分比（neutrophils percentage，NEUT%）水平对诊断肺结核合并细菌性肺炎的临床应用价值

方法 本研究收集 2021 年 10 月至 2022 年 12 月川北医学院附属医院感染科收治的肺结核患者，共纳入研究 107 例，根据 2 组肺泡灌洗液 PCT、外周血 PCT、外周血进行测定，比较不同指标间的差异性以及相关性。同时绘制受试者操作特征曲线（receiveroperatingcharacteristic curve, ROC）评估上述指标早期诊断 PTB 合并细菌性肺炎的性能。

结果 1.肺结核合并细菌性肺炎患者中，BALF 中 PCT 水平高于单纯性肺结核组，差异具有统计学意义（P<0.05），血清 PCT 水平也高于单纯肺结核组，差异具有统计学意义（P<0.05）。2.在肺结核合并细

菌性肺炎组及单纯性肺结核组中，BALF 中 PCT 水平均高于其血清 PCT 水平，差异均具有统计学意义（P<0.05）。3.肺结核合并细菌性肺炎组外周血 WBC、NEUT%水平高于单纯性肺结核组，差异具有统计学意义（P<0.05)。 4.在肺结核合并细菌性肺炎组中 BALF 中 PCT 与血清 PCT 水平具有正相关性（rs=0.431，P=0.005<0.05），而与外周血 WBC、NEUT%水平不相关（P>0.05）。5.BALF 中 PCT 诊断肺结核合并细菌性肺炎的最佳临界值 0.62ng/ml，曲线下面积（AUC）为 84.7%，敏感度为 78.0%，特异度为 78.8%。血清中 PCT 的最佳临界值为 0.25ng/ml，AUC 为 80.2%，敏感度为 70.7%，特异度为 78.8%。血清中 WBC 的的最佳临界值为 7.7×10^9/L，AUC 为 65.9%，敏感度为 65.9%，特异度为 68.2%。NEUT%的最佳临界值为 77.5%,AUC 为 77.20%，敏感度为 61.0%，特异度为 89.4%。

结论 BALF 中 PCT 检测对于诊断肺结核合并细菌性肺炎具有较好的价值。

关键字：肺结核合并细菌性肺炎；肺泡灌洗液 降钙素原

中心静脉相关血流感染的病原学特点和预后影响因素

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目的 尽管医疗机构严格遵守预防中心静脉相关血流感染（CLABSI）的预防与控制措施，但 CLABSI 仍然是危及生命的并发症，是医院感染死亡的重要原因。本研究将探讨 CLABSI 患者的病原学特点及影响预后的危险因素。

方法 回顾性收集 2018 年 1 月至 2021 年 12 月期间在四川省某三甲医院确诊的中心静脉相关血流感染的住院患者的临床资料，并进行统计分析，探索 CLABSI 患者死亡的危险因素。

结果 共纳入 63 例确诊为 CLABSI 的患者，其中生存组 45 例，死亡组 18 例，死亡率为 28.6%。总体病原学特点显示，CLABSI 的病原体主要为革兰阳性菌（ 44.44%），其次为革兰阴性菌（ 39.68%），不同年份 CLABSI 的病原菌感染构成情况不同。多因素 logistic 回归分析结果提示，机械通气[比值比（odds ratio，OR）=22.415，95%置信区间（confidence interval，CI）=（1.966，255.564），P=0.012]是 CLABSI 患者死亡的独立危险因素。

结论 机械通气是CLABSI 患者死亡的独立危险因素，对于存在机械通气的 CLABSI 患者，需严格落实感染防控措施，积极评估停机指征，早日脱机，以降低患者死亡风险。

关键字：中心静脉导管相关血流感染，预后，危险因素

Predictive Model Development and Risk Assessment of Piperacillin/Tazobactam-Associated Hypokalemia in Neonates: A Retrospective Study

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Objective This retrospective study aimed to investigate the incidence, severity, and determinants of piperacillin/tazobactam (TZP)-associated hypokalemia (TAH) in neonates and to develop a predictive model for the early detection of neonatal TAH

Methods Neonates treated with TZP between January 1, 2019, and December 31, 2023, at Xiamen Women and Children's Hospital in China were included. Demographic data, laboratory indicators, and medication details were extracted from electronic medical records. The Naranjo probability scores were used to evaluate TAH causality. Multivariate logistic regression was performed to identify independent predictors, and a nomogram was constructed to predict TAH occurrence. Discrimination, calibration and and utility (patient stratification into low-risk vs high-risk groups) were assessed to determine the predictive accuracy of the nomogram

Results Among 1,027 neonates, 358 were analyzed, with a TAH incidence of 20.4%. Independent predictors of TAH included baseline serum creatinine (P = 0.012, OR 1.017, 95% CI 1.004-1.031), dopamine (P = 0.002, OR 3.366, 95% CI 1.5393-7.361), and serum calcium (P = 0.049, OR 0.313, 95% CI 0.098-0.994). A nomogram integrating these factors demonstrated good predictive accuracy (AUC = 0.771) and net benefit. The cumulative incidence curves plotted by the Kaplan-Meier method revealed that, the high-risk group displayed a higher cumulative incidence of hypokalemia than low-risk group (Log-rank test P < 0.001)

Conclusion This study highlights baseline serum creatinine, dopamine, and serum calcium as independent predictors of neonatal TAH. The developed nomogram provides a user-friendly tool for TAH prediction, potentially enhancing early detection and management in clinical practice. This study provides an empirical basis for early detecting, diagnosing and intervening in neonatal TAH

关键字：Neonates,piperacillin/tazobactam,hypokalemia ,incidence,risk factor,Nomogram

Candida Albicans Combined with Mycobacterium Intracellulare Infection Caused by CARD9 Deficiency: Case Report and Literature Review

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Background Invasive candidiasis poses a significant mortality risk, proves challenging to treat, and is most commonly caused by Candida albicans. CARD9 represents a class of proteins incorporating the caspase recruitment domain (CARD). CARD9 deficiency follows a strict autosomal recessive inheritance pattern and results in an impaired immune response to fungi, consequently leading to infection

Case Presentation This report delineates the case of a 51-year-old middle-aged male who was admitted to the hospital 3 years ago due to recurrent fever (maximum temperature 38.8℃) accompanied by headache. The causative factor remained elusive, and symptomatic treatment yielded unsatisfactory results. Next-generation sequencing (NGS) of cerebrospinal fluid (CSF) at our hospital identified C. albicans infection. Following antifungal therapy, the patient experienced relief from fever and headache; however, he subsequently developed hydrocephalus. CSF culture indicated the presence of non-tuberculous mycobacteria (NTM)—Mycobacterium intracellulare, prompting initiation of anti-NTM treatment. Given the recurrent infections, peripheral blood was collected for exome sequencing, revealing a CARD9-deficient homozygote with the mutation site identified as c.175 C>T (p.Arg59Trp). The patient underwent hospitalization at West China Hospital of Sichuan University on 8 occasions for diagnostic assessments and treatments. Presently, antifungal treatment has been discontinued, while anti-NTM therapy is being maintained, with the patient reporting no fever or other discomforts.

Conclusion In managing fungal infections among non-HIV/AIDS patients, clinicians should consider immune impairment as a contributing factor. For such patients, conducting multiple CSF and blood cultures and employing new technologies such as NGS are advisable. There is currently no definitive evidence supporting the necessity of long-term or even lifelong antifungal drug use to prevent recurrence; thus, diligent long-term follow-up should not be overlooked

关键字：CARD9, candida albicans, mycobacterium intracellulare, immune deficiency, case report

耳念珠菌研究进展的可视化分析

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目的 运用文献计量学工具分析耳念珠菌的研究热点和前沿，为今后的研究提供参考资料。

方法 从 Web of Science 核心合集(WOSCC)中筛选 2009—2022 年关于耳念珠菌的文章和综述。利用 CiteSpace 软件对该领域的国家、机构、作者、关键词进行可视化分析。

结果 共纳入耳念珠菌相关文献 1042 篇。美国是这一领域最有影响力的国家。美国 Centers for Disease Control and Prevention 和荷兰 Canisius Wilhelmina Hospital 机构的论文数量并列第一。Jacques F Meis 发表的相关文献最多。一段时间以来，“antifungal resistance”,“Candida albican” and “identification” 一直是该领域的研究热点。“antifungal activity”则是近年来的研究热点。

结论 自 2009 年耳念珠菌被真正分离以来，我们对其流行病学资料和相关致病机制有了一些初步的研究，但在其迅猛传播的现在，需要我们对其进一步探索。

关键字：耳念珠菌，Citespace，可视化分析；

2019-2023 年四川省飞沫传播法定传染病的流行趋势分析

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目的 分析四川省 2019—2023 年飞沫传播法定传染病的流行趋势，为飞沫传播传染病的院感防控策略提供科学依据。

方法 根据“四川省卫生健康委员会”官网公布的 2019—2023 年四川省法定传染病概况，整理归纳经飞沫传播法定传染病（包括流行性感冒、流行性腮腺炎、猩红热、百日咳、麻疹、风疹、麻风病、流行性脑脊髓膜炎）的发病数据，人口数据来自四川省统计局及国家统计局，采用描述流行病学及趋势卡方，分析经飞沫传播传染病年均发病率的变化趋势。

结果 2019-2023 年经飞沫传播法定传染病累计报告 2742890 例，年均报告发病率为 655.72/10 万。2019 年年均发病率（282.73/10 万）高于 2020-2022 年（107.04/10 万），2019-2022 年年均发病率呈下降趋势（χ^2 趋势＝29856，P＜0.001）；2020-2022 年年均发病率低于 2023 年（2676.31/10 万），2020-2023 年年均发病率呈上升趋势（χ^2 趋势＝3516542，P＜

0.001），且季节分布较为明显。

结论 2020-2022 年社会各界为响应重大突发公共卫生事件，严格落实防控措施：包括正确佩戴口罩、减少聚集性活动、加强手卫生、保持社交距离等，也降低了其它经飞沫传播法定传染病的发病率，可为今后常态下的飞沫传播传染病院感防控工作提供科学依据。

关键字：飞沫传播；法定传染病；流行趋势；防控措施；

我院 161 例抗菌药物不良反应分析

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目的 分析我院近五年来抗菌药物发生的不良反应，了解我院药物不良反应的上报及处理情况。提高医务人员上报药物不良反应的积极性，促进抗菌药物在临床合理使用，为临床提供精准用药服务。

方法 首先采用回顾性研究方法，从国家药品不良反应监测系统平台收集我院2018年1月到2023年12月抗菌药物不良反应共计 161 例进行分析。其次使用统计学方法，对患者基本信息、年龄、症状、给药途径、药品类别以及结果等方面进行汇总分析。

结果 在 161 例报告中，0-15 岁患者用药后不良反应发生率最高，占比（45.68%），16-30 岁患者发生率最低，占比（6.79%）等；给药途径：静脉滴注给药 156 例，占比最高为（96.89%），其次为口服给药 4 例，占比（2.48%）等；报告类型及转归：一般 140 例，占比（86.96%），结果为症状消失、症状痊愈等，其次新的一般 12 例，占比（7.45%），严重 7 例，占比（4.35%）等；不良反应累及器官系统、患者临床表现：不良反应累及皮肤及其附件占比（76.40%），伴随临床表现包括瘙痒、皮疹等；其次累及消化系统占比（4.35%），伴随临床表现包括恶心、呕吐、腹泻等。

结论 药品不良反应的发生与患者年龄、给药途径、药品种类等因素存在相关性。加强药品不良反应监测，有利于提高医务人员对药品不良反应的防范意识，防止严重药害事件的发生、蔓延和重演，提高临床合理用药水平。

关键字：药品不良反应；抗菌药物；合理用药；

感染性疾病学科发展（细菌真菌为发展方向）

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目的 感染性疾病严重威胁人类健康、国家安全和社会稳定，而感染性疾病学科建设发展对于保障人民健康，促进社会经济持续发展具有重大意义。“十四五”国家临床专科能力建设规划对于对临床专科能力建设作出整体性、系统性、制度性安排。本研究系统回顾分析 2016 年-2023 年以细菌真菌感染诊治为主的天津市感染性疾病学科建设发展情况，比较新冠疫情前后学科建设发展影响，总结发现问题短板以进一步促进学科建设发展。

方法 本研究回顾分析天津市 2016 年、2019 年、2023 年全市二三级医疗机构感染性疾病学科调研数据，就感染性疾病科设置、普通病房设置、普通感染门诊设置、隔离病房设置情况、人员配置情况等进行汇总统计分析。

结果 天津市 2023 年三级医疗机构具有建制感染科数量、普通感染门诊数量、隔离病房数量、普通病房数量、高级职称医师数量、发热门诊数量等较 2019 年分别增长 57.14%、26.32%、153.85%、47.06%、222.06%、189.74%，二级医疗机构具有建制感染科数量、普通感染门诊数量、隔离病房数量、普通病房数量等较 2019 年分别增长 75.00%、133.33%、333.33%、75.00%。

结论 2023 年至 2019 年感染学科建设各数据较 2016 至 2019 年增幅显著。实际全面运行感染性疾病科数量仍有限。

关键字：细菌真菌感染，学科建设，发展

基于基因组序列的 ST11-KL10 CRKP 的进化路径分析

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目的 ST11 型是我国医院获得性碳青霉烯类耐药肺炎克雷伯菌（CRKP）的主要流行克隆，其荚膜血清型以 KL47 和 KL64 为主，且 KL64 逐渐取代 KL47。然而，一项覆盖全国的 CRKP 流行病学研究中显示，存在一簇具有独特遗传特性的 ST11-KL10 型 CRKP 菌株，其进化路径迄今尚未阐明，解析其分子起源对于 CRKP 防控至关重要。

方法 通过对全国范围内收集到的 528 株 ST11 型 CRKP 菌株进行单核苷酸多态性（SNP）分析以揭示潜在的重组区域。为确定重组区域的可能供体，将提取到的重组区域与所有 KL10 的不同 ST 型肺炎克雷伯菌基因组进行系统发育分析，包括从美国国家生物技术信息中心（NCBI）数据库中检索到的 185 株具有遗传背景多样的菌株以及本次流行病学

研究中的菌株（34 株 ST11-KL10、1 株 ST76-KL10）。对去除重组区域的同一 ST11 下的不同 KL 型菌株进行亲缘关系分析，明确 ST11-KL10 进化来源。

结果 基于 SNP 的系统发育分析表明，ST11-KL10 型 CRKP 的演化进程与 2 个特定重组区域的获取（分别为 95 kb、480 kb）密切相关。绝大多数 ST11-KL10 由 ST11-KL47 通过同源重组产生，获得一个来自 ST76-KL10 的 95 kb 的片段，其中包含荚膜多糖（CPS）、脂多糖（LPS）。而其中一离群株 GCA 900501195.1 可能衍生自 ST11-KL13，在 ST11-KL13 的基础上与来源于 ST629-KL10 基因组中一段 480 kb（包含 CPS、LPS 及前述的 95 kb）区域的片段进行替换所得。

结论 ST11 型 CRKP 在中国的广泛传播与其获得碳青霉烯酶基因有关，肺炎克雷伯菌毒力与荚膜类型息息相关。重组事件促进了 ST11 型 CRKP 内的亚克隆进化，ST11-KL10 这一亚克隆进化路径的多样性和遗传性应受到高度关注，避免其演变为高危克隆，从而确保公共卫生安全。

关键字：碳青霉烯类耐药肺炎克雷伯菌，ST11-KL10，重组，进化

基于信息化集成平台的多重耐药菌防控管理新模式探讨

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目的 探讨基于信息化集成平台的多重耐药菌综合防控管理新模式在多重耐药菌医院感染防控中的应用成效。

方法 选取 2020 年 01 月 01 日-2023 年 12 月 31 日期间住院患者 MDRO 相关资料，根据是否应用信息化集成平台综合管控 MDRO，分为干预前组和干预后组，比较两组临床分离菌及其来源分布、抗菌药物耐药性差异，及主要 MDRO 菌株检出率/医院感染发生率、三管一切口 MDRO 感染发生率、医院总体感染率等。

结果 两组分别收集非重复临床分离菌 2691/3342 株，其中革兰阴性菌株占 76.85%/81.10%，革兰阳性菌株占 17.69%/16.06%，菌株主要来源呼吸道、血液、尿液标本；两组多重耐药鲍曼不动杆菌检出率最高，耐药情况最为突出，对大多数抗菌药物的耐药率＞50%，对碳青霉烯类药物耐药率＞60%。干预后 MRSA、CRKP、CREC 院内感染率较前显著下降，医院主要多重耐药菌总感染例次发病率由 0.68‰下降至 0.45‰（P＜0.05）；导尿管相关尿路 MDRO 感染率由 0.24％降至 0.10％、中央血管导管相关血流 MDRO 感染率由 0.75%降至 0.13%，差异均有统计学意义。此外，信息化综合管理实施后医院感染率、医院感染漏报率、住院患者抗生素使用率均较前显著降低（$\chi2$=7.372、7.597、6.956，P＜0.05），医院感染送检率、医护人员手卫生依从性、手卫生正确率及 MDRO 防控措施完全落实率均显著改善。

结论 该信息化综合管理模式可有效改善医院多重耐药菌感染现况，降低医院多重耐药菌感染率，值得医疗机构广泛推广应用，但亦需根据自身情况进行量身改进。

关键字：多重耐药菌；医院感染；信息化；管理；预防与控制

1 例误判断为左氧氟沙星导致中性粒细胞缺乏的皮肤软组织感染病例

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目的 对 1 例误判断为左氧氟沙星导致中性粒细胞缺乏的患者抗感染治疗过程进行分析，以提高临床对药物所致中性粒细胞缺乏的认识。

方法 收集 1 例抗感染治疗过程中出现中性粒细胞缺乏患者的临床资料，并对不良反应关联性进行评价。

结果 患者为 49 岁男性，因右下肢疼痛、发凉 10 天、加重 2 天入院，入院后诊断为下肢动脉硬化闭塞症，血栓闭塞性血管炎，右下肢缺血，先后 3 次行动脉溶栓及取栓术，术后出现坏疽、横纹肌溶解、多脏器功能损害表现，于入院第 8 天给予哌拉西林他唑巴坦，入院第 9 天行右下肢大腿截断术，入院第 11 天联合利奈唑胺抗感染治疗（4 天后停用），入院第 19 天，白细胞计数(WBC)7.57x10^9/L，中性粒细胞数(ANC)6.14 x10^9/L，C 反应蛋白(CRP)20.85mg/L。入院第 23 天，分泌物培养回报为产 oxa-23 型碳氢霉烯酶的鲍曼不动杆菌及全敏感的阴沟肠杆菌，临床药师建议调整抗感染方案为头孢哌酮钠舒巴坦钠联合左氧氟沙星。入院第 26 天，WBC 1.77x10^9/L，ANC 0.18 x10^9/L，CRP 118.20mg/L，抗感染方案改为美罗培南。入院第 28 天，WBC 2.17x10^9/L，ANC 1.02x10^9/L，CRP 206.42mg/L。临床医师上报左氧氟沙星导致中性粒细胞缺乏的药品不良反应，临床药师梳理治疗过程并复习文献，哌拉西林他唑巴坦诱导中性粒细胞减少可能是由于髓系细胞的增殖阻滞所致，长疗程用药（疗程≥14 d）及较高的累积使用剂量是危险因素，ANC 多在停药 7d 内恢复正常水平。有学者建议哌拉西林他唑巴坦使用疗程>10d、累积量>150g 的患者要高度警惕血液系统不良反应。利奈唑胺所致中性粒细胞减少与患者性别、年龄、疗程、剂量等相

关，用药超过 2 周发生率明显上升，发生机制可能与免疫介导或直接毒性相关。氟喹诺酮类引起白细胞减少的发生时间为 (5.82±1.93) d，其中左氧氟沙星最常见，相关中性粒细胞减少的报道少见，有报道用药 10d 后出现粒细胞缺乏，停药后 4-5d 后恢复正常。以上三种药物均可能导致中性粒细胞缺乏，利奈唑胺使用时间较短考虑可能性不大，患者的中性粒细胞缺乏出现在左氧氟沙星使用 3 天后，此时哌拉西林他唑巴坦使用 15 天（累积剂量为 202.5g）停用 3 天，ANC 恢复出现在左氧氟沙星停用 1 天、哌拉西林他唑巴坦停用 5 天后 。经不良反应关联性评价，患者的粒细胞缺乏很可能与哌拉西林他唑巴坦相关。

结论 哌拉西林他唑巴坦可能引起罕见的粒细胞缺乏，建议长疗程使用过程中密切监测患者的血常规，一旦发现药物不良反应应及时停药及调整治疗方案。

关键字：中性粒细胞缺乏，哌拉西林他唑巴坦

微生物实验室药敏预报告模式的建立和临床应用评价

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目的 通过优化实验室信息系统建设，建立药敏结果自动预报告规则，并评价其临床应用效果。

方法 首先完善微生物实验室信息系统，基于实验室既往药敏复查结果和 VITEK2 compact 专家系统，建立实验室的自动审核药敏拦截规则及相应数据汇总分析程序。收集 2023 年 9 月-2023 年 11 月广州市第一人民医院检验科微生物室发出的药敏报告，分析预报告和最终报告药敏结果的一致率以及报告时效。

结果 自 2023 年 9 月 15 日至 11 月 11 日，实施药敏预报告工作流程期间，共发出预报告药敏结果的临床标本 87 份，其中肠杆菌目细菌药敏 34 份、不动杆菌属细菌药敏 12 份、铜绿假单胞菌药敏 13 份、肠球菌属细菌药敏 5 份、其他细菌药敏 5 份，一致率为 100%。葡萄球菌属细菌药敏 18 份，因最终报告时加测 β 内酰胺酶试验修正了青霉素敏感这一结果，总体一致率为 94%。时效性方面，与传统药敏报告模式相比，药敏预报告模式施行后，进行药敏试验第一天发出药敏结果标本的比例由 2.3%提升至 45%，进行药敏试验第二天上午 8 时前发出药敏报告标本的比例由 2.3%提升至 61%。药敏报告 TAT 中位数时间缩短 16.5 小时。

结论 实验室现试行的药敏预报告模式，预报告药敏结果较准确。通过药敏报告模式的改变，可为临床提供更及时的药敏结果。

关键字：药敏试验，自动审核

非编码小 RNA RSaX28 通过结合 RNAIII 调控 ST398 型金黄色葡萄球菌致病

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目的 金黄色葡萄球菌（简称金葡菌）是重要的临床机会致病菌。RNAIII 等非编码小 RNA 在金葡菌毒力、耐受能力等方面发挥重要的调控作用。RNAIII 是重要的全局调控性非编码 RNA，在金葡菌的各个生长阶段均有较高的转录水平。ST398 型金葡菌是重要的社区相关性感染分离菌株，均有较高的毒力，同时也有一定的耐药性和耐受能力。本研究旨在通过分析临床分离的 ST398 型金葡菌的转录组，筛选新的重要的非编码小 RNA，并研究其在金葡菌致病能力中的调控作用。

方法 选取三株临床分离的 ST398 型金葡菌，收集其在半对数生长期（4h）和平台期（8h）两个生长时相的菌体进行转录组学分析。选取两个生长时相转录水平均较高的非编码小 RNA（TPM>1000）并构建敲除株，以溶血情况改变作为毒力筛选指标。选择改变较大的非编码小 RNA 进行后续研究。通过 cDNA 末端快速克隆实验确定小 RNA 的转录起始位点和转录终止位点，通过 Northern blot 实验验证非编码小 RNA 的转录水平和长度。通过细菌感染小鼠生存曲线、血流感染模型肾定植能力以验证非编码小 RNA 对金葡菌毒力的调控作用。通过在线工具筛选靶标 RNA 并通过 EMSA 实验验证。通过利福平转录抑制实验和启动子报告基因实验验证小 RNA 对靶标 mRNA 的影响，构建非编码小 RNA 的完整调控通路。

结果 通过筛选发现非编码小 RNA—RSaX28 在 ST398 型金黄色葡萄球菌的半对数生长期和平台期均有较高的转录水平，且敲除 RSaX28 后金黄色葡萄球菌溶血能力明显减弱。RACE 实验显示 RSaX28 长度为 534nt，有独立的启动子和终止位点。通过 Northern blot 可验证其大小如是，且转录水平在平台期最高。RSaX28 敲除株感染小鼠生存能力强于野生株感染组（P<0.05）；RSaX28 敲除株引发血流感染后，小鼠肾脏大体观察可见肾脓肿面积更小，HE 染色显示肾损伤较轻，证明 RSaX28 敲除株肾定植能力相对较弱，毒力更低。筛选后并通过 EMSA 验证 RNAIII 能与 RSaX28 结合。利福平转录抑制实验显示 RSaX28 能通过促进 RNAIII 的稳定性而促进细菌的毒力，并通过报告基因发现下游 alpha-toxin 的翻译水平随之改变。

结论 RSaX28 通过促进 RNAIII 的稳性，正向调控下游的毒力基因 hla。从而促进 ST398 型金葡菌的毒力，以导致更为严重的临床感染。

关键字：金黄色葡萄球菌，社区相关性克隆株 ST398，非编码小 RNA，RSaX28，RNAIII，毒力

1 例美罗培南致中性粒细胞减少症个案报道并文献分

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目的 分析美罗培南致中性粒细胞减少症的临床特点，为临床安全用药提供参考。

方法 梳理临床药师参与 1 例美罗培南致中性粒细胞减少症的治疗过程，并采用计算机检索中国知网（CNKI）、万方（WanFang）、维普（VIP）、PubMed、MedSci 等数据库中美罗培罗致中性粒细胞减少症的相关文献，检索时限为自建库起至 2023 年 2 月 10 日，从患者人口学特征，美罗培南用法用量，中性粒细胞减少症发生时间、严重程度及临床表现，干预及转归等方面分析美罗培南致中性粒细胞减少症的临床特征。

结果 共检索到文献 5801 篇，最终纳入 9 篇，涉及 9 例患者。纳入分析的 10 例患者（包含本研究报道案例 1 例和文献检索案例 9 例）中，男 6 例，女 4 例；年龄不超过 3 岁的 5 例；10 例患者均有明确的用法用量；原发疾病主要为颅内感染和血流感染；药品不良反应的潜伏期为 8～20 d（平均 14. 5 d）；8 例患者为重度中性粒细胞减少症，2 例患者合并发热及皮疹；5 例患者停药后中性粒细胞计数自行恢复正常，5 例患者在停药的基础上加用人粒细胞刺激因子注射液升白细胞治疗后中性粒细胞计数亦恢复正常；1 例患者因未定期随访而未知康复时间，其余 9 例患者平均康复时间为 6. 9 d。

结论 美罗培南致中性粒细胞减少症是罕见和可逆的，潜伏期长，多数患者无明显临床表现，但程度较重。临床使用美罗培南时应密切监测患者的中性粒细胞计数，以便及时发现、及时治疗，保证患者用药安全。

关键字：美罗培南，中性粒细胞减少症，药品不良反应

Mendelian Randomization and Transcriptomic Analysis Reveal The Protective Role of NKT Cells in Sepsis

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Objective Sepsis is a life-threatening clinical syndrome caused by dysregulated host response to infection. The mechanism underlying sepsis-induced immune dysfunction remains poorly understood. Natural killer T (NKT) cells are cytotoxic lymphocytes that bridges the innate and adaptive immune systems, the role of NKT cells in sepsis is not entirely understood and NKT cell cluster differences in sepsis remain unexplored. This study aimed to explore the role of NKT cells and its subtypes in sepsis

Methods Mendelian randomization (MR) analyses were first conducted to investigate the causal relationship between SSC-A on NKT cells and 28-day mortality of septic patients. A prospective and observational study was conducted to validate the relationship between the percentage of NKT cells and 28-day mortality of sepsis. Then the single-cell RNA sequencing (scRNA-seq) data of peripheral blood mononuclear cells (PBMCs) from healthy controls and septic patients were profiled

Results MR analyses first revealed the protective roles of NKT cells in 28-day mortality of sepsis. Then 115 septic patients were enrolled. NKT percentage was significantly higher in survivors (n=84) compared to non-survivors (n=31). Patients with lower levels of NKT cells exhibited a significantly increased risk of 28-day mortality. According to scRNA-seq analysis, NKT cell clusters exhibited multiple distinctive characteristics, including a distinguishing cluster defined as FOS+NKT cells, which showed a significant decrease in sepsis. Pseudo-time analysis showed that FOS+NKT cells were characterized by upregulated expression of crucial functional genes such as GZMA and CCL4. CellChat revealed that interactions between FOS+NKT cells and adaptive immune cells including B cells and T cells were decreased in sepsis compared to healthy controls

Conclusion Our findings suggest that NKT cells may provide protection for sepsis. And percentage of NKT cells can predict the 28-day mortality of sepsis. Additionally, we identified a distinctive FOS+NKT subtype, which is pivotal in the immune response during sepsis, providing novel insights into the underlying immunopathogenesis of sepsis

关键字：Natural Killer T (NKT) cells; Sepsis; Outcome；Mendelian research

肺曲霉菌病合并新型冠状病毒感染的危险因素和预后分析

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目的 目前，新型冠状病毒感染（COVID-19）已经进入“常态化管理”阶段。新型冠状病毒感染后继发曲霉菌感染日益受到重视。此外，我们观察到越来越多既往确诊的侵袭性肺曲霉菌病（IPA）患者合并感染了新型冠状病毒。因此，本研究旨在探究肺曲霉菌（感染或定植）患者伴有或不伴有新型冠状病毒感染的临床特征的差异，探究预后相关的危险因素。同时，我们首次研究了 COVID-19 相关性肺曲霉菌病（COVID-19-associated pulmonary aspergillosis, CAPA）和 IPA 继发感染新型冠状病毒的两组患者之间的差异。

方法 本研究是一项单中心回顾性研究，根据 EORTC/MSG 和 ECMM/ISHAM 2020 共识标准定义，纳入我院 2022 年 11 月 1 日至 2023 年 10 月 31 日期间 181 名曲霉菌感染或定植的住院患者，其中 72 名患者感染了新型冠状病毒，152 名患者诊断为侵袭性肺曲霉菌病（包括确诊、临床诊断或者拟诊）。随后，我们根据感染先后顺序将 152 例患者分为 CAPA 与 IPA 继发新型冠状病毒感染两组，并分析了两组临床特征的差异。

结果 通过分析有无合并 COVID-19 的肺曲霉菌病患者的临床特征，我们发现合并 COVID-19 组的患者年龄更大，住院天数更长，需要高流量吸氧和有创通气者更多，淋巴细胞计数更低，SII、AST、Cre、BUN、BUN/Cre、APTT、D 二聚体指标更高，休克发生率、入住 ICU 机率、病死率更高（P 值均＜0.05）。单因素回归分析显示 SARS-CoV-2 感染、SII、ALB、Cre、CRP 和 D-二聚体与患者的预后有关（P 值均<0.05）。根据多因素回归模型，SII、SARS-CoV-2 感染、确诊 IPA 和 CRP 是预后相关独立危险因素，模型曲线下面积为 0.759（CI 95%：0.683-0.835，P＜0.001）。与 CAPA 患者相比，IPA 继发 SARS-CoV-2 感染的患者在体重、Cre 和 D 二聚体中有统计学差异（P 值均<0.05），并且死亡率相对较低（33.3% vs 63.2%，P=0.037）。在我们的研究中，IPA（确诊/拟诊）大多通过痰培养、血清 GM 和 BALF mNGS 诊断。无论是否合并 COVID-19，烟曲霉都是最常检测到的菌种。

结论 肺曲霉菌病患者的高死亡率与 SARS-CoV-2 感染、确诊 IPA、CRP 和 SII 明显相关。与 CAPA 患者相比，IPA 继发 SARS-CoV-2 感染的患者死亡率也很高，这同样需要引起临床的高度关注。

关键字：COVID-19，COVID-19 相关性肺曲霉菌病（CAPA），侵袭性肺曲霉菌病（IPA），IPA 继发 SARS-CoV-2 感染，危险因素

Virus-Inspired Nanoparticles Dual-Penetrate Microbial Membranes and Biofilms for Conquering Antimicrobial-Resistant Infections and Promoting Wound Healing

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Methicillin-resistant Staphylococcus aureus (MRSA) forming into biofilms could trigger chronic inflammation and disrupt the well-coordinated progression of skin wound-healing processes. Prolonged and excessive use of antibiotics can expedite the development of resistance, primarily because of their limited ability to penetrate microbial membranes and biofilms effectively. Herein, a strategy is devised for virus-inspired nanoparticles to guide antibiotic penetrate into both bacterial cells and biofilms for defeating antimicrobial-resistant infections and promoting skin wound healing. Tailor-made lipid-based nanoparticles based on stearamine and cholesterol are designed to mimic viral highly ordered nanostructures. For mimicking the arigininе-rich fragments in viral protein transduction domains, the primary amines on the surface of the lipid-based nanoparticles are modified to guanidine segments. Hyaluronic acid (HA) as a capping agent is coated on the surface of nanoparticles to achieve bacterial-specific degradation and guanidine explosion in bacterial microenvironment with highly produced hyaluronidases for the dual-penetration of microbial cell membranes and biofilm structures, mimicking viral specific invasion within target cell microenvironment. As predicted, our virus-inspired nanoparticles display long-acting antibacterial effect and powerful biofilm elimination for conquering antimicrobial-resistant infections and promoting skin wound healing in vitro and in vivo. This work represents the first-ever demonstration of molecular and supramolecular engineering of virus-inspired nanoparticles to achieve the long-awaited dual-penetration of microbial cell membranes and biofilm structures, contributing to the development of a novel way for addressing antimicrobial-resistant infection and triggering skin wound healing.

关键字：virus-inspired particles, biofilm penetration, antibiotic resistance

基于 VOSviewer 和 CiteSpace 的碳青霉烯耐药革兰阴性杆菌文献研究现状和可视化分析

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目的 利用 VOSviewer 及 CiteSpace 软件进行计量文献分析,了解我国碳青霉烯耐药革兰阴性杆菌（CRO）领域的研究进展、研究热点以及未来的发展趋势。

方法 以中国知网 CNKI 辅以万方、维普网等数据库作为计量文献分析的数据来源,以“SU %=(耐碳青霉烯革兰阴性杆菌 + 碳青霉烯耐药革兰阴性杆菌 + 耐碳青霉烯类肠杆菌目细菌 + 耐碳青霉烯鲍曼不动杆菌 + 耐碳青霉烯类肠杆菌科细菌 + 耐碳青霉烯肺炎克雷伯菌 + 耐碳青霉烯类大肠埃希菌 + 耐碳青霉烯类铜绿假单胞菌)”为检索式,检索 2000 年 1 月 1 日至 2024 年 1 月 20 日期间发表的碳青霉烯耐药革兰阴性杆菌领域的相关文章。对检索到的文献进行数据清洗。利用 VOSviewer （版本 1.6.20）和 Cite space（版本 6.1.R3）对文献的作者、期刊、机构、关键词共现和聚类进行可视化图谱构建和可视化分析。

结果 共检索到 CRO 研究领域 3693 篇文献，经过数据清洗去除重复文献等，共引入 3672 篇文献。整体来看，近 20 年关于 CRO 研究领域的文献发文量呈现波浪式增加趋势，其中以 2018-2020 年期间发文量最多,近 5 年平均年发文量在 250 篇左右。该领域发文主要期刊包括中华医院感染学杂志、中国感染与化疗杂志、中国抗生素杂志、中国卫生检验杂志等，其中载文量最高的期刊为中华医院感染学杂志，为 262 篇，占总发文量的 18.52%。根据普莱斯定律进行判定，该领域核心作者发文量最小值为 7 篇。共计 172 位核心作者，共发文 1708 篇（46.2%），未达到 Price 提出的半数（50%）标准。发文量较多的作者包括俞云松、徐英春、沈继录、季萍、徐元宏、倪语量、卓超、胡付品等。各个作者之间合作不甚密切，跨地区合作较少。在研究机构中，发文量在 50 篇以上的有 5 所机构，前三位依次为安徽医科大学第一附属医院、复旦大学附属华山医院、南昌大学。对关键词进行聚类图谱分析，文献共生成 11 个聚类：“#0：同源性”“#1：预后”“#2：耐药性”“#3：美罗培南”等，聚类结果均可靠。由关键词突现图谱可见，耐药性、抗菌药治疗、碳青霉烯酶、肺炎克雷伯菌是当前研究的热点问题。

结论 该研究领域有重要的研究前景和学术价值。CRO 领域研究热点已经向危险因素、耐碳青霉烯肺炎克雷伯菌、血流感染、毒力基因、重症医学等方面转移。目前围绕耐药机制以及抗菌药物方面研究较多。同时应加强作者间、机构间的研究交流,开展多学科合作、高质量的研究。

关键字：碳青霉烯，耐药，细菌，可视化，计量文献分析

多主体协同治理视阈下优化抗菌药物集中采购政策效能分析——以湖南省为例

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目的 本研究旨在多主体协同治理视阈下为促进抗菌药品集中采购政策的可持续发展、优化抗菌药物管理提供参考意见。

方法 本研究于 2023 年在湖南省长沙市和娄底市对被访者包括副院长、药剂科主任、临床医生等不同职业群体进行了集体非结构访谈以获取一手资料，并使用“药品集中采购政策”、“协同治理”等关键词搜索相关文献以获取二手资料，旨在了解目前药品集中采购政策的实施现状及问题，并运用协同治理理论对资料中所反映的问题进行分析并提出相应对策。

结果 研究表明，卫健部门与医保部门、医保部门与医疗机构、医保部门与药企之间的协同问题影响药品集中采购政策效能的发挥。政策叠加引发的政策冲突是卫健部门与医保部门之间的主要问题，监管不到位是医保部门与药企之间的主要问题。医保部门与医疗机构之间的协同问题最为突出，例如政策本身过于严苛；集采任务量与医院实际需求不符；药品品种无法很好满足医院需求；医保不同限制导致医院临床医生人为不合理用药；医保部门针对医院的激励机制不健全；医院缺少自主选择权和价格知情权等等。

结论 推动药品集中采购政策的可持续发展、优化药品集中采购政策效能、实现抗菌药物的科学管理必须通过加强卫健部门与医保部门之间的政策协同、赋予医疗机构更多自主权、加强对中标企业的监管来实现。

关键字：药品集中采购，抗菌药物，协同治理

应用 FNEA 管理降低重症医学科 CAUTI 发生率

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目的 2020 年-2022 年，重症医学科尿管相关性尿路发生率在 0.12‰-0.42‰之间，高于全省中位数。通过对 CAUTI 的发生的原因进行分析，制定了一系列的防止策略，降低 CAUTI 的发生率，为临床有效防治 CAUTI 提供科学依据。

方法 对 2020 年 1 月-2022 年 12 月发生 CAUTI

的患者进行回顾性的根因分析，找出我科室患者发生 CAUTI 的原因。做为护理质量管理的重点改进项目，制定一系列防治策略，通过目标性监测，降低重症医学科 CAUTI 发生率。

科室组建 CAUTI 改进小组，结合预防 CAUTI 护理管理质量评价标准，进行分析，找出重点改进项目，制定降低科室 CAUTI 改进方法。方法如下：

结合科室现状制定了尿管相关的全流程管理：1.1 置管前的环境准备 1.2 ICU 留置尿管护理 SOP。1.3 制定了尿培养的正确采集方法.1.4 录制操作视频并人人掌握。1.5 制定了督查标准。1.6 规范更换集尿袋以及倾倒尿液的方法。

2.多形式分层级培训:2.1 对医护人员采取现场教学、理论授课、操作示范等多形式分层级的理论结合实践的培训。2.2 对科室卫生人员分时段培训，每日抽查，每月院感小组质控考核。

3.穿刺前干预:3.1 提前对整个会阴部进行清洁并对周围皮肤进行去定值。3.2 置管前 及安置尿管过程中停止床旁打扫卫生和更换床单元。

4.建立最大无菌屏障:4.1 与消毒供应中心沟通，根据需求制定无菌包布增加无菌屏障屏障。4.2 院感护士对责任护士置管过程进行监督，保障置管过程中无菌。

5.日常督查：5.1 每日落实三管监测。5.2 对尿管管理的督查结果进行分析整改。5.3 对可能感染 CAUTI 高风险情况进行梳理，与医生讨论留置或更换必要性。

结果 通过量改进,2023 年重症医学科病房的 CAUTI 发生率由实施前的 0.12‰-0.42‰下降至 0.025%,特别是无菌屏障、集尿袋更换方法、尿培养采集、无菌操作不严格等得到明显改善

结论 应用 FNEA 管理能及时发现工作中存在的问题，能够提升医护人员的感控意识与能力，提升医院的护理质量。

关键字：FNEA, CAUTI

嗜麦芽窄食单胞菌血流感染，源头何在？

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目的 通过一例连续 7 次血培养为嗜麦芽窄食单胞菌的病例，揭示龋齿可能为血流感染的来源。

方法 报道一例嗜麦芽窄食单胞菌血流感染的诊治经过。

结果 患者男性，64 岁，因“体检发现右上肺结节 2 月”2023-10-19 入胸外科。入院后排除手术禁忌症，10-20 行胸腔镜下右上肺癌根治术。10-21 患者出现声嘶、呛咳、咳痰，逐渐出现发热、气促，予抗感染、化痰等治疗，症状改善不明显。10-24 进食后出现气促加重，血气分析提示 II 型呼吸衰竭（P/F180mmHg，PaCO2 52mmHg），转 ICU，经鼻气管插管接呼吸机辅助通气。经验性抗感染（亚胺培南）、肺保护性通气、营养支持等治疗，患者逐渐退热，10-29～10.31 连续 3 天无发热，PCT 由 1.51ng/ml（10-25）降至 0.58ng/ml（10-30），复查胸片双肺炎症改善，呼吸机支持力度下调。10-31 下午患者出现呕吐，呕吐物为肠内营养液，胃镜发现慢性胃炎伴胆汁反流，胃镜下留置空肠营养管。11-1 凌晨出现寒战、高热，体温 39℃，伴感染性休克，予液体复苏、停“亚胺培南西司他丁”，改“美罗培南”抗感染。11-2 再次寒战、高热，体温 40℃，PCT 升至 1.58ng/ml。10-30 留取的痰培养回报为嗜麦芽窄食单胞菌，“美罗培南”改“头孢哌酮钠舒巴坦钠”。11-3 热峰略有回落，接报 11-1 寒战时留取的外周血及中心静脉导管血培养均提示“嗜麦芽窄食单胞菌”（第 1 次），拔除原深静脉导管（10-24 置入）。患者仍每天发热，热峰波动于 38.5℃～39℃，11-2、 11-4、11-5 复查血培养均于 48 小时内报外周血及中心静脉导管血培养为嗜麦芽窄食单胞菌（第 2、3、4 次），且外周血报阳时间更早。11-6 加用“复方磺胺甲恶唑”，热峰略下降，PCT 可回落至 0.93ng/mL(11-11)。11-7 复查 CT 双肺炎症明显吸收，腹部未见病理性表现。多次复查心脏彩超未见瓣膜赘生物。11-12 体温再次升至≥38.5℃，分别于 11-12、11-15、11-18 复查外周血及中心静脉导管血培养均提示嗜麦芽窄食单胞菌（第 5、6、7 次），患者的肺炎及呼吸衰竭逐步控制，11-15 拔除气管插管。嗜麦芽窄食单胞菌血流感染持续存在，来源无法用肺部、消化道、导管来解释，发现患者存在严重龋齿，11-22 取牙菌斑（两个部位）标本，培养 2 天发现嗜麦芽窄食单胞菌。11-19、11-22 连续两次血培养阴性，热退；11-22 转出 ICU，11-24 转口腔科处理龋齿。出院后随访 2 月，未再发热。

结论 嗜麦芽窄食单胞菌血流感染，当排除常见的感染源，应关注少见的感染源如龋齿。

关键字：嗜麦芽窄食单胞菌，血流感染，龋齿

Evaluating The Impact of Prone Position Ventilation on Oxygenation and Survival Outcomes in Severe ARDS Patients Treated with Extracorporeal Membrane Oxygenation: A Protocol For Prospective Multicenter Randomized Controlled Trial

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Background Acute Respiratory Distress Syndrome (ARDS) remains one of the most formidable challenges in critical care, characterized by a high mortality rate and significant management complexities. Extracorporeal Membrane Oxygenation (ECMO) has emerged as a pivotal intervention for severe ARDS, providing essential respiratory support when conventional therapies fail. Despite advancements, optimizing outcomes for these critically ill patients requires continued innovation. Prone Position Ventilation (PPV) has shown promise in improving oxygenation and reducing mortality in ARDS patients not on ECMO, yet its efficacy and safety when integrated with ECMO therapy are not well-defined. Addressing this knowledge gap, our study proposes a multicenter prospective randomized controlled trial aimed at evaluating the impact of PPV on severe ARDS patients undergoing ECMO. This research endeavors to enhance clinical practice by providing evidence-based guidelines for the concurrent use of PPV and ECMO in managing severe ARDS, with the ultimate goal of improving patient outcomes in intensive care units

Objective This study aims to systematically assess the efficacy and safety of Prone Position Ventilation (PPV) in severe Acute Respiratory Distress Syndrome (ARDS) patients undergoing Extracorporeal Membrane Oxygenation (ECMO) through a multicenter, prospective, randomized controlled trial. Specifically, the study seeks to determine whether PPV, when used in conjunction with ECMO, can improve oxygenation parameters, reduce the duration of ICU stay and mechanical ventilation, and decrease mortality rates in this patient population, thereby filling a significant research gap in current treatment practices

Methods The study is set in the ICUs of several tertiary hospitals across China, targeting patients with a diagnosis of severe ARDS who are eligible for ECMO treatment. Following informed consent, eligible participants will be randomized into two groups: a control group receiving standard ARDS care and an intervention group receiving PPV in addition to standard care. Primary outcomes will include mortality rates at 30, 60, and 90 days, improvements in oxygenation parameters (PaO2/FiO2 ratios), and the duration of ICU stay and ECMO support. Secondary outcomes will focus on the incidence of adverse events and complications, and the success rate of weaning from ECMO and mechanical ventilation. Advanced statistical methods, including Kaplan-Meier survival analysis, Cox proportional hazards models, and logistic regression, will be utilized to analyze the data, ensuring a comprehensive evaluation of the intervention's impact

Results We anticipate that PPV, when integrated with ECMO for the management of severe ARDS, will result in significant improvements in patient outcomes. Specifically, we expect to observe a notable enhancement in oxygenation parameters, a reduction in the duration of ICU stays and mechanical ventilation requirements, and a decrease in mortality rates compared to standard care. Additionally, the study aims to establish a detailed safety profile for the combined use of PPV and ECMO, providing critical insights into managing this complex patient population

Discussion The integration of PPV with ECMO represents a potential paradigm shift in the treatment of severe ARDS, offering a novel approach that could significantly improve clinical outcomes. This study's findings are expected to contribute substantially to the body of knowledge on ARDS management, providing a strong evidence base for the adoption of PPV in conjunction with ECMO. Moreover, the research will shed light on the safety of this combined treatment modality, enabling clinicians to make informed decisions in the care of critically ill ARDS patients.

Limitations Acknowledge potential study limitations, including the challenges of managing complex interventions like PPV and ECMO in a multicenter trial setting.

Future Research Directions Suggest areas for future investigation, such as long-term outcomes of PPV use in ARDS patients or exploring PPV's effects on specific ARDS subtypes.

Conclusion By meticulously evaluating the efficacy and safety of Prone Position Ventilation in severe ARDS patients treated with ECMO, this prospective multicenter randomized controlled trial aims to address a critical gap in current medical practice. The anticipated findings promise to provide a new therapeutic strategy that could enhance the clinical management and survival outcomes of critically ill patients with severe ARDS, laying the groundwork for significant therapeutic advancements in one of the ICU's most challenging patient populations

关键字：ARDS，prone position ventilation，Critical Care，ECMO

列题

细菌真菌感染的流行病学

111 例侵袭性肺曲霉菌病的临床特征及预后危险因素分析

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关键字：肺曲霉菌病；预后；危险因素

新冠患者继发真菌感染的临床特征及预后影响因素分析

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关键字：新型冠状病毒感染；真菌感染；预后；影响因素

脑卒中患者发生卒中相关性肺炎的危险因素分析

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关键字：脑卒中；肺炎；危险因素

MNGS Combined with Traditional Microbiology Identifies The First Case of Candida Auris in Southwest China

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关键字：Candida auris; next generation seqence; South Asian clade; antifungal susceptibility; China

艾滋病患者马尔尼菲篮状菌病相关免疫重建炎症综合征临床特征与预后

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关键字：马尔尼菲篮状菌病，免疫重建炎症综合征，艾滋病

Microevolution of Salmonella 4,[5],12:i:- Derived From Salmonella Enterica Serovar Typhimurium Through Complicated Transpositions

Qiuchun Li[1], Zhenyu Wang[1], Dan Gu[1], Yaming Hong[1], Yachen Hu[1], Jiaojie Gu[1], Yuanyue Tang[1], Xiaohui Zhou[2], Yunzeng Zhang[1], Xinan Jiao[1]
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关键字：Salmonella; monophasic variant; microevolution; IS26

广东地区耐碳青霉烯类肺炎克雷伯菌临床分布特征和耐药性变迁

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关键字：肺炎克雷伯菌；耐碳青霉烯类；检出率；耐药率

基于 GeoDa 的江西省某三甲医院在院病人肺结核流行特征研究

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关键字：肺结核；流行特征；空间自相关；后疫情时期

甘肃省某三甲医院耐碳青霉烯类肠杆菌科细菌流行病学特征

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关键字：耐碳青霉烯类肠杆菌；流行病学特征；肺炎克雷伯菌

血清幽门螺杆菌在健康人群中的感染现状研究

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关键字：幽门螺杆菌，幽门螺杆菌抗体，感染，检测，ELISA 方法学

新冠流行前、中、后期通过 NGS 检测 ICU 患者下呼吸道病原菌差异及对预后的影响

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关键字：新冠，微生物组学，重症患者，肺泡灌洗液

新出现的耐红霉素 ptxP3 克隆百日咳杆菌在中国上海处于优势地位

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关键字：百日咳，耐药基因，抗生素，全基因组测序

耐碳青霉烯类铜绿假单胞菌的分子流行病学及群体感应信号系统相关基因的研究

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关键字：铜绿假单胞菌，耐药，流行特征

Microbiology and Clinical Outcome of Bloodstream Infections in Patients After Hematopoietic Stem Cell Transplantation

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关键字：blood infections, hematopoietic stem cell transplantation, antibiotic resistance

Analysis of The Spectrum of Common Pathogens and The Resistance of Mycoplasma in Sialidase-Positive Bacterial Vaginosis

Qiongfang Zhu* Yili Shen Jie Xu
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关键字：Sialidase, Vacterial vaginosis, pathogenic spectrum, Mycoplasma

23 株图宾根曲霉分离患者临床特征及体外抗真菌药物敏感性分析

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关键字：图宾根曲霉，临床特征，药物敏感性

基于 Web of Science 的阴道微生态与早产相关性研究的文献计量学

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关键字：阴道微生态，早产，文献计量学，可视化分析

细菌真菌感染的病原诊断技术

镰刀菌血流感染所致急性淋巴细胞白血病缓解后角膜炎病例实验室诊断分析

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关键字：血流感染，镰刀菌属，血培养新技术，二代测序，病例报告

ALIFAX 尿液细菌培养技术在尿路感染诊断中的应用价值

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关键字：尿路感染、快速细菌培养、诊断效能、ALIFAX、性能评估。

心脏移植患者术后感染解甘露醇罗尔斯顿菌 1 例

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关键字：解甘露醇罗尔斯顿菌；心脏移植；宏基因组检测测序；细菌培养；药敏结果。

基于拉曼技术的耐碳青霉烯类肺炎克雷伯菌快速分型

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关键字：拉曼光谱技术；肺炎克雷伯菌；碳青霉烯类；快速耐药分型；机器学习算法

宏基因组测序诊断鹦鹉热衣原体肺部感染

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关键字：鹦鹉热衣原体；肺炎；宏基因组二代测序；肺泡灌洗液；多西环素

Metagenomic Next-generation Sequencing for The Microbiological Diagnosis of Geriatric Sepsis Patients

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关键字：Metagenomic Next-generation Sequencing, Sepsis, Geriatric, Microbiological, Diagnosis

无乳链球菌的检测方法学比较

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关键字：无乳链球菌，细菌培养，液体显色，荧光 PCR，灵敏度，特异性

Case Report and Literature Review: A Rare Case of Successful Treated Community-acquired Pseudomonas Aeruginosa Sepsis with Host-response Biomarkers Negative

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关键字：sepsis, Pseudomonas aeruginosa, metagenomic next generation sequencing, blood culture

不同新型冠状病毒感染疫情阶段呼吸道感染细菌的分布特征及药敏分析

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关键字：呼吸道感染；细菌；新冠病毒感染；

DdPCR 技术指导老年血流感染的诊疗价值

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关键字：ddPCR，BC，BSI，诊断，治疗，预后

Metagenomic Next-generation Sequencing Assists Early Diagnosis of Community-Acquired Legionella Pneumonia in Three Immunocompetent Patients in A Limited Resource Area: Case Report and Literature Review

Yuanyuan Chen Yue Wang Yan Gao*
PeKing University People's Hospital

关键字：Legionella pneumonia, metagenomic next-generation sequencing, community-acquired pneumonia, Legionella pneumophila, pathogen diagnosis

微滴数字 PCR 快速检测真菌病原菌临床价值的研究

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关键字：微滴数字 PCR ，侵袭性真菌感染 ，真菌培养

入院早期 PCT、NLR、Lac 对脓毒症患者病情分级及 预后预测的价值

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关键字：脓毒症；降钙素原；中性粒细胞/淋巴细胞比值；血清乳酸

MNGS 技术快速加测感染阿萨西毛孢子菌的实验研究及临床分析

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关键字：阿萨希毛孢子菌 感染 mNGS 技术

1 例肺普通裂褶菌感染所致变应性支气管肺真菌病的诊疗和思考

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关键字：普通裂褶菌；宏基因测序；肺组织培养；变应性支气管肺曲霉病；变应性支气管肺真菌病

经宏基因二代测序诊断小孢根霉致老年肺部感染一例

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关键字：宏二代基因检测，老年肺部感染，毛霉菌病，小孢根霉

T-SPOT 和分子生物学在存在肺部结核表现的患者中的诊断和应用及敏感性分析

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关键字：结核感染，结核病，肺结核，T-SPOT，分子生物学，肺泡灌洗液

宏基因组测序在肾移植肺部感染患者中的价值探讨及相关影响因素分析

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关键字：宏基因组，测序，肾移植，肺部感染，诊断

肝硬化腹水并发自发性细菌性腹膜炎的危险因素及病原学分析

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关键字：肝硬化，腹水，自发性细菌性腹膜炎，危险因素，诊断模型，病原菌

肝衰竭合并医院感染的危险因素分析

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关键字：肝衰竭，医院感染，危险因素，肺部感染，细菌性腹膜炎

1 例老年肺结核合并多重感染的诊治体会

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关键字：老年肺结核 多重感染 诊治体会

MNGS 和改良罗氏培养基诊断皮肤海分枝杆菌感染的比较

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关键字：mNGS，改良罗氏培养基，海分枝杆菌

直接药敏纸片扩散方法在肠杆菌目细菌血流感染诊断的准确性分析

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关键字：血培养，肠杆菌目细菌，快速鉴定，直接快速药敏

Multiple Organ Dysfunction Due To Leptospira Infection: A Case Reprort

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关键字：multiple-organ dysfunction,leptospirosis,Next-Generation gene Sequencing

急性胃肠炎伴菌血症患者分离血嗜冷杆菌的鉴定及生物学特性研究

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关键字：血嗜冷杆菌; 基质辅助激光解吸电离飞行时间质谱; 16S rRNA

(1,3)-β-D 葡聚糖检测与真菌培养检测对侵袭性真菌感染的诊断价值分析

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关键字：G 试验，真菌培养，侵袭性真菌感染

MNGS 在侵袭性肺真菌感染中的诊疗价值

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关键字：真菌感染，诊断，mNGS，传统检测

应用 tNGS 技术诊断耶氏肺孢子菌肺炎临床特征分析

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关键字：耶氏肺孢子菌，肺炎，靶向高通量测序（tNGS）

群集裂褶菌肺部感染病例报道并文献复习

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关键字：群集裂褶菌，真菌，感染

Blood Culture Quality and Turnaround Time

of Clinical Microbiology Laboratories in Chinese Teaching Hospitals: A Multicenter Study

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关键字：blood culture, key performance indicators, clinical microbiology laboratory, turnaround time, laboratory workflow

细菌真菌感染的治疗

1 例嗜肺军团菌致重症肺炎及多器官功能不全患者的抗感染治疗及药学监护

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关键字：嗜肺军团菌；重症肺炎；多器官功能不全；奥马环素；临床药师；药学监护

1 例儿童复杂先心术后合并重症感染病例分析及文献回顾

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关键字：儿童，先心病术后，解甘露醇罗尔斯顿菌，嗜麦芽窄嗜单胞菌 ，抗菌药物选择

嵌合抗原受体 T 细胞治疗后继发肺毛霉菌病 1 例

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关键字：毛霉菌；儿童；两性霉素 B；泊沙康唑；血药浓度监测

一例儿童血液恶性肿瘤肺毛霉菌病的抗感染治疗

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关键字：儿童；毛霉菌病；抗感染治疗；两性霉素 B；泊沙康唑

1 例儿童 CRE 感染后骨髓炎病例分析

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关键字：骨髓炎； CRE； 头孢他啶/阿维巴坦； 氨曲南

靶向可变剪接激活脓毒症期间的免疫反应

曹敏[1] 刘涛[1] 苏伟[1] 赵勇[2], Rosalind E Jenkins[3], Simon T, Abrams[4], Guozheng Wang[4], Cheng-Hock Toh[4] 谢剑锋[1]
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3.利物浦大学药理学和治疗学系
4.利物浦大学临床感染、微生物学和免疫学系

关键字：脓毒症；RNA 可变剪接；磷酸蛋白组组学；转录组学；剪接调节剂

替加环素治疗合并肾功能不全的腹腔感染患者的案例分析

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关键字：替加环素，腹腔感染，屎肠球菌，肾功能不全

一例腹腔感染患者的抗菌药物选择分析

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关键字：临床药师，腹腔感染，亚胺培南西司他丁钠，万古霉素

伏立康唑治疗失败侵袭性肺曲霉菌病一例

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关键字：发热；呼吸系统；侵袭性肺曲霉菌病；抗真菌治疗；初始治疗失败

阑尾穿孔伴周围脓肿继发大面积坏死性筋膜炎 1 例

张丽琴[1] 苗开辉[2] 袁媛[1,3] 孙志江[1] 鲁品[1] 赵婧[1] 周慧茹[1] 张雪[1] 焦亚军[1] 连符言[1]
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关键字：坏死性筋膜炎，阑尾穿孔，VSD，耐碳青霉烯类鲍曼不动杆菌

泛耐药肺炎克雷伯菌多部位感染 1 例

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关键字：临床药师；泛耐药肺炎克雷伯菌；肺部感染；尿路感染；药学监护

1 例鹦鹉热衣原体社区获得性肺炎抗感染治疗和药学监护

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关键字：鹦鹉热衣原体；社区获得性肺炎；米诺环素；临床药师；药学监护

新生儿 3 例曲霉菌感染患儿临床分析

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山西省儿童医院

关键字：曲霉菌感染，慢性肉芽肿病，新生儿，胸部CT，基因检测

磷霉素钠联合美罗培南治疗 1 例难治性化脓

性 脑膜炎诊疗体会

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关键字：化脓性脑膜炎，大肠埃希菌，美罗培南，磷霉素钠，硬膜下积脓

1 例严重肾功能不全合并阿莫西林过敏患者抗感染用药选择的病例分析

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关键字：严重肾功能不全；阿莫西林过敏；抗感染用药

临床药师参与 1 例人粒细胞无形体病抗感染治疗的病例分析

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天水市中西医结合医院

关键字：发热待查，人粒细胞无形体病，蜱虫，临床药师

临床药师参与 1 例菌血症患者的抗感染治疗方案分析

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关键字：坏死梭杆菌；菌血症；临床药师

一例难治性单核细胞增生性李斯特菌脑膜炎合并肺炎患者的抗感染治疗

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关键字：中枢神经系统感染，李斯特菌性脑膜炎，下一代测序（NGS）

泊沙康唑肠溶片治疗 PCNSL 合并泌尿系统尖孢镰刀菌感染一例

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关键字：PCNSL；尖孢镰刀菌；泊沙康唑肠溶片

1 例剖宫产后切口感染合并坏疽性脓皮病患者的病例分析及药学监护

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关键字：剖宫产，伤口感染，坏疽性脓皮病，药学监护

临床药师参与 1 例放线菌性胸部脓肿抗感染治疗分析

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关键字：胸脓肿，放线菌，抗感染治疗，药学监护，临床药师

新型冠状病毒感染合并混合曲霉菌感染 1 例并文献复习

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关键字：新型冠状病毒，COVID-19，侵袭性肺曲霉菌病，新型冠状病毒相关肺曲霉菌病，混合曲霉菌感染，临床特征

尖端赛多孢子菌椎体感染一例

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关键字：尖端赛多孢子菌，椎体感染，伏立康唑

一例消化道穿孔患者术后继发念珠菌血流感染的病例分析

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关键字：卡泊芬净；念珠菌感染；氟康唑

1 例肺结核合并侵袭性肺曲霉、铜绿假单胞菌感染伴肾功能不全患者的抗感染治疗与药学监护

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关键字：铜绿假单胞菌，肺结核，侵袭性肺曲霉，肾功能不全，临床药师

依拉环素联合用药用于治疗碳青霉烯耐药肠杆菌科细菌及碳青霉烯耐药鲍曼不动杆菌导致的肺部感染的临床疗效和安全性研究

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关键字：依拉环素，碳青霉烯耐药，肺部感染

临床药师参与 1 例耶氏肺孢子菌肺炎治疗的案例报告

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关键字：耶氏肺孢子菌肺炎，复方磺胺甲恶唑，治疗药物监测，血药浓度

Antibacterial Therapy of Listeriosis: Experience and Perspective From A Tertiary First-class Teaching Hospital in China

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关键字：Listeria monocytogenes; listeriosis; antibiotic treatment; questionnaire survey; clinicians

依拉环素与厄他培南对比治疗中国成人复杂性腹腔感染的疗效和安全性

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5.首都医科大学附属北京友谊医院

关键字：复杂性腹腔感染，依拉环素，厄他培南，III 期临床试验

Fluconazole Combined with Fire Needle Therapy Against Chromoblastomycosis: A Case Report and Literature Review (

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关键字：chromoblastomycosis, fluconazole, fire needle, adjuvant therapy

急性髓系白血病合并侵袭性真菌病临床治疗分析

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关键字：急性髓系白血病，侵袭性真菌病，两性霉素 B，伏立康唑

巴西奴卡菌致左上臂瘘管形成 1 例

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关键字：奴卡菌、瘘管、免疫力、药物治疗

艾沙康唑预防血液肿瘤化疗后骨髓抑制真菌感染的疗效分析

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关键字：真菌感染；艾沙康唑；血液肿瘤；骨髓抑制；疗效

神经外科术后嗜麦芽窄食单胞菌脑膜炎：一例病例报告

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关键字：神经外科，嗜麦芽窄食单胞菌，脑膜炎

A Case of Cervical Colonization by Group B Streptococcus Causing Vaginal Bleeding

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关键字：GBS; cervical colonization; abortion.

齐多夫定联合呋喃妥因对多药耐药肺炎克雷伯菌的体外活性研究

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关键字：肺炎克雷伯菌，多药耐药，齐多夫定，呋喃妥因，联合用药

The First Report of Apiotrichum Mycotoxinivorans Isolation From Cerebrospinal Fluid in Human

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关键字：Apiotrichum mycotoxinivorans, rare fungus, cerebrospinal fluid, natural products

以皮炎外瓶霉感染致皮肤坏死为首发症状的猫抓病一例及文献回顾

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关键字：皮炎外瓶霉；皮肤坏死；猫抓伤；宏基因组二代测序技术；

纹带棒状杆菌所引起的呼吸机相关性肺炎的临床特征及死亡预测因素

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关键字：纹带棒状杆菌感染；呼吸机相关性肺炎；临床特征；死亡率；预测因子

肺炎克雷伯菌所致肝脓肿合并感染性心内膜炎 1 例并文献复习

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关键字：肺炎克雷伯菌；肝脓肿；感染性心内膜炎；第三代头孢菌素；氨基糖苷类

1 例由 emm22/ST46 型化脓性链球菌引起的中毒性休克综合征

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关键字：化脓性链球菌、中毒性休克综合征、二代测序

青霉素联合头孢曲松治疗粪肠球菌所致感染性心内膜炎 1 例并文献复习

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关键字：粪肠球菌；感染性心内膜炎；青霉素 G；氨苄西林；头孢曲松

脑脊液检查正常的小肠结肠炎耶尔森菌颅内感染 1 例报道

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关键字：小肠结肠耶尔森菌 ，颅内感染

Multidrug-resistant Aeromonas Caviae Causing Cystitis in A Renal Failure Patient

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关键字：Aeromonas caviae; multidrug-resistant; cystitis; multiple myeloma; renal failure

被膜微环境响应的纳米粒子用于可视化成像引导的抗菌治疗

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关键字：生物被摸，环境响应，纳米粒子，抗菌作用，可视化成像

巨噬细胞膜包覆黑磷纳米片用于低温热动力治疗生物被膜效果的研究

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关键字：黑磷纳米片，生物被膜，低温热动力治疗，细菌感染

人型支原体致剖宫产术后血流感染 2 例并文献回顾

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关键字：人型支原体；血流感染；剖宫产

碳青霉烯类耐药肠杆菌科细菌血流感染临床特征的回顾性分析

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关键字：碳青霉烯类耐药肠杆菌科细菌，血流感染，临床特征

ICU 中 COVID-19 相关肺曲霉菌病患者的风险因素和短期预后

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关键字：COVID-19，肺曲霉菌病，ICU

康替唑胺成功治疗肝移植术后屎肠球菌所致脓毒症 1 例报告

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关键字：肝移植；屎肠球菌；康替唑胺

细菌真菌耐药监测与耐药机制

耐碳青酶烯类肠杆菌科细菌血流感染的临床特征分析及预后研究

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关键字：耐碳青霉烯类肠杆菌科；血流感染；预后危险因素

某医院 2019 年耐碳青霉烯类肺炎克雷伯菌流行特征及同源性分析

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关键字：耐碳青霉烯类肺炎克雷伯菌；耐药基因；流行特征；同源性分析

重症医学科肺炎克雷伯菌耐药率变迁及中外数据库对比

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关键字：肺炎克雷伯菌，MIMIC-IV 数据库，重症医学科，标本分布，耐药性变迁

Cyp51A 突变合并 hmg1 突变所致三唑类耐药烟曲霉导致的慢性空洞性肺曲霉病一例

梁天宇[1] 李征途[2] 李准[2] 李若瑜[1] 叶枫[2] 刘伟[1]
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关键字：烟曲霉，三唑类，耐药机制，hmg1，cyp51A

Distribution and Drug Resistance of Bacteria Isolated From Blood Samples in The Intensive Care Unit

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关键字：Blood culture; drug resistance; pathogens; intensive care unit

CRE 血流感染危险因素及耐药基因分析

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关键字：碳青霉烯类耐药肠杆菌目细菌；血流感染；危险因素；耐药基因

In Vitro Activity of Cefiderocol Against Carbapenem-resistant Escherichia Coli (CREC): A Multicenter Study in China

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关键字：carbapenem-resistant Escherichia coli, cefiderocol, CirA, NDM

6155 例泌尿生殖道感染患者支原体培养及药敏结果分析

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四川省医学科学院·四川省人民医院

关键字：泌尿生殖道，支原体，药物敏感性

Epidemiology and Antifungal Susceptibility of Candida Species Isolated From Aseptic Body Fluids in Sichuan Province of China

Xiren Deng Xiangning Huang Lin Yin Aibo Liu Shanshan Long Min Zhong Daiwen Xiao Xin Liu Kai

Zhang Xiao Wang Jie Zhang Hua Yu*
Academy of Medical Sciences & Sichuan Provincial People's Hospital

关键字：Candida Species, Aseptic Body Fluids, Antifungal Susceptibility, Epidemiology

常见真菌感染种类及耐药性分析

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关键字：真菌，体液感染，耐药性分析

Epidemiological Statistics and Drug-resistance Genotype of CRE Infection in Patients with Hematological Diseases

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关键字：Blood diseases, Carbapenem-resistant Enterobacteriales (CRE), Ertapenem resistant CRE (ETP-CRE)， metallo-β-lactamases, serine-carbapenemase, genotypes

BLBLIs-nonsusceptible ESBL-producing Enterobacteriaceae Bloodstream Infections: An Underestimated Clinical Entity

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关键字：extended spectrum β-lactamase, β-lactam/β-lactamase inhibitors combinations, bloodstream infections, Enterobacteriaceae

643 例儿童皮肤软组织感染病原分布及耐药性分析

马芷茵 张交生* 王敏敏
深圳市儿童医院

关键字：儿童，皮肤软组织感染，病原，耐药性

124 例儿童骨关节感染病原菌及抗菌药物应用分析

王敏敏 张交生*
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关键字：骨关节感染，儿童，病原菌，抗菌药物

Mining Staphylococcus Aureus Genomic Data for Identifying Fosfomycin Resistance Genes

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关键字：fosfomycin; Staphylococcus aureus; fosSA

抗菌药物的 PK/PD 研究与临床试验

肿瘤患者万古霉素血药浓度达标情况影响因素分析

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关键字：肿瘤；万古霉素；血药浓度；影响因素

抗菌药物管理与院感防控

Current Status of Antibiotic Allergy Assessment in Tertiary Hospitals in China: Empirical Research (Quantitative)

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Zhongshan Hospital

关键字：antimicrobial allergy over-labelling, allergy assessment teams, drug safety

Control of The Carbapenem-resistant Klebsiella Pneumoniae Outbreak in The Digestive Department: Whole-genome Sequencing and Active Screening Powered Investigation

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关键字：Carbapenem-resistant Klebsiella pneumoniae, nosocomial infection, outbreak, whole-genome sequencing, active screening

一例万古霉素药物热退热延迟的病例分析

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关键字：临床药师，药物热，退热延迟，万古霉素，抗菌药物

重症监护室耐碳青霉烯类肺炎克雷伯菌的耐药现状及感染危险因素分析

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关键字：碳青霉烯类耐药肺炎克雷伯菌；重症监护室；耐药菌感染；危险因素

洋葱伯克霍尔德菌在医院重症监护室的分布和耐药性分析及采取集束化管理后科室现状

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关键字：关键词：洋葱伯克霍尔德菌；重症监护病房；医院感染；多重耐药菌；

2019-2021 年甘肃省呼吸内科病原菌分布及耐药性

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关键字：呼吸内科；病原菌；耐药性；合理用药

感染指标对金黄色葡萄球菌感染诊断效能评估

刘德华*
昆明市第一人民医院

关键字：金黄色葡萄球菌，感染指标，PCT，CRP，IL-6，WBC

临床药师对抗菌药物使用的合理性干预效果分析

黄琴*
乐山市人民医院

关键字：临床药师，抗菌药物，干预

基于微信小程序的抗菌药物院外服药管理云平台的设计

李欢* 罗云婷 梁欢 胡思靓
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关键字：抗菌药物，院外，服药管理，微信小程序，设计

临床药师干预 I 类切口手术预防用药的效果分析

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关键字：临床药师，I 类切口手术，围手术期，抗菌药物，干预

基质辅助激光解吸电离飞行时间质谱在医院感染 目标性监测中的应用价值

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关键字：基质辅助激光解吸电离飞行时间质谱, ICU 病房, 医院感染监测

COPD 患者使用抗生素后发生抗生素相关性腹泻的危险因素分析

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关键字：AECOPD，抗生素相关性腹泻，危险因素

其他微生物及其感染

ERCP 与 LCBDE 治疗胆总管结石的医院感染相关因素分析

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关键字：ERCP；LCBDE；胆总管结石；医院感染；影响因素

Pseudomonas Oleovorans Sepsis in A 72-year-woman: The First Reported Case in China

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关键字：Pseudomonas oleovorans, Sepsis, Bloodstream infection, Fever, MALDI-TOF MS, Case report

A Case Report and Literature Review: Mycobacterium Leprae Infection Diagnosed by Metagenomic Next-generation Sequencing of Cerebrospinal Fluid

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Center of Infectious Diseases, West China Hospital

关键字：Mycobacterium leprae, leprosy, Listeria monocytogenes, metagenomic next-generation sequencing, systemic lupus erythematosus, case report

Listeria Monocytogenes Meningoencephalitis in The Elderly Caused by Needle

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West China School of Public Health. West China Fourth Hospital.

关键字：Listeria monocytogenes meningoencephalitis, elderly, needle injection

Fusobacterium Nucleatum-triggered Neutrophil Extracellular Traps Facilitate Colorectal Carcinoma Progression

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关键字：Fusobacterium nucleatum, colorectal carcinoma, neutrophil extracellular traps, ROS, TLR4, NOD1/2

浙江省儿童肺炎支原体感染血清学检测结果分析

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杭州迪安医学检验中心有限公司

关键字：浙江省，儿童，支原体肺炎，化学发光法

Clinical and Microbiological Characteristics of Patients with Candiduria

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关键字：Candiduria; Candidemia; Risk factor; Yeast-like cell counting; Candida score

经鼻高流量氧疗治疗重症新冠肺炎疗效及治疗失败的预警 因素分析

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关键字：新型冠状病毒肺炎 ，经鼻高流量吸氧 ，疗效 ， 危险因素

一例鹦鹉热衣原体重症肺炎的诊治与思考

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关键字：鹦鹉热衣原体，重症肺炎，mNGS

其他

人费克蓝姆菌感染 1 例报道

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关键字：人费克蓝姆菌 ； 面部脓肿 ； 诊断 ； 治疗

MNGS 诊断 7 例 Q 热立克次体并文献复习

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联勤保障部队第九 00 医院

关键字：Q 热立克次体，宏基因组二代测序，mNGS，贝纳柯克斯体

扶正解毒利水法治疗老年新型冠状病毒感染合并心功能不全的临床研究

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关键字：扶正解毒利水法，奥密克戎，新型冠状病毒感染，心功能不全，老年

临床药师参与一例腰椎感染脓肿分枝杆菌合并金黄色葡萄球菌患者的药学监护

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关键字：临床药师、腰椎感染、脓肿分枝杆菌、药学监护

布鲁氏菌性脊柱炎一例

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关键字：布鲁氏杆菌；脊柱感染；布鲁氏菌性脊柱炎；干酪样坏死

Streptococcus Salivarius Pneumonia-induced Pneumomediastinum: A Case Report and Literature Review

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关键字：Pneumonia, Streptococcus salivarius, Pneumomediastinum

临床药师参与老年患者感染病例会诊分析

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关键字：临床药师，老年患者，会诊

度洛西汀在抑郁症患者中血药浓度/剂量比的影响因素研究

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关键字：度洛西汀；血药浓度/剂量比；影响因素；抑郁症

基于 Web of Science 的非酒精性脂肪性肝病的研究现状及趋势可视化分析

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关键字：非酒精性脂肪肝病，Web of Science，CtieSpace，VOSviewer，可视化分析

托珠单抗治疗特发性多中心型 Castleman 病 1 例

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关键字：Castleman 病；托珠单抗；特发性；多中心；紫罗兰色丘疹

Metallo-β-lactamases Immobilized by Magnetic Zeolitic Imidazolate Frameworks-8 for Degradation of B-lactam Antibiotics in The Water Environment

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关键字：Zeolitic imidazolate frameworks-8, Metallo-β-lactamases, Magnetic nanoparticles, β-lactam antibiotics, Water treatment

江苏省医院感控专职人员岗位胜任力现状及其影响因素

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关键字：医院感染管理；专职人员；岗位胜任力；影响因素；现况调查

Association between Muscular Atrophy and Mortality Risk in Patients with COPD: A Systematic Review

Wenyan Li*
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关键字：Chronic obstructive pulmonary disease; Muscular atrophy; Sarcopenia; Mortality; Systematic review

免疫功能正常宿主肺盖尔森基兴诺卡菌病 1 例及文献复习

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关键字：盖尔森基兴诺卡菌；圣乔治教堂诺卡菌；肺部感染；肺诺卡菌病

Spotlight on Endoplasmic Reticulum Stress in Acute Kidney Injury: A Bibliometric Analysis Andvisualization From 2000 To 2023

Yuan Yang Xin Li*
The Third Hospital of Changsha

关键字：Acute kidney injury, Endoplasmic reticulum stress, Bibliometric analysis, Web of Science, Visualization.

肠道菌群对多重耐药菌定植抗性的研究进展综述

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关键字：定植抗性，肠道菌群，多重耐药菌

A Case of Primary Echinococcus Multilocularis in The Abdominal Cavity and Abdominal Wall of The Patient

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关键字：Echinococcus multilocularis,abdominal cavity, abdominal wall

新冠病毒感染后 Good's 综合征伴巨细胞病毒、肺孢子菌混合感染 1 例并文献复习

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关键字：Good's 综合征,免疫缺陷,胸腺瘤,机会性感

染,混合感染

关键字：驻科化，管理模式，合理用药，

品管圈提高多重耐药菌患者防控措施落实率效果观察

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杭州市第一人民医院

关键字：多重耐药菌，医院感染，防控措施，品管圈

马尔尼菲篮状菌磷脂酶 A 基因家族的生物信息学与表达分析

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关键字：马尔尼菲篮状菌，磷脂酶 A，生物信息学

提升实验室生物安全管理：从理论到实践的综合策略

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关键字：实验室生物安全，质量体系文件，风险评估，传染病院感系统，测评体系

隐球菌脑膜炎患者头痛的非药物干预措施：一项范围综述

魏利琴 侯姝婷 李欢*
四川大学华西医院

关键字：隐球菌脑膜炎，头痛，非药物干预

去除噬菌体制剂中内毒素的不同方法的比较研究

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关键字：耐碳青霉烯肺炎克雷伯菌；噬菌体；内毒素

碳青霉烯类耐药肠杆菌目细菌去定植，能成为现实吗？

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关键字：碳青霉烯类耐药肠杆菌目细菌；去定植；选择性消化道去污；粪菌移植

甲状腺激素水平对慢重症患者预后的影响

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中国医科大学附属第一医院

关键字：关键词：非甲状腺疾病综合征，慢性危重病，三碘甲状腺原氨酸，预测模型，预后

急性髓系白血病患者化疗后中性粒细胞缺乏与感染的危险因素分析

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关键字：急性髓系白血病；化疗；中性粒细胞缺乏；感染

临床药师驻科化管理模式提升我院临床合理用药水平

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隐匿性胃腺癌双肺转移误诊为肺炎一例

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关键字：胃腺癌，肺转移癌，肺炎支原体肺炎，肺炎，肺肿瘤血栓性微血管病

Study of The Effect of Intestinal Microbes on Obesity: A Biblio- 1 Metric Analysis

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关键字：obesity, intestinal microbiota, bibliometric analysis, visualization, co-occurrence analysis

血液肿瘤科儿童伏立康唑谷浓度影响因素分析

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关键字：伏立康唑，治疗药物监测， CRP，儿童，血液肿瘤

Excellent Performance of XGBoost in Predicting Bloodstream Infections

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关键字：bloodstream infection, XGBoost, Machine learning

ICU 患者院内感染因素分析及护理对策

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关键字：ICU 院内感染因素 病原菌 护理管理

Case Report: Minocycline-induced Drug Reaction with Eosinophilia and Systemic Symptoms Syndrome: A Case Report and Literature Review

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关键字：minocycline, drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, adverse event, case report, literature review.

主办单位： 中华医学会

中华医学会细菌感染与耐药防治分会

承办单位： 四川省医学会

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