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目 录

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CONTENTS

感控	001-047
感染	048-242
呼吸	243-254
临床药理	255-278
微生物	279-391
血液	392-415
真菌	416-444
重症	445-488
专家课件	489-558

CONTENTS

感控 001

根据药敏数据动态指导抗菌药物临床应用对大肠埃希菌及肺炎克雷伯菌药敏结果的影响 002

远程指导居家精神障碍患者 开展院前感染防控的应用效果 003

Remote guidance for patients with mental disorders at home The application effect of pre-hospital infection prevention and control 004

基层精神病医院开展 院外感染智慧防控管理的创新实践 005

外科重症监护病房院内感染细菌分布及耐药性分析 006

综合干预对降低血管导管相关感染发病率的效果评估 007

集束化干预降低导尿管相关尿路感染的效果 008

线上开展精神障碍患者 居家感控对医院感控的价值分析 009

基于信息化集成平台的多重耐药菌医院感染防控新模式探讨 010

新型冠状病毒感染疫情前后临床病原菌分布特征及耐药性变化研究 011

ICU 靶向干预和 COVID-19 间隔后碳青霉烯耐药鲍曼不动杆菌种群变化：一项基于基因组的纵向全球监测研究 012

Antibiotic prophylaxis after 48 h postoperatively are not associated with decreased surgical site infections and other healthcare associated infections in pancreatic surgery patients: a retrospective cohort study 013

The symptoms and interval of Omicron SARS_x0002_CoV-2 reinfection among healthcare workers in a hospital of Southern China: a cross sectional study 014

神经外科术后颅内感染 Nomogram 模型的建立与验证 015

医院感染诊断病原学送检标本 与目标感染部位的匹配情况 016

非 MDRO 型 CRPA 临床分布特点 及分层防控模式探讨 017

药敏结果“中介”是否纳入“耐药”统计 对多药耐药菌监测数据的影响 018

非重症监护病房多重耐药菌感染来源及分布研究 019

CONTENTS

Characteristics and Occurrence Scenarios of Staff Exposed to SARS-CoV-2 Omicron in Shanghai Lingang Fangcang Shelter Hospital, CHINA 020

What is the status of nucleic acid contamination in 2019-nCOV vaccination sites? Can it be avoided? 021

Antibiotic Prophylaxis After Pancreatic Surgery: A Critical Analysis 022

头孢菌素类注射剂皮试的规范化管理及分析 023

基于 CiteSpace 的 CRE 医院感染防控可视化研究 024

基于 PDCA 理论在 ICU CRE 感染防控中的精准管理实践 025

Implications of deduplication on the detection rates of multidrug-resistant organism (MDRO) in various specimens: insights from the hospital infection surveillance program 026

2014-2023 年术后肺炎临床分布特点及变化趋势 028

脊柱手术围手术期抗菌药物预防性使用合理性分析 029

Association between TLR2 +2477G/A polymorphism and bacterial meningitis: a meta-analysis 030

我院抗菌药物处方点评制度与成效对比 031

基于信息化监测的维持性血透患者中心静脉导管相关血流感染危险因素分析及预测模型构建与验证 032

来源于不同菌群的 10 个耐药基因及其突变导致耐多粘菌素肺炎克雷伯菌的传播 033

TEM-135 型产青霉素酶淋球菌的突变分析及进化趋势 034

间歇性次氯酸消毒对供水管路消毒效果及宏基因组测序分析 035

四川地区 2017-2023 年呼吸道病毒感染的流行病学特征分析 036

ERCP 与 LCBDE 治疗胆总管结石的医院感染相关因素分析 037

江苏省医院感控专职人员岗位胜任力现状及其影响因素 038

Increased Transmission of Pseudomonas aeruginosa in ICU Settings During the COVID-19 Pandemic 039

CONTENTS

Discovery of novel BfmR inhibitors restoring carbapenem susceptibility against carbapenem-resistant Acinetobacter baumannii by structure-based virtual screening and biological evaluation 040

Knowledge, Attitudes, and Practices of Chinese Residents Regarding Antibiotics and Antibiotic Resistance 041

重症监护病区（ICU）抗生素耐药性防控策略研究进展 043

江苏省某大型三甲医院静脉药物调配中心 2019 年—2023 年环境卫生学监测结果分析 044

《粒缺伴发热患者血培养病原菌分布及耐药性：一项为期 10 年的单中心回顾性研究》 045

Establishment and validation of a nomogram based predictive model for Carbapenem-resistant organism infection 046

Global, regional, and national time trends in incidence for tuberculosis,1990-2019: An age-period-cohort analysis for the Global Burden of Disease 2019 study 047

感染 048

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 049

P2X7 和 TRAF1/C5 基因多态性与结核病易感关联性的家庭病例对照研究 050

DRESS syndrome caused by comprehensive effects of multiple drugs-a case report 051

头孢他啶阿维巴坦用于儿童术后产超广谱 β 内酰胺酶大肠埃希菌脑膜炎和脑脓肿的病例报道 052

MRSA 菌血症患者万古霉素个体化治疗方案分析 053

马尔尼菲青霉菌病 1 例 054

肺结核合并噬血细胞综合征 1 例 055

Adoptive transfer of CMV-specific TCR-T cells for the treatment of CMV infection after haploidentical hematopoietic stem cell transplantation 056

225 株鲍曼不动杆菌的耐药性分析与 OXA-23 型碳青霉烯酶检测在神经重症中应用 057

心脏外科手术围术期抗菌药物的使用与术后切口感染发生率的研究 058

CONTENTS

一例肺组织胞浆菌患者的诊疗 059

分享 1 例妊娠中期重度支原体肺炎的诊治 060

Colistin methanesulfonate is efficacious and safe for the management of serious infections in hematological diseases patients: a retrospective study in China 061

b-Hydroxyisovalerylshikonin regulates macrophage polarization via the AMPK/ Nrf2 pathway and ameliorates sepsis in mice 062

耐多黏菌素和碳青霉烯类肺炎克雷伯菌的危险因素分析 063

高龄尿路感染患者的病原学特征分析 064

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 065

从药学角度对硫酸黏菌素的临床应用评价与分析 066

肺炎克雷伯菌尿路感染 167 例碳青霉烯耐药风险列线图 预测模型的构建 067

CRISPR/Cas13a 技术助力戊型肝炎病毒 RNA 准确、便携式检测 068

马尔尼菲篮状菌持续成为福建省艾滋病患者血流感染的压倒性病原体 069

耐甲氧西林金黄色葡萄球菌致 5 例 PICC 导管相关性血流感染的血液肿瘤患者的护理分析 070

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 071

伏立康唑治疗肝衰竭合并侵袭性肺曲霉病的临床研究 072

Infection with Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae: clinical, virulence and molecular epidemiological characteristics 073

代谢途径中的磷酸烯醇丙酮酸（PEP）在肿瘤免疫微环境中作用 074

The first case report: diagnosis and management of necrotizing fusobacterium lung abscess via BALF next generation sequencing 075

大肠埃希菌感染引起肝脓肿、肠系膜脓肿合并肝假性动脉瘤一例 076

社区获得性耐甲氧西林金黄色葡萄球菌致感染性心内膜炎合并肺脓肿病例报道及文献复习 077

中国不同城市 61 例鹦鹉热衣原体肺炎病例分析 078

CONTENTS

Maraviroc, an inhibitor of chemokine receptor type 5, alleviates Sepsis associated liver injury via regulating MAPK/NF-κB signaling 079

于临床宏基因组测序技术快速预测中枢神经系统感染耐多药细菌表型研究 080

血药浓度监测下伏立康唑致肝酶升高及视觉异常的药学监护 081

PIRO（易感因素、损害、反应、器官功能障碍）评分与其他六个临床预测评分对 COVID-19 患者预后预测的比较：一项基于急诊科数据的研究 082

Presepsin 作为 COVID-19 患者预后预测的生物标志物：结合临床评分系统和实验室炎症指标的预测研究 083

中国西部地区 HIV 阴性结核性脑膜炎发生矛盾反应的临床特征研究 084

Quality assessment of therapeutic drug monitoring guidelines for voriconazole using AGREE II instrument 085

化学发光法检测胃功能的方法学评价 086

PDCA 循环模式在干眼理疗眼部感染发生率中的应用 087

基于 COM-B 理论模型的口腔卫生管理对造血干细胞移植后患者口腔感染的影响 088

药师参与 1 例啮蚀艾肯菌致腰大肌脓肿患者的药物治疗实践 089

肺部混合感染并抗合成酶抗体综合征活动 1 例 090

腺病毒肺炎和鹦鹉热衣原体肺炎的临床特征比较 091

大浪淘沙，寻因高热肺脓肿 092

宏基因组二代测序和血培养在血液病粒缺患者革兰阴性杆菌感染中的对比研究 093

新冠患者继发真菌感染的临床特征及预后影响因素分析 094

临床药师参与 1 例铅黄肠球菌血流感染的体外膜肺氧合患者抗感染治疗的药学监护 095

二代测序技术在皮肌炎并发肺部感染患者中的作用：1 例报告 096

宜春市人民医院感染 CRKP 患者的预后数据分析 097

临床药师参与 1 例毗邻颗粒链菌菌血症合并化脓性脑膜炎患者抗感染治疗的药学实践 098

CONTENTS

耶氏肺孢子菌肺炎诱发哮喘急性发作 1 例 099

Mycobacterium paragordonae pulmonary disease with rapidly growing solitary lesions: a case report and literature review 100

硫酸黏菌素不同给药方式治疗碳青霉烯类耐药革兰阴性菌所致肺部感染的临床应用分析 101

基于 FAERS 数据库万古霉素在老年患者中的不良事件信号挖掘 102

miR-223 Regulates FOXO1 Expression, Autophagy, and Im-mune Function in CD4+T lymphocytes during Sepsis: ex-hibiting a potential application of small RNA (miR-223) in solving the immune imbalance during sepsis 103

Efficacy and Safety of Eravacycline (ERV) in Treating Infections Caused by Gram-Negative Pathogens: A Systematic Review and Meta-Analysis 104

咽峡炎后败血症（lemierre 综合征）个案报道并文献复习 105

Clinical features and risk factors of Klebsiella pneumoniae infection in premature infants: a retrospective cohort study 106

113 例艾滋病相关淋巴瘤患者的治疗结局及影响因素 108

流感相关肺曲霉菌病与新冠相关肺曲霉菌病临床特征及预后分析：一项多中心回顾性研究 109

tNGS 对高毒力肺炎克雷伯杆菌感染的诊断价值分析 110

Optimizing Antimicrobial Strategies and Prognosis Prediction in Corticosteroid-Sensitive Diffuse Parenchymal Lung Diseases with Negative mNGS Results 111

某院 360 例氨基糖苷类抗感染药物合理用药分析 112

类器官共培养模型的研究进展 113

Optimizing Pharmacokinetics: Insights into Antimicrobial Agents in the Elderly Population 114

1 例慢性阻塞性肺疾病急性加重伴肺部感染患者药源性血小板减少症的药学监护 115

噬菌体与抗生素联合清除细菌生物膜的研究进展 116

亚胺培南 / 瑞来巴坦和 ceftolozane/tazobactam 对肠杆菌目细菌、铜绿假单胞菌的抗菌活性：SMART 2020~2021 117

CONTENTS

EBV-LPDs 患者免疫紊乱及早期诊断预测指标研究 118

持续炎症刺激下耐受型树突状细胞的细胞模型 119

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 120

奥马环素治疗急性细菌性皮肤和皮肤软组织感染的疗效和安全性：随机对照试验的系统评价和荟萃分析 121

替考拉宁在老年人群中的血药谷浓度监测结果及影响因素探讨 122

替考拉宁治疗脓毒症患者的血药谷浓度与临床疗效和安全性的相关性分析 123

3 例鹦鹉热衣原体重症肺炎临床特征及诊治特点 124

不同乳杆菌对脓毒血症保护作用 125

Polymyxin B resistance rates in carbapenem-resistant Pseudomonas aeruginosa isolates and a comparison between Etest ® and broth microdilution methods of antimicrobial susceptibility testing 126

新型冠状病毒感染患者炎症指标及细胞因子检测的临床价值 127

鄞州地区结核患者营养风险和营养指标调查分析 128

CD8+ 组织驻留记忆 T 细胞在新型冠状病毒感染中的研究进展 129

高黄芩素抑制鲍曼不动杆菌多聚磷酸盐激酶 PPK1 的作用及机制 130

Copper metabolism-mediated virulence evolution of omadacycline in carbapenem-resistant Klebsiella pneumoniae ST11 131

123 例免疫缺陷人群肺孢子菌肺炎合并急性呼吸衰竭临床特征分析 133

基于微信小程序的 OTO 药学服务在抗菌药物科学化管理中的应用 134

影像类似肺水肿表现的常见疱疹病毒肺炎 135

合并隐球菌、白色念珠菌感染 1 例 135

第三章基因二代测序（mNGS）在气管食管瘘病原学检测中的应用研究 136

Diagnostic sensitivity of immune-inflammatory cell proportion in early diagnosis of endometrial cancer 137

CONTENTS

神经型布鲁菌病 20 例病例系列 138

Practice of standardization of CLSI M45 A3 antimicrobial susceptibility testing of Infrequently Isolated or Fastidious Bacteria strains isolated from blood specimens in Guangdong Province 2017 -2021 140

Association between serum vitamin E and bacterial vaginitis in women: a cross-sectional study 141

广泛耐药鲍曼不动杆菌肺部感染的危险因素与抗菌药物治疗方案 分析 143

宏基因组二代测序在骨关节感染病原学诊断中的应用 144

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 145

妊娠期糖尿病孕妇尿路感染的临床特征与危险因素分析 146

危重症监护室血流感染预后危险因素分析 147

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 148

孕妇尿路感染的病原菌分布及危险因素分析 149

基于真实世界数据的集采注射用头孢唑林钠预防手术部位感染（SSI）的临床综合评价 150

Increased Co-Infection of Mycoplasma and Chlamydia Pneumoniae Among COVID-19-Positive Kidney Disease Patients 151

Oridonin protects LPS-induced acute lung injury by modulating Nrf2-mediated oxidative stress and Nrf2-independent NLRP3 and NF-κB pathways 152

Oridonin attenuates carrageenan-induced pleurisy via activation of the KEAP-1/Nrf2 pathway and inhibition of the TXNIP/NLRP3 and NF-κB pathway in mice 153

肺泡灌洗液 mTGS 检测流程的优化和临床验证 154

发热半年的罪魁竟然是它? 155

外周血宏基因组二代测序诊断侵袭性曲霉菌病的价值：一项单中心回顾性研究 156

Negative associations between folate and bacterial vaginosis in the NHANES 2001 to 2004 157

CONTENTS

1 例紫色尿袋综合征患者的治疗体会 158

同型半胱氨酸与细菌性阴道病之间的关联：来自 2001-2004 年 NHANES 数据 159

降糖药物的服用与脓毒症的不良预后：基于药物靶点遗传代理的孟德尔随机化研究 160

隐球菌病的临床病例分析 161

Ceftazidime/avibactam resistance characteristics emerged diversely in carbapenem-resistant Klebsiella pneumoniae and carbapenem-resistant Pseudomonas aeruginosa from an intensive care unit 162

Glucose oxidase@Ruthenium-copper Nano-enzyme Aerogels in the Treatment of Biofilm Infections 164

Association Between Red Blood Cell Folate and Trichomonas vaginalis Infection among Women 166

杭州市 2021-2023 年诺如病毒流行病例状况分析 167

布鲁菌性脊柱炎危险因素及预后分析 168

慢性阻塞性肺疾病急性加重期及慢性阻塞性肺疾病下呼吸道感染患者的病原菌分布及耐药性研究进展 169

通过生物信息学分析和机器学习来识别结核病和 SARS-CoV-2 感染之间的相互作用 170

血浆 mcfDNA 宏基因组二代测序揭示血液病与造血干细胞移植患者感染病原谱特征 171

A five-year retrospective cohort study of patients with acinetobacter baumannii bloodstreaminfection: clinical characteristics, treatment, prognosis and their consequences 172

脓毒症和脓毒性休克 1h 集束化治疗实施现状调查 173

Metagenomic Sequencing Reveals Differences in Lung Microenvironment among Patients with Nontuberculous Mycobacterial Pulmonary Disease under Different Immune States 174

微滴式数字聚合酶链反应在病原体检测中的研究进展 176

创伤弧菌感染引起双足坏死继发脓毒血症一例 177

双歧杆菌四联活菌片及联合凝结芽孢杆菌活菌片对移植后患者粘膜炎的影响 178

CONTENTS

碳青霉烯类抗生素耐药铜绿假单胞菌菌血症不同抗菌治疗方案疗效分析 179

脓毒症引起的肌萎缩与白介素 -6 相关研究的综述 180

发热伴血小板减少综合征患者合并侵袭性肺曲霉病的危险因素：一项多中心研究 181

Temporal trends in global, regional, and national tuberculosis mortality, 1990-2019: An age-period-cohort analysis for the GBD 2019 study 182

Global Publication Trends in Monkeypox Research: An Analysis through Bibliometrics 184

浙江地区普通人群戊型肝炎病毒感染情况调查分析及研究 186

Efficacy and safety of combination of colistimethate sodium aerosol and injection in the treatment of pulmonary infection caused by carbapenem-resistant organism: a real-world evaluation study 187

Incidence, Risk Factors, Microbiology and Outcomes of Bloodstream Infection During Conditioning before Allogeneic Hematopoietic Stem Cell Transplantation 189

Efficacy of Short Course Antibiotic Therapy for Uncomplicated Staphylococcus aureus bacteremia in Neutropenic Patients with Hematological Diseases: A Retrospective Comparative Study 190

Analysis of the Burden of Disease and Attributable Risk Factors for Myocarditis in the Western Pacific Region, 1990-2019 192

基于生物信息学筛选并验证识别脓毒症相关凝血功能障碍新型生物标志物研究 194

中国临床金黄色葡萄球菌对磷霉素耐药性分析及耐药机制研究 195

MRSA ST764 克隆传播和克隆变迁机制研究 196

多黏菌素 B 治疗感染 CRO 肾移植患者相关性急性肾损伤的影响因素分析 197

基于单细胞转录组测序技术的肺曲霉菌感染的免疫机制研究 198

动态血脂谱对新冠肺炎患者死亡率的预测价值 199

In vitro activity of cefiderocol against carbapenem-resistant Escherichia coli (CREC): A multicenter study in China 200

CONTENTS

The downregulation of Tapasin in dendritic cell regulates CD8+ T cell autophagy to hamper hepatitis B viral clearance in the induced pluripotent stem cell-derived hepatocyte organoid 201

低频超声通过抑制 TNFR1-NF-κB 途径减轻肺炎克雷伯菌诱导的小鼠肺部炎症 202

mNGS 技术在危重症患者病原学诊断中的应用价值 203

医院获得性肺炎患者多粘菌素 B 的药代动力学及其影响因素分析 204

不同益生菌补充治疗对于干细胞移植患者感染的影响 205

多粘菌素 B 药代动力学参数与 HAP 患者临床预后的相关性研究 206

VAP 患者静脉联合雾化应用多粘菌素 B 的 PK/PD 临床研究 207

营养支持时机对不同病原菌所致脓毒症患者预后的影响：一项单中心、回顾性、队列研究 208

支气管扩张患者合并活动性肺结核风险因素分析及列线图预测模型的建立 209

多黏菌素 B 治疗碳青霉烯耐药革兰阴性杆菌所致血流感染的疗效与安全性分析 210

重症 COVID-19 患者继发细菌、真菌感染的危险因素与临床特征 211

RT-LAMP 诊断赛卡病毒感染的系统评价和 Meta 分析 212

A single center retrospective clinical epidemiological study on infections in renal transplant recipients 213

肾脏血流动力学联合生物标志物对脓毒症相关急性肾损伤患者肾脏预后的预测价值 215

Pathogen spectrum and clinical characteristics in Lung cancer patients: a 10 years retrospective study 216

内皮细胞外囊泡重编程单核细胞在脓毒症相关 ARDS 中的作用和机制研究 218

基于真实世界不同厂家美罗培南治疗肺部感染的有效性与安全性评价 219

喀什地区细菌性脑膜炎的临床特征及结局的回顾性研究 220

恶性血液病患者发生铜绿假单胞菌感染的临床特征及预后分析 221

识别肺炎克雷伯菌肝脓肿患者发生菌血症的生物标志物探索 222

CONTENTS

耶尔森菌素在经典肺炎克雷伯菌肺部感染中发挥关键毒力作用 223

基于 MIMICIV 数据库中 ICU 患者动态体温特征构建辅助识别脓毒症的模型 224

成人肺炎支原体感染对大环内酯类抗生素耐药的研究 225

造血干细胞移植过程中肠道微菌群与血清 / 尿液代谢物的动态变化及其临床意义 226

搭建用于病原高通量测序的感染性病理样本核酸提取流程 228

固有免疫反应在 HAdV 感染疾病进程中的关系探讨 229

伏立康唑成功治愈奥默柯达血流感染 1 例 230

重症患者体内多黏菌素 B 药物浓度监测及评价指标 231

Identifying mortality-related risk factors of bloodstream infections due to Escherichia coli and Klebsiella pneumoniae in hematological patients 232

Risk factors for hospitalization and pneumonia development of pediatric patients with seasonal influenza during February-April 2023 234

Analysis of Pulmonary Bacterial Infection and Antimicrobial Agent Use in Elderly Patients 235

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 236

不同益生菌补充治疗方案对于干细胞移植患者感染的影响 237

Antithrombotic strategies in adult COVID-19 patients: a systematic review and Bayesian network meta-analysis 238

Omicron caused stronger macrophage pyroptosis than wild-type strains 240

1 例支气管扩张并感染患者住院期间高热处理经验分享 242

呼吸 243

新型冠状病毒肺炎病情严重程度与预后指标相关性的 Meta 分析 244

热毒宁注射液治疗老年急性肺炎的临床疗效 245

CONTENTS

烟曲霉胶霉毒素抑制巨噬细胞自噬及炎症的机制研究 246

布地格福吸入气雾剂在慢性阻塞性肺病中的临床研究进展 247

低密度中性粒细胞在结核病发病中的表达及功能影响 248

基于多样化筛选的儿童重症腺病毒肺炎全因素分析及预测模型构建与评价 249

降糖药使用引起的细菌性肺炎发生风险和获益——基于遗传基因水平的孟德尔随机化研究 250

服用降糖药物引发的病毒性肺炎发生：基于药物靶点遗传代理的孟德尔随机化研究 251

临床药师参与一例多重耐药非结核分支杆菌肺病治疗的药学监护 252

一例百日咳肺炎合并心力衰竭患儿的护理 253

机化性肺炎的多组学免疫景观 254

临床药理 255

基于一体化闭环药学服务的国家骨科医学中心抗菌药物合理应用实践 256

基于院科上下联动事前事中事后服务闭环的抗菌药物管理实践及规范 257

Antibacterial Therapy of Listeriosis: Experience and Perspective from a Tertiary First-class Teaching Hospital in China 258

Evaluations of prescribing practices of ceftazidime-avibactam at a tertiary first-class teaching hospital in China: A retrospective analysis for future improvement 259

The enhancement effect of small molecule Lyb24 reveals AzoR as a novel target of polymyxin B 260

TBAJ-587 对临床相关非结核分枝杆菌的体外抗菌活性研究 262

Therapeutic drug monitoring of ceftazidime-avibactam concentrations in carbapenem-resistant K. pneumoniae-infected patients with different kidney statuses 263

慢性炎症的中医疗法 264

Vancomycin combined with piperacillin-tazobactam increases the risk of acute kidney injury compared with vancomycin plus other anti-pseudomonal beta-lactams: a systematic review and network meta-analysis 265

CONTENTS

苦练内功强本领，真抓实干出实招—明光市人民医院多措并举推进抗菌药物管理取得实效 267

TBAJ-587 对临床相关非结核分枝杆菌的体外抗菌活性的研究 268

The impact of polymyxin B pharmacokinetics on clinical outcomes in critically ill patients: A single-center retrospective study 269

Effect of Ceftazidime- Avibactam Combined with Different Antimicrobials against Carbapenem-Resistant Klebsiella pneumoniae 271

Comparative Pharmacokinetics of Polymyxin B in Critically Ill Elderly Patients with Extensively Drug-Resistant Gram-Negative Bacteria Infections 272

替加环素致低纤维蛋白原血症的危险因素 273

TDM 指导下美罗培南治疗耐药菌感染的重症成人糖尿病患者 274

模型引导下西他沙星对目标病原菌药动学 / 药效学界值的制定及给药方案评价 275

Development, validation and application of an LC-MS/MS method for the simultaneous quantification of four triazole antifungal concentrations in human plasma 276

PBPK study of contezolid in the central nervous system 277

微生物 279

FOCUS—PDCA 在降低感染科住院患儿血培养污染率中的应用 280

Strong homology between colonising and bloodstream carbapenem-resistant Acinetobacter spp.: implications for empiric antibiotic therapy in haematological patients 281

A training program for Improving the capacity of infection high-throughput sequencing and Diagnosis in China 282

以腹泻为首发表现的 C 群沙门菌全身侵袭性肝脓肿 1 例 284

抗菌肽 Aurein 1.2 衍生物的设计、合成和活性评价 285

鲍曼不动杆菌碳青霉烯耐药代谢变化及逆转效应代谢物功能的研究 286

全靶向宏基因组二代测序技术对脓毒症病原体诊断价值及临床评估治疗研究：一项多中心前瞻性观察研究 287

CONTENTS

质谱鉴定联合直接快速药敏试验在细菌血流感染中的应用 288

某三级医院耐碳青霉烯铜绿假单胞菌的临床分布及其检出率与碳青霉烯类抗菌药物使用频度DDDS 的相关性研究 289

Quorum sensing coordinates phage defense mechanisms in Pseudomonas aeruginosa 290

Synergistic Effect of N-acetylcysteine and Ambroxol Hydrochloride in Combination with Phage against Pseudomonas aeruginosa and Klebsiella pneumoniae 291

脓肿分枝杆菌致婴幼儿迁延性肺炎 1 例并文献复习 293

Comparison of metagenomic next-generation sequencing and conventional culture for the diagnostic performance in febrile patients with suspected infections 294

Highly sensitive SERS platform for pathogen analysis by cyclic DNA nanostructure@AuNP tags and cascade primer exchange reaction 295

Study on the Detection and Infection Distribution of Multidrug-Resistant Organisms in Different Specimens 296

2012-2022 年某综合医院门诊男性患者人乳头瘤病毒感染状况和基因型分布 297

Tracing the Possible Evolutionary trends of Morganella morganii: Insights from Molecular Epidemiology and Phylogenetic Analysis 298

应用定量测序技术评估呼吸机相关下呼吸道感染患者的早期微生物反应 299

Whole genome sequence of Porphyromonas pogonae PP01-1, ahuman strain harboring blaOXA-347 and tet(Q)with chromosomal location 300

Performance of Disk Diffusion Method for Aztreonam in Combination with Avibactam against Enterobacteriales 301

Extraintestinal pathogenic Escherichia coli (ExPEC) O-serotype distribution and antibiotic resistance profiles among aging population in China: a longitudinal, multi-center study 303

基于 Nanopore 技术的宏基因组测序在肺炎患者 Balf 病原诊断价值的临床观察研究 304

KPC-2 和 NDM-1- 共携带含 IncR 质粒的弗劳地柠檬酸杆菌在中国的出现和克隆传播 305

CONTENTS

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 306

新型 β - 内酰胺酶抑制剂 FL058 提高亚胺培南抗脓肿分枝杆菌活性 307

新型 InhA 还原酶抑制剂 NITD-916 对脓肿分枝杆菌的体内外活性研究 308

A Simple Disk Stacking Plus Micro-Elution Method for Rapid Detection of the Synergistic Effect of Aztreonam and Ceftazidime/Avibactam Against Metallo- β -Lactamase Producing Enterobacterales 309

2021 - 2022 监测年度枣庄市乙型流感病毒 Victoria 系全基因组测序分析 310

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 311

2016-2023 年常州恙虫病的临床特征和实验室诊断 312

宏基因组测序诊断鹦鹉热衣原体肺部感染 313

耐碳青霉烯类肺炎克雷伯菌 ST11 的分子流行病学特征 314

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 315

In vitro activities of the essential antimicrobial including aztreonam/avibactam, eravacycline, colistin, and other comparators against carbapenem-resistant organisms: a multicenter study in China, 2021 316

Involvement of Tn3 Transposon in Formation and Transmission of Hypervirulent and Carbapenem-resistant Klebsiella pneumoniae 318

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 319

Analysis of the Spectrum of Common Pathogens and the Resistance of Mycoplasma in Sialidase-Positive Bacterial Vaginosis 320

59 例咽峡炎链球菌群感染脑脓肿患者临床特征分析 321

The peripancreatic microbiota is associated with the severity of acute pancreatitis 322

抗心律失常药物决奈达隆通过抑制 LuxS 发挥增强多粘菌素抗菌活性的机制研究 323

Global epidemiology and evolutionary trajectory of mcr-positive Klebsiella pneumonia from 2000 to 2023 324

CONTENTS

从 ST11 新突变株识别耐碳青霉烯肺炎克雷伯菌的多种潜在耐药基因靶标 325

Dissemination of clinical Escherichia coli strains harboring mcr-1, blaNDM-7 and siderophore-producing plasmids in a Chinese hospital 326

Transmission of non-conjugative virulence plasmid of ST65 carbapenem-resistant and hypervirulent Klebsiella pneumoniae strains 327

人源性非伤寒沙门菌感染中由质粒介导的阿奇霉素耐药性 328

Epidemiology of Meyerozyma guilliermondii species complex isolated from invasive fungal diseases: a multicenter study in China 329

2013-2022 年孕产妇血流感染的临床特点及病原菌分布 331

Complex evolutionary trajectories in vivo of two novel KPC variants conferring ceftazidime-avibactam resistance 332

A novel KPC-179 variant conferring ceftazidime-avibactam resistance in a carbapenem-resistant Klebsiella pneumoniae isolate 333

Blood-rsCDM: a New Rapid and Simplified Carbapenemase Detection Method for Detecting Carbapenemases in Enterobacterales Directly from Positive Blood Cultures 334

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 335

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 336

孕产妇生殖道无乳链球菌的血清型分布及耐药基因分析 337

Genome sequencing unveils blaKPC-2-harboring plasmids as drivers of enhanced resistance and virulence in nosocomial Klebsiella pneumoniae 338

Excellent performance of XGBoost in predicting bloodstream infections 339

Dynamic evolution of ceftazidime-avibactam resistance from a single patient through the IncX3_NDM-5 plasmid transfer and blaKPC mutation 340

A large-scale surveillance revealed that KPC variants mediated ceftazidime-avibactam resistance in clinically isolated Klebsiella pneumoniae 341

CONTENTS

In vivo divergent evolution of cross-resistance to new β-lactam/β-lactamase inhibitor combinations in Pseudomonas aeruginosa following ceftazidime/avibactam treatment 342

IS26 mediated recombination poses contribution to the formation of blaKPC and blaNDM hybrid plasmid 343

The Novel, Unprecedented Photodynamic Therapy of Ionic Aggregation-induced Emission Compounds for the Treatment of Superbug Candida auris Infections 345

头孢他啶 - 阿维巴坦压力下 KPC 突变的体外模拟：表型、分子机制、遗传结构和动力学研究 347

肺炎链球菌感染研究进展 348

Xpert Carba-R 技术在 CRE 耐药基因快速检测中的应用及其诊断效率 349

多粘菌素耐药性：机制、挑战与防控策略 350

基于 MALDI-TOF MS 与机器学习快速检测热带念珠菌氟康唑耐药性研究 351

Antimicrobial application of multimodular functional materials constructed based on alkyne amine click reaction against carbapenem-resistant gram-negative bacilli 352

A case report of elbow joint cyst caused by Nocardioides zeae infection 354

The rapid transform of blaKPC variant within ST11 carbapenem-resistant and hypervirulent Klebsiella pneumoniae contributed to ceftazidime/avibactam resistance during in vivo severe infection 355

新型分子技术用于非结核分枝杆菌菌种鉴定的效能比较分析 356

微滴式数字 PCR 检测淋病奈瑟菌方法的建立 357

微滴式数字 PCR 检测阴道加德纳菌方法的建立及应用 358

杭州市某三级医院 2015-2020 年院内鲍曼不动杆菌耐药性及种群特征分析 359

基于基因组序列分析 ST11-KL10 CRKP 的进化路径 360

SSK2 基因影响 VG Ⅰ型格特隐球菌对两性霉素 B 药物治疗敏感性的研究 361

利用宏转录组学对肺炎患者下呼吸道样本病原体鉴定的案例报告 362

CONTENTS

微滴式数字 PCR 检测解脲支原体方法的建立及应用 363

深圳市人民医院 2019—2023 年铜绿假单胞菌的临床分布及耐药性分析 364

疥疮 638 例的临床特征分析 365

头孢他啶 - 阿维巴坦耐药相关肺炎克雷伯菌 blaKPC-90 的鉴定及 IS26 介导的耐药基因易位和截短 366

A novel COE-D8-Fosfomycin conjugate effectively against first line antibiotic resistant uropathogenic E.coli. 367

2021-2023 年西北地区某中医医院多重耐药菌感染检出情况调查分析 369

Microbial community of municipal drinking water in Hangzhou using metagenomic sequencing 370

Assessment of microorganisms in drinking water disinfected by catalytic ozonation with fluorinated ceramic honeycomb and NaClO disinfectants under laboratory and pilot conditions 376

Application of Total Laboratory Automation for Direct Rapid Antimicrobial Susceptibility Testing from Enterobacterales-Containing Blood Cultures 384

High-fat diet changed salmonella infection pattern associated with increasing intestinal permeability and altering gut microbiota 385

微滴式数字聚合酶链式反应在临床诊断中的研究进展 386

不携带 mecA 基因的甲氧西林耐药金黄色葡萄球菌的检出及分子特征 387

Persistent dissemination of β-lactam resistant Streptococcus pneumoniae clones in China linked to distinct Penicillin-Binding-Protein mutational combination 388

急性髓性白血病患者的肠道菌群 - 宿主代谢物的时间变化及临床预测价值 390

Screening of potential biomarkers involved in Lyme disease infection via bioinformatics analysis with machine learning algorithm 391

CONTENTS

血液 392

Acinetobacter spp. bloodstream infection in hematological patients: a 10-year single-center study 393

浙江地区健康体检人群血清水平调查 394

The pathogenesis of severe aplastic anemia may be influenced by Poxviridae and Retroviridae through metabolic pathways 395

基于社会生态系统理论的白血病患者恢复居家生活体验的质性研究 396

血液系统恶性肿瘤患者粒缺发热时期宏基因组二代测序技术分析病原微生物的临床研究 397

结核 398

CD7 CAR-T 桥接 allo-HSCT 显著提高难治 / 复发 T 细胞急性淋巴细胞白血病 / 淋巴瘤的无病生存 399

曲美替尼在 RAS 突变的恶性血液肿瘤维持治疗中可显著降低复发率改善预后生存 400

TP53 突变恶性血液病行异基因造血干细胞移植后应用奥拉帕利的维持治疗 401

PD-1 单抗在治疗移植后早期播散性腺病毒感染中的应用 402

异基因造血干细胞移植后耶氏肺孢子菌肺炎临床特征分析 403

宏基因二代测序技术在 allo-HSCT 后 军团菌肺炎的 6 例临床应用观察 404

Clinical Characteristics and Treatment Response of Chronic Disseminated Candidiasis in Patients with Hematological Disorders 405

磁微粒发光法检测抗 IAA 抗体的性能验证 407

自身抗体和补体在狼疮肾病的应用价值 408

血小板参数联合 CRP 在类风湿关节炎活动度中的相关性研究 409

母亲抗核抗体阳性对新生儿的影响 410

儿童造血干细胞移植骨髓空巢期使用康替唑胺联合抗结核治疗案例报告 411

来特莫韦治疗及二级预防异基因造血干细胞移植后巨细胞病毒感染的临床研究 412

CONTENTS

Increased Epstein-Barr virus reactivation but comparable post-transplant lymphoproliferative disorders incidence following allogeneic hematopoietic cell transplantation in letermovir era for cytomegalovirus prophylaxis 413

一例误诊为播散性感染的间变大细胞淋巴瘤 415

真菌 416

泊沙康唑与伏立康唑经验治疗或诊断驱动治疗免疫功能低下患者侵袭性霉菌病的成本—效果分析 417

毛霉菌感染患者艾沙康唑治疗药物监测的价值 418

Integrated analysis of microbiome and host transcriptome unveils correlations between lung microbiota and host immune in bronchoalveolar lavage fluid of pneumocystis pneumonia patients 419

马尔尼菲篮状菌感染淋巴结引起的上腹部肿块：病例报告 421

初始抗真菌治疗策略对重症侵袭性肺曲霉菌病患者的临床预后影响：一项单中心、回顾性研究 422

伏立康唑分散片致骨髓抑制不良反应分析 423

Successful management of chronic pulmonary mucormycosis with multi-facet diagnosis and non-surgical therapy: a case series 424

重度肝硬化患者合并侵袭性肺曲霉菌病的临床特征和短期预后 425

真菌感染与肿瘤免疫治疗之纽：基于 C 型凝集素受体调控的抗真菌免疫预测黑色素瘤免疫治疗效果 426

Research trends and hotspots of invasive pulmonary aspergillosis: bibliometric and visual analysis 427

基于 LASSO 回归的心脏外科术后侵袭性真菌病患者短期死亡风险预测模型的建立与验证 428

1 例由迟缓曲霉感染引起的心脏瓣膜置换术后并发侵袭性肺曲霉病 429

经验性抗真菌治疗对非粒缺 ICU 患者病死率的影响：一项倾向性评分匹配的回顾性队列研究 430

耶氏肺孢子菌感染与定植的临床特征分析 431

CONTENTS

曲霉 PCR、宏基因组测序及半乳甘露聚糖对血液病患者 侵袭性肺曲霉病的诊断性能研究 432

尖端赛多孢菌椎体感染 1 例 433

基于动态表面增强拉曼光谱法的代谢轮廓分析用于克服白念珠菌耐药性 434

一例播散性毛霉菌病合并肺马尔尼菲篮状菌的诊治 435

成人灰色小克银汉霉侵袭性毛霉菌病 1 例 436

mNGS Combined with Traditional Microbiology Identifies the First Case of Candida auris in Southwest China 437

The Diagnostic Value of Metagenomic Next-Generation Sequencing for Mucormycosis and the Risk Factors of Poor Prognosis in Mucormycosis 438

2021-2023 年某院烟曲霉临床分离株的分布 及流行病学特征 440

淮安地区公立医疗机构真菌感染检测能力调查 441

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 442

耳念珠菌持续血流感染及血管移植物感染一例 443

一例急性 B 淋巴细胞白血病 CART 治疗后播散性镰刀菌感染的诊治 444

重症 445

头孢他啶阿维巴坦双组分在重症感染患者中的药代动力学 446

血清 CA125 检测与心力衰竭疾病的相关性 447

血清 25- 羟基维生素 D 与成人脓毒症患者死亡风险的荟萃分析 448

糖尿病与脓毒症患者死亡风险的一项荟萃分析 449

维生素 D 水平在脓毒症患者中与营养状况和炎症反应之间的关系 450

2022 年某院神经外科 ICU 多重耐药菌分布及耐药性分析 451

揭秘！发热合并低氧血症背后的单一真相究竟为何？ ——1 例脓毒症休克合并 ARDS 患者的救治心得体会 452

CONTENTS

短效 β 受体阻滞剂在治疗 1 例脓毒症合并持续交感应激反应患者中的应用体会 453

Plasma and blood-cell co-metagenomic sequencing in precise diagnosis and severity evaluation of sepsis, a prospective cohort study 454

新生儿重症监护室规范化护理干预对红臀发生率的影响分析 455

The value of ursodeoxycholic acid and mesenchymal stem cells in the treatment of critical COVID-19 456

Effectiveness of polymyxin B-immobilized hemoperfusion in adult patients with sepsis and septic shock: a systematic review and meta-analysis 457

血清唾液酸检测的临床价值 458

临床药师参与 1 例暴发型流行性脑脊髓膜炎（休克型）重症感染患者的药学监护与治疗体会 459

脓毒血症治疗和防护的纳米药物 460

特重度烧伤患者术后反复难治性铜绿假单胞菌血流感染治疗 1 例及文献复习 461

Serum Exosome Proteomics Reveals Molecular CharacteristicsSevere Sepsis 462

Dynamic expression analysis of peripheral blood derived exosome miRNAs in sepsis progression 463

Effect of one dose of ceftriaxone during endotracheal intubation on the incidence of aspiration pneumonia in cerebral hemorrhage patients 464

液滴数字 PCR 在脓毒症患者队列中快速、敏感地鉴定病原体：一项前瞻性诊断研究 465

脓毒症相关肺损伤中 JAK/STAT 通路介导巨噬细胞极化的机制及潜在治疗靶点 466

The value of the proportion of perfused vessels change rate in the evaluation of early organ function deterioration in septic shock and ARDS 467

Trex1 介导 Irf3 入核促进单核 / 巨噬细胞免疫耐受的机制研究 468

Global research trends and focus of Sepsis bundle research from 2000-2024: A bibliometric and visualized study 469

机械通气患者抗菌药物雾化吸入的临床实施 472

CONTENTS

Dynamic Decline of Lymphocytes Predicts Extracorporeal Membrane Oxygenation-related Infections: A Retrospective Observational Study 473

Efficacy and Safety of Prone Position Ventilation in Severe Acute Respiratory Distress Syndrome Patients Undergoing Extracorporeal Membrane Oxygenation: A Prospective Multicenter Randomized Controlled Study 474

SepsisSCA: a comprehensive database integrating single-cell transcriptome atlas of sepsis 475

Effect of individualized positive end-expiratory pressure titrated by electrical impedance tomography on ventilation-perfusion distribution in patients with acute respiratory distress syndrome 476

脓毒症发病机制及潜在治疗靶点 477

Endothelial cell-derived extracellular vesicles modulate the therapeutic efficacy of mesenchymal stem cells through IDH2/TET pathway in ARDS 478

CD39-A2aR 通路介导肺驻留 NK 细胞功能障碍在脓毒症肺损伤中的作用研究 480

Clinical performance and impact of hybridization Probe Capture Next-generation sequencing for sepsis diagnosis and therapeutic adjustment: a multicenter and prospective study 481

Left ventricular global longitudinal strain is independently associated with mortality in hyperdynamic patients with sepsis 482

Left ventricular global longitudinal strain is associated with mortality in hyperdynamic patients with sepsis 483

染色体外环状 DNA 相关基因作为脓毒症脑病的生物标志物研究 484

超声图像相位分析在重症患者膈肌连续厚度超声测量应用中的可靠性研究 485

Ultrasound echo characteristics of respiratory muscles and weaning outcomes in mechanically ventilated patients with sepsis: a prospective observational study 486

右美托咪定与脓毒症所致急性肺损伤患者的死亡率降低相关 487

基于贝叶斯预测的万古霉素个体化给药在重症患者中的应用研究 488

CONTENTS

专家课件 489

血流感染病原分子诊断靶向 NGS 初露锋芒 490

病毒感染在支气管扩张中的作用 497

引起人类感染的环境病原真菌特征研究——Nat Microbiol 工作分享 501

感染性休克中 β 受体阻滞剂可以使用吗? 505

Viral Pneumonia in Immunocompromised Patients 509

呼吸道病毒疫苗的选择 514

细胞治疗在病毒性肺炎治疗中的作用 518

从皮肤到系统：探索皮肤表现对成人 Still 病诊治的意义 522

肺部侵袭性霉菌感染治疗策略之疗程管理
——重症新冠合并侵袭性肺曲霉 / 毛霉病诊治专家共识 526

病毒感染罹患侵袭性肺曲霉病 2 例 530

《侵袭性霉菌感染实验室诊断临床应用专家共识》解读 534

老年视角谈感染预防 538

“根”本不能忽视，mNGS 主力下的精准治疗 542

异基因造血干细胞移植患者的毛霉感染诊治 546

非结核分枝杆菌感染与实验室检测 551

感染标志物的质量管理对临床诊疗的意义 555



感控

根据药敏数据动态指导抗菌药物临床应用对大肠埃希菌及肺炎克雷伯菌药敏结果的影响

赵春坦
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目的 分析我院根据药敏数据指导抗菌药物临床应用后对大肠埃希菌及肺炎克雷伯菌药敏结果的影响。

方法 收集大肠埃希菌、肺炎克雷伯菌的药敏数据，根据药敏数据指导抗菌药物在相应病原菌感染性疾病中的应用，评价指导前后大肠埃希菌、肺炎克雷伯菌的药敏变化。

结果 经规范性指导后，肺炎克雷伯菌对抗菌药物的敏感率较指导前明显升高，尤其是对哌拉西林他唑巴坦、氨苄西林舒巴坦、头孢他啶、头孢吡肟、头孢唑林、头孢曲松、头孢替坦、氨曲南、亚胺培南、妥布霉素、庆大霉素、阿米卡星、左氧氟沙星、环丙沙星、呋喃妥因和复方新诺明的敏感率较 2019 年 1 季度均明显上升（P < 0.05），其中对亚胺培南敏感率从 76.86% 上升到 96.81%，对哌拉西林他唑巴坦敏感率从 76.03% 上升到 95.74%，对头孢曲松敏感率从 57.85% 升高等到 93.62%。2022 年 1 季度大肠埃希菌对氨苄西林舒巴坦、头孢吡肟、庆大霉素以及呋喃妥因敏感率较 2019 年明显升高（P < 0.05），对哌拉西林他唑巴坦、头孢他啶、头孢唑林、氨曲南等敏感率较 2019 年稍有升高。全院抗菌药物使用强度由 2019 年 1 季度的 52.62 DDDs 降到 2022 年 1 季度的 40.23 DDDs。

结论 通过药敏指导抗菌药物使用可减少细菌耐药性的发生。

远程指导居家精神障碍患者 开展院前感染防控的应用效果

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如皋市精神病防治医院

目的 探讨医务人员借助 “互联网 +” 模式（微信等），线上对居家精神病患者（家属）开展院前感染防控，远程指导居家防控细菌病毒感染、提高抵御感染的健康知识、基本技能、身体素质，降低患者携带病毒细菌等感染源进入精神病专科医院门诊和住院治疗的风险几率的应用实践效果分析。

方法 随机选取长期在门诊治疗、居家服药的精神病患者共有 126 名，在 2023 年 1 月 ~2023 年 12 月期间，对其中的 63 例患者为对照组，进行门诊窗口常规感染防控指导，另外的 63 例患者为观察组，在门诊窗口常规指导外，再借助微信（群）给予强化居家防控细菌病毒等院前抗感染远程指导。对比两组患者的感染防控效果。

结果 观察组患者在线上获得医务人员的居家（院前）防控感染强化指导干预后，发生季节流行性病毒性感冒、细菌性感染比例、感染后病程等都明显降低，相比于对照组，具有明显的优势，$P < 0.05$。

结论 医务人员开展院前感控宣传、线上强化防控感染指导，能够有效增加精神病长期居家患者的健康卫生知识、感染防控技能，降低病毒细菌感染的几率和病程，提高其健康卫生知识、身体素质、生活质量和社会适应能力，提升患者对医务人员服务的满意度、有利于精神疾病的康复；同时，借助微信远程指导患者（家属）做好院前感染防控工作，能够大大降低患者携带病毒细菌等感染源进入医院门诊和住院治疗的风险几率！值得借鉴推广、持续开展。

Remote guidance for patients with mental disorders at home The application effect of pre-hospital infection prevention and control

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Rugao City Psychiatric Prevention and Treatment Hospital

Abstract Content Objective To explore the practical effect of medical staff in carrying out pre-hospital infection prevention and control of homebound psychiatric patients (family members) online with the help of the "Internet+" mode (WeChat, etc.), remotely guiding the prevention and control of bacterial and viral infections at home, improving the health knowledge, basic skills and physical fitness of resisting infection, and reducing the risk probability of patients carrying viruses and bacteria and other infection sources into hospitals for outpatient and inpatient treatment.

Methods A total of 126 psychiatric patients who have been treated in outpatient clinics for a long time and taken medication at home were randomly selected, and during the period of January 2023~December 2023, 63 patients were taken as the control group for routine infection prevention and control guidance in the outpatient window, and the other 63 patients were given in the observation group. The infection prevention and control effect of the two groups was compared.

Results After receiving the intensive guidance intervention of medical staff for home (pre-hospital) infection prevention and control online, the proportion of seasonal viral influenza and bacterial infection, and the course of infection in the observation group were significantly reduced, which was significantly superior to that of the control group, $P<0.05$.

Conclusion Medical staff carrying out pre-hospital infection control publicity and online strengthening of infection prevention and control guidance can effectively increase the health and hygiene knowledge and infection prevention and control skills of patients with long-term mental illness, reduce the probability and course of viral and bacterial infection, improve their health and hygiene knowledge, physical fitness, quality of life and social adaptability, and improve patients' satisfaction with medical staff's services. At the same time, with the help of WeChat to remotely guide patients (family members) to do a good job in pre-hospital infection prevention and control, it can greatly reduce the risk probability of patients carrying viruses and bacteria and other sources of infection into the hospital for outpatient and inpatient treatment!

基层精神病医院开展 院外感染智慧防控管理的创新实践

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目的 探讨基层精神病医院线上开展院外感染智慧防控管理，即医务人员借助 “互联网 +”模式（微信等），远程对居家精神病患者（家属）开展院外感染防控，远程指导居家防控细菌病毒感染、提高抵御感染的健康知识、基本操作技能、身体素质，以降低患者携带病毒细菌等感染源进入医院门诊和住院治疗的风险几率的创新管理实践效果分析。

方法 随机选取长期在门诊治疗、居家服药的精神病患者共有 126 名，在 2023 年 1 月 ~2024 年 1 月期间，对其中的 63 例患者为对照组，进行门诊窗口常规感染防控指导，另外的 63 例患者为观察组，在门诊窗口常规指导外，再借助微信（群）给予强化居家防控细菌病毒等院外抗感染远程指导、智慧防控管理。对比两组患者的感染防控效果。

结果 观察组患者在线上获得医务人员的居家（院外）防控感染强化指导干预后，发生季节流行性病毒性感冒、细菌性感染比例、感染后病程等都明显降低，相比于对照组，具有明显的优势，$P < 0.05$。

结论 基层精神病防治医院医务人员开展智慧防控管理，院外感控宣传、线上强化防控感染指导，能够有效增加精神病长期居家患者的健康卫生知识、感染防控技能，降低病毒细菌感染的几率和病程，提高其健康卫生知识、身体素质、生活质量和社会适应能力，提升患者对医务人员服务的满意度、有利于精神疾病的康复；同时，借助微信远程指导患者（家属）做好院前感染防控工作，能够大大降低患者携带病毒细菌等感染源进入医院门诊和住院治疗的风险几率！院外感染智慧防控管理，具有创新性、实用性，值得借鉴推广、持续开展。

外科重症监护病房院内感染细菌分布及耐药性分析

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目的 了解上海交通大学医学院附属新华医院外科重症监护病房近 3 年院内感染患者分离细菌的分布以及对常用抗菌药物的敏感性耐药性，为临床经验用药提供参考依据。

方法 收集 114 例 2021 年 1 月至 2023 年 12 月入住该院 SICU 的发生院内感染患者的标本，包括呼吸道、尿液、血液、伤口分泌物、静脉导管、引流液，采用标准纸片扩散法或自动化仪器检测法进行药敏试验，对细菌耐药监测数据进行统计分析。

结果 共分离出 399 株非重复临床分离菌，其中革兰阴性菌 246 株（61.65%），革兰阳性菌 153 株（38.35%）。在所有细菌中分离率名列前 5 位的分别是大肠埃希菌（11.53%）、肺炎克雷伯菌（10.53% ）、鲍曼不动杆菌（9.02% ）、屎肠球菌（7.52% ）、嗜麦芽窄食单胞菌（6.02%）。 革兰阳性菌中，金葡菌均为耐甲氧西林金黄色葡萄球菌（100%），耐甲氧西林凝固酶阴性葡萄球菌占凝固酶阴性葡萄球菌的 90.54%，葡萄球菌属中未发现万古霉素耐药株；粪肠球菌对测试抗菌药物的耐药率均明显低于屎肠球菌。革兰阴性菌中，大肠埃希菌和肺炎克雷伯菌中产超广谱 β - 内酰胺酶菌株分离率分别为 71.43% 和 14.29% ，两者对三代头孢菌素的耐药率为 64.29-78.57%，大肠埃希菌对碳青霉烯类抗菌药物耐药率低。肺炎克雷伯菌、鲍曼不动杆菌和铜绿假单胞菌对碳青霉烯类抗菌药物耐药率高，分别为 72.01%、91.67% 和 71.43%；肺炎克雷伯菌和鲍曼不动杆菌对替加环素敏感性好，敏感率分别为 92.85% 和 85.71%。

结论 外科重症监护病房患者标本分离菌的耐药率较高，多重耐药菌的检出率也较高，为减少多重耐药和广泛耐药菌的产生及传播，需进行实时细菌耐药性监测及回顾性分析细菌耐药变迁，采取有效的医院感染控制措施，临床药师参与院内抗菌药物管理并与临床、检验三方联动共同推进我院抗菌药物的合理使用。

综合干预对降低血管导管相关感染发病率的效果评估

刘厚荣
东莞市人民医院

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。

集束化干预降低导尿管相关尿路感染的效果

刘厚荣
东莞市人民医院

目的 评估集束化干预措施降低导尿管相关尿路感染（CAUTI）的效果。

方法 2017年1-6月对某院留置导尿管患者进行目标性监测的基线调查（干预前期），7-12月结合PDCA工具找出主要原因并制定集束化干预措施（过渡期），2018年1-6月落实干预措施（干预后期），对比干预前后导尿管使用率、人均留置导尿管日数、日发病率的差异。

结果 干预后手卫生依从率、防控措施执行率、防控措施知晓率分别为81.94%、95.37%、97.98%，高于干预前的64.66%、66.31%、65.02%，干预后每日评估执行率达96.15%。CAUTI日发病率从干预前的1.71‰降至干预后的1.22‰，导尿管使用率从干预前的10.02%降至干预后的7.69%，内科系统CAUTI日发病率从干预前的3.73‰降至干预后的1.56‰，干预前后上述指标比较差异均有统计学意义（均$P < 0.05$）。

结论 开展CAUTI目标性监测，结合PDCA工具能发现医院感染防控的薄弱环节，为制定专项防控措施提供循证依据，落实集束化干预措施能有效降低CAUTI发病率。

线上开展精神障碍患者 居家感控对医院感控的价值分析

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如皋市精神病防治医院

目的 探讨医务人员线上开展精神障碍患者居家（院外）感染智慧防控管理，即“互联网 +”模式（微信、群、公众号、视频号等），远程指导居家防控细菌病毒感染、提高抵御感染、安全合理用药的健康知识、基本卫生操作技能、身体自我免疫素质后，对患者降低携带病毒细菌等感染源进入医院、及在门诊和住院治疗期间发生院内感染几率的实践价值和效果分析。

方法 随机选取门诊治疗、居家服药的精神病患者共有 300 例，在 2020 年 4 月 ~2024 年 3 月期间，对其中的 150 例患者为对照组，进行门诊窗口常规感染防控处置不良反应等指导，另外的 150 例患者为观察组，在门诊窗口常规指导外，再借助微信（群）公众号朋友圈视频号等给予强化居家防控细菌病毒等院外抗感染和处置不良反应等远程指导、智慧防控管理。对比两组中部分患者因精神病发作住院期间发生院内感染情况。

结果 观察组患者在线上获得医务人员的居家（院外）防控感染强化指导干预后，感控知识提升、病情发作住院期间发生院内季节流行性病毒性感冒、细菌性感染比例、感染后病程等都明显降低，相比于对照组，具有明显的优势，$P < 0.05$。

结论 基层精神病防治医院医务人员开展智慧防控管理，院外感控宣传、线上强化防控感染指导，能够大大降低患者发生院内感染的风险几率！院外感染智慧防控管理，具有创新性、实用性，值得借鉴推广、持续开展。

基于信息化集成平台的多重耐药菌医院感染防控新模式探讨

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目的 探讨基于信息化集成平台的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，比较两组临床分离多重耐药菌及其来源分布、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、部分侵入性操作 MDRO 感染发生率、医院感染率等。

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%，菌株均主要来源呼吸道、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 院内感染例次率较前显著下降，主要多重耐药菌院内总感染例次率由 0.68‰下降至 0.45‰（P < 0.05）；导尿管相关尿路 MDRO 感染率由 0.40‰降至 0.14‰、中央血管导管相关血流 MDRO 感染率由 0.65‰降至 0.15‰，差异均有统计学意义。此外，干预后医院感染率、医院感染漏报率、住院患者抗生素使用率均较前显著降低（χ^2=7.372、7.597、6.956，P < 0.05），医院感染病例病原学送检率、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 基于信息化集成平台的综合管理模式可有效改善医院内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。

新型冠状病毒感染疫情前后临床病原菌分布特征及耐药性变化研究

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目的 探讨新型冠状病毒感染（COVID-19）疫情前后安徽省某三甲医院临床病原菌的分布情况及其耐药性变迁，为医院感染的防控及临床合理使用抗菌药物提供参考。

方法 回顾性分析 2017 年 1 月 1 日—2019 年 12 月 31 日（COVID-19 疫情前组）、2020 年 1 月 1 日—2022 年 12 月 31 日（COVID-19 疫情后组）医院所有送检标本中病原菌的临床分布及对临床常用抗菌药物的耐药性进行统计学分析。

结果 2017-2022 年共分离出 34734 株细菌，其中 COVID-19 疫情前组占比 40.95%，COVID-19 疫情后组占比 59.05%，均以革兰阴性菌为主。COVID-19 疫情后组肺炎克雷伯菌、大肠埃希菌和铜绿假单胞菌占比升高，鲍曼不动杆菌和金黄色葡萄球菌占比较前下降，差异具有统计学意义（均 $P < 0.05$）。肺炎克雷伯菌和大肠埃希菌对碳青霉烯类抗菌药物较敏感，耐药率均 < 10%，COVID-19 疫情后组肺炎克雷伯菌对亚胺培南、厄他培南耐药率较前升高，差异具有统计学意义（均 $P < 0.05$）；COVID-19 疫情后组鲍曼不动杆菌对头孢吡肟、庆大霉素耐药率均下降（均 $P < 0.05$）；COVID-19 疫情后组铜绿假单胞菌对亚胺培南、头孢类、喹诺酮类药物的耐药率均升高（均 $P < 0.05$）；COVID-19 疫情后组金黄色葡萄球菌对多数抗菌药物的耐药率均下降（均 $P < 0.05$），未检出对万古霉素和利奈唑胺耐药的菌株。耐碳青霉烯类铜绿假单胞菌、耐碳青霉烯类肺炎克雷伯菌、耐碳青霉烯类大肠埃希菌检出率较疫情前升高，而耐甲氧西林金黄色葡萄球菌检出率较疫情前下降（均 $P < 0.05$）。

结论 COVID-19 疫情后医院分离细菌耐药性较前发生了较大变化，其中肺炎克雷伯菌、铜绿假单胞菌对碳青霉烯类的耐药率持续上升，应引起临床高度重视。

ICU 靶向干预和 COVID-19 间隔后碳青霉烯耐药鲍曼不动杆菌种群变化：一项基于基因组的纵向全球监测研究

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目的 碳青霉烯耐药鲍曼不动杆菌 (CRAB) 是一种持续存在的医院病原体，对全球公共卫生尤其是重症监护病房 (ICU) 构成重大威胁。本研究旨在了解针对性干预后的 ICU CRAB 群体变化，并进一步探讨新兴 ST164 CRAB 谱系的整体特征和可能的进化路径。

方法 继 2019 年第一个为期三个月的研究之后，2021 年在同一 ICU 进行了另一项为期三个月的纵向研究，伴随着 COVID-19 相关的延误和针对患者、工作人员和 ICU 环境的干预措施。确定了所有分离株的九种抗生素的最低抑制浓度。 通过基因组学方法分析了全球克隆 2 (GC2) 分离株到新兴 ST164 克隆的动态变化。 进一步探讨了全球 ST164 CRAB 的系统发育、地理分布及其演化。

结果 该 ICU 中分离出的大多数鲍曼不动杆菌为 CRAB（80.9%；419/518）。 亚胺培南的 MIC50/MIC90 从 2019 年研究中的 32/64 mg/L 增加至 64/128 mg/L。 与此同时，GC2 分离株的比例从 2019 年的 99.5% 下降到 2021 年的 50.8% (213/419)。GC2 的系统发育多样性增加，显然是由与患者相关的不同簇的定期引入所驱动的。其余的 CRAB（40.2%；206/419）是 ST164 的高度克隆群体，全球监测显示 ST164 菌株主要分布在亚洲，可分为 7 个具有巨大多样性的进化枝（3-4,919 个 cgSNP）。 ST164 CRAB 可能通过 Tn2006 和 Tn6924 转座子介导的两条途径进化。

结论 ST164 CRAB 是全球高风险谱系之一。 应实施有针对性的感染预防和控制（IPC）策略来控制该克隆在 ICU 中的传播。

Antibiotic prophylaxis after 48 h postoperatively are not associated with decreased surgical site infections and other healthcare associated infections in pancreatic surgery patients: a retrospective cohort study

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Abstract Content Background It is controversial whether antibiotic should be used prophylactically 48 h after pancreatic surgery. Hence, the association of antibiotic prophylaxis (AP) after 48 h postoperatively with the incidence of surgical site infec- tions (SSIs) and other healthcare-associated infections (HAIs) in patients receiving pancreatic surgery was evaluated.

Methods A retrospective cohort analysis was performed on 1073 patients who underwent pancreatic surgery. These patients were categorized into the non-AP after 48 h postoperatively group (n=963) and the AP after 48 h postop- eratively group (n=110) based

Results The incidence of SSIs in the non-AP after 48 h postoperatively group (98/963, 10.2%) was notably lower than that in the AP after 48 h postoperatively group (22/110, 20.0%) (P=0.002). Other HAIs incidence was not signif- cantly diferent between the non-AP after 48 h postoperatively group (77/963, 8.0%) and the AP after 48 h postopera- tively group (11/110, 10.0%) (P=0.468). Multiple regression analysis demonstrated that AP after 48 h postoperatively was a risk factor for SSIs (OR=2.14, 95% CI 1.28–3.59) but not for other HAIs (OR=1.24, 95% CI 0.63–2.42) after adjust- ment for age, gender, and diabetes. Subsequent to adjustment for all confounding factors, AP after 48 h postopera- tively was not a infuence factor for SSIs (OR=2.13, 95% CI 0.76–5.99) and other HAIs (OR=3.69, 95% CI 0.99–13.81).

Conclusion AP after 48 h postoperatively following pancreatic surgery was not associated with the lower morbidity rate of SSIs and other HAIs. Nonetheless, this study may facilitate further development of strategies towards standardi- zation of the duration of AP management of pancreatic surgery.

The symptoms and interval of Omicron SARS_x0002_CoV-2 reinfection among healthcare workers in a hospital of Southern China: a cross sectional study

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Abstract Content Background :The prevalence and distinction between first Severe acute respiratory syndrome coronavirus 2 (SARS_x0002_CoV-2) infection and reinfection with the Omicron variant among healthcare workers (HCWs) remain unclear.

Methods A cross-sectional study was conducted at a hospital in Southern China. The study included 262 HCWs who were infected with SARS-CoV-2 between April and June 2023, with 101 cases of first infection and 161 ones of reinfection. Student's t-test, Analysis of Variance (ANOVA), and Mann-Whitney U tests were used based on the distribution of quantitative variables. Pearson's chi-square and Fisher's exact tests were used based on the expected frequencies of categorical variables

Results The reinfection rate among HCWs was 11.5% (161/1406). The majority of the infected HCWs were female (212/262, 80.9%, first infection vs. reinfection: 76.2% vs. 83.9%). The nursing staff, had the highest percentage of SARS_x0002_CoV-2 infection (42.0%), especially of its reinfection (47.8%). Out of the 262 infected individuals, 257 had received SARS-CoV-2 vaccination, primarily inactivated vaccines (243/257, 91.1%). The first infection group, which received four doses (24, 23.8%), was significantly higher than that in the reinfection group (6, 3.7%) ($P<0.001$). The proportion of asymptomatic infections among HCWs in the two groups was 1.0% and 1.2%. The main symptoms during the first infection and reinfection were fever (83.2% and 50.9%) and sore throat (78.2% and 77.0%). There were significant differences in the prevalence of fever (83.2% vs. 50.9%), rhinorrhea (45.5% vs. 60.9%) and myalgia (56.4% vs. 37.9%) between the first infection and reinfection ($P < 0.05$). The average interval for SARS-CoV-2 reinfection was 149.9 (range: 114–182, SD=11.9) days. Notably, physicians had the shortest average interval of 142.8 (8.8) days, while management and administrative staff had the longest average interval of 153.8 (13.5) days.

Conclusion Although the symptoms of HCWs during reinfection with SARS-CoV-2 were milder, the high reinfection rate and short interval between infections indicate the need to enhance monitoring and protective measures for HCWs during the epidemic.

神经外科术后颅内感染 Nomogram 模型的建立与验证

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目的 探讨神经外科术后患者颅内感染危险因素，建立并验证 Nomogram 预测模型。

方法 回顾性分 析 2019 年 1 月 1 日—2022 年 12 月 31 日南京某医院 978 例神经外科手术患者资料，经 logistic 单因素和多因素分 析筛选独立危险因素。通过 Lasso 回归筛选建模变量，采用 logistic 回归构建 Nomogram 模型并进行内部验证，采用 受试者工作特征（R OC）曲线、校准曲线、决策曲线测评模型效果。

结果 978 例神经外科手术患者中，293 例发生 术后颅内感染，医院感染发病率为 29. 96% 。感染组和非感染组患者的年龄、性别、冠心病、脑梗死、糖尿病和高血 压的比例等基本情况比较，差异均无统计学意义（均 P ＞ 0. 05）。logistic 多因素分析结果显示，术后颅高压、发热、血常规中性粒细胞百分比升高，脑脊液浑浊、潘氏试验阳性、葡萄糖浓度降低、脑脊液 / 血清葡萄糖比值异常、微生 物培养阳性，以及未留置脑室外引流管（EVD）、留置腰大池置管引流管（LD）、使用免疫抑制药物和手术时间长是 神经外科术后患者颅内感染的独立危险因素（均 P ＜ 0. 05）。通过 Lasso 回归筛选 15 个变量，经共线性筛查、缺失 数据插补（随机森林法）、检查两两交互作用项后最终纳入 14 个变量建模。建立 Nomogram 预测模型，其 R OC 曲线 下面积、灵敏度、特异度和准确度分别为 0.885、0.578、0.896、0.704，对模型进行内部验证，建模组和验证组效果相 近，校准曲线和决策曲线同时提示模型有良好的预测能力。

结论 本研究构建的神经外科术后颅内感染 Nomogram 预测模型，预测指标科学且容易获取，稳定性与可靠性强，具有较高的应用价值和较广的适用范围，可为神经 外科术后颅内感染的判定提供参考。

医院感染诊断病原学送检标本 与目标感染部位的匹配情况

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目的 研究医院感染诊断病原学送检标本与目标感染部位的匹配情况。

方法 纳入 2021 年 1 月 1 日 - 2021 年 12 月 31 日南京医科大学第一附属医院发生医院感染的住院患者，纳入 2591 例医院感染患者，包含 2827 个感染诊断，分析医院感染诊断相关病原学送检率、医院感染诊断相关病原学送检标本匹配率、不同感染部 位医院感染诊断相关病原学送检标本匹配率。

结果 全院医院感染率为 1.53%(2951/192584)，医院感染诊断 相关病原学送检率为 95.72%(2480/2591)；不同片区间送检率差异有统计学意义 (P<0.001)，其中 ICU 的医院 感染诊断相关病原学送检率最高 (99.83%)，外科组 (93.09%) 和急诊组 (91.30%) 相对较低；全院医院感染诊断相 关病原学送检 标 本 匹 配 率 为 87.44%，不 同 片 区 间 匹 配 率 差 异 有 统 计 学 意 义 (P <0.001)，其 中 ICU 最 高 (94.61%)，内科最低 (76.27%)，其中血液科为 76.69%(181/236)；医院感染诊断相关病原学送检标本匹配率最高 的三个感染部位分别为血液系统 (98.13%)、泌尿系统 (92.97%) 和手术部位 (87.56%)；送检标本匹配率 <80% 的 感染部位主要有皮肤与软组织和眼耳鼻喉部位感染。

结论 不同科室与不同部位医院感染送检标本的匹配性差 异较大，医疗机构应根据不同科室以及不同感染部位的特点采取针对性改进措施，提高医院感染送检标本匹配 率，进一步提升抗菌药物合理使用。

非 MDRO 型 CRPA 临床分布特点 及分层防控模式探讨

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目的 分析非多药耐药菌 (Non-MDRO) 型耐碳青霉烯类铜绿假单胞菌 (CRPA) 的临床分布特点，并提出 其分层防控模式的建议。

方法 选择南京医科大学第一附属医院 2020 年 1 月 -2022 年 6 月临床标本中分离的 CRPA、耐碳青霉烯类肠杆菌目细菌 (CRE)、耐碳青霉烯类鲍氏不动杆菌 (CRAB) 为研究对象，根据 MDRO 定义，将其分别分为 Non-MDRO 组和多药耐药菌 (MDRO) 组，对比分 析 Non-MDRO 组 比 例。分 析 Non-MDRO 组 CRPA 临床分布、影响因素以及耐药性特点。

结果 医院感染重点监测的 MDRO，针对铜绿假单胞菌 (PA)，2015 年之前均为多药耐药铜绿假单胞菌 (MDR-PA)，2015 年之后则都是 CRPA；CRPA 中 Non-MDRO 占比 62.15% (770/1239)，CRE 和 CRAB 中 Non-MDRO 占比则分别为 0.51%(9/1758) 和 0.91%(21/2308)；Logistic 多因素 分析结果显示年龄和病区分布是 Non-MDRO 型 CRPA 的影响因素 (P<0.05)；CRPA 中 Non-MDRO 组耐药率 低于 MDRO 组（均 P<0.05），其中 Non-MDRO 组除了对碳青霉烯类药物耐药率较高外，其余抗菌药物耐药率均 低于 20%。

结论 非 MDRO 型 CRPA 基数较大，危害较小，且占据一定的防控资源，建议根据情况对 CRPA 进 行分层防控管理，即耐药菌并不多见、防控资源宽松的医疗机构可以将 CRPA 全部纳入常规重点监测菌，而对于 部分耐药菌泛滥、防控资源紧张的大型三甲医院，则可以将重点监测菌中的 CRPA 更改为 MDR-PA 或难治型耐耐药（DTR）-PA。

药敏结果“中介”是否纳入“耐药”统计 对多药耐药菌监测数据的影响

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目的 探讨药敏结果“中介”是否纳入“耐药”统计对多药耐药菌 (MDRO) 监测数据的影响。

方法 选择南 京医科大学第一附属医院 2020 年 1 月 -2022 年 6 月微生物送检标本中分离出的医院重点监测 MDRO, 分别将 “中介”纳入耐药和“中介”不纳入耐药统计 , 对比分析两种情况下 MDRO 检出率、MDRO 感染例次发生率、感染 构成比。

结果 国内不同指南和共识的 MDRO 定义中 , 对于中介是否纳入耐药统计存在差异 ; 参与调研的 20 所 医疗机构 ,15 所判定 MDRO 时将药敏结果中介纳入耐药统计 ,5 所判定 MDRO 时未将药敏结果中介纳入耐药统 计 ; 中介纳入和不纳入耐药的情况下 ,CRKP、CRECO、CRAB、MRSA 的检出率差异无统计学意义 , 中介纳入耐药 时的 CRPA 检出率 (42.45%) 高于中介不纳入耐药时检出率 (34.17%)(P<0.001); 中介纳入和不纳入耐药的情 况下 ,CRKP、CRECO、CRAB、MRSA 的感染例次发生率差异无统计学意义 , 中介纳入耐药时的 CRPA 感染例次率 (0.26%) 高于中介不纳入耐药时检出率 (0.22%)(P<0.001); 中介纳入和不纳入耐药的情况下 ,CRKP、CRE_x0002_CO、CRAB、CRPA、MRSA 的感染构成比差异无统计学意义。

结论 MDRO 判定时 , 中介纳入和不纳入耐药统 计的情况下 ,CRPA 检出率、CRPA 感染例次发生率差异显著。建议相关部门统一 MDRO 监测标准 , 进一步提升 数据监测的同质化水平。

非重症监护病房多重耐药菌感染来源及分布研究

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目的 分析非重症监护病房（ICU）多重耐药菌（MDRO）感染来源及分布，为制定精准 化 MDRO 防控措施提供依据。

方法 选取南京医科大学第一附属医院 2017 年 10 月至 2019 年 9 月 802 例自 非 ICU 科室 MDRO 感染者体内分离出的 1 116 株 MDRO 菌株作为研究对象，依据来源将 MDRO 分为院 外感染（外院转入、社区获得）和院内感染（本院转入、科室获得）两大类型共 4 个组别进行分析。

结果 本院非 ICU 科室感染的 MDRO 以 CRE（34.41%）及 MRSA（29.66%）为主；4 种常见 MDRO 感染最多的科室为老年医学科（113.17%）、神经外科（10.04%）和康复医学科（8.51%）。CRE、MRSA、CRAB 和 CRPA 检出率分别为 10.69%（704/6 584）、43.83%（554/1 264）、33.72%（376/1 115）和 27.11%（475/1 752），均显著低于全院科室 CRE、MRSA、CRAB、CRPA 的平均检出率（25.35%、51.48%、79.15% 和 46.99%），差异均有统计学意义（P 均< 0.001）；非 ICU 科室间以上 4 种 MDRO 检出率差异均有统计学意义（P 均< 0.001）。MDRO 感染部位主要为下呼吸道（48.39%）、手术部位（11.83%）和泌尿道（11.02%）。院外感染者占 57.44%，包括外院转入（33.42%）和社区获得（24.01%）；院内感染者占 42.56%，包括本院转入（4.66%）和科室获得（37.90%）。

结论 本院非 ICU 科室 MDRO 感染近 2/3 来源于院外输入和院内转入，需重视感染控制基本措施落实并通过信 息系统早期识别，且各科室间 MDRO 感染来源及分布不同，应根据其特点制定针对性措施，实现精准化防控。

Characteristics and Occurrence Scenarios of Staff Exposed to SARS-CoV-2 Omicron in Shanghai Lingang Fangcang Shelter Hospital, CHINA

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Abstract Content Objective To analyze the characteristics and occurrence scenarios of occupational exposure of staff in the Shanghai Lingang Fangcang Shelter Hospital

Methods We collected the data of 80 staff with occupational exposure (including doctors, nurses, cleaning, security guards, and maintenance staff) in the Shanghai Lingang Fangcang Shelter Hospital from April 5 to May 20, 2022. The basic information of occupational exposure, factors influencing different occupational exposure types, ways to discover occupational exposure, discovery places of occupational exposure, and specific occurrence scenarios were compiled and analyzed among these data.

Results Occupational exposure mainly occurred in nurses (37, 46.25%), and cleaning (21, 26.25%). After the occurrence of occupational exposure, 20 staff (25%) did not know the occurrence time. Moreover, occupational exposure types were listed from high to low proportion as follows: broken protective clothing (56, 70%), mask loosening or displacement (13, 16.25%), skin exposure (6, 7.5%), and sharp object injuries (5, 6.25%). Occupational exposure was discovered mainly through self-discovery (56, 70%), while other discovery ways were majorly colleague discovery (12, 15%) and infection control supervisor discovery (12, 15%). Furthermore, occupational exposure was discovered principally in the public area (53.75%) and the office area (25%) of the cabin, but the proportion of mask loosening or displacement (38.46%) and skin exposure (50%) was also high in the first unloading area. Broken protective clothing occurred in the following scenarios: scratching while working in the cabin (37, 66.07%) and not knowing its occurrence time (25%). The occurrence scenarios of mask loosening or displacement were mainly not knowing its occurrence time (6, 46.15%), self_x0002_discovery (3, 23.08%), and at the time of removal (3, 23.08%).

Conclusion Targeted training and prevention of occupational exposure should be performed to decrease infection risk and ensure staff safety in Fangcang shelter hospitals.

What is the status of nucleic acid contamination in 2019-nCOV vaccination sites? Can it be avoided?

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Abstract Content This study aimed to investigate the environmental contamination of nucleic acid at 2019 novel coronavirus (2019-nCOV) vaccination site and to evaluate the effect of improvement to the vaccination process.

Methods Nucleic acid samples were collected from the surface of the objects in 2019-nCOV vaccination point A (used between 15 November 2020 and 25 December 2020) and point B (used after 27 December 2020) in a comprehensive tertiary hospital. Samples were collected from point A before improvement to the vaccination process, and from point B (B1 and B2) after improvement to the vaccination process. The real-time fluor_x0002_escence polymerase chain reaction method was used for detection.

Results The positive rate of vaccin_x0002_ation room was 47.06% (24/51) at point A. No positive result was found in point B1 both at working hours (0/27) and after terminal disinfection (0/27). In point B2 , the positive results were found in vaccine's outer packaging and staff gloves at working hours, with a positive rate of 7.41% (2/27). The positive rate was 0 (0/27) after terminal disinfection in point B2 .

Conclusion The nucleic acid contamination in the vaccination room of 2019-nCOV vaccine nucleic acid sampling point is serious, which can be avoided through the improvement and intervention (such as personal protection, vaccination operation and disinfection methods).

Antibiotic Prophylaxis After Pancreatic Surgery: A Critical Analysis

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Abstract Content Objective To analyse the current status and factors influencing antibiotic prophylaxis (AP) after pancreatic surgery.

Methods A total of 1073 patients who underwent pancreatic surgery at the First Affiliated Hospital of Nanjing Medical University from January 2022 to December 2022 were selected. These patients were categorized into AP >24 h group (135) and Non-AP >24 h group (938) based on whether AP were administered from 24 hours to 30 days after surgery. Univariate and multivariate logistic regression analyses were performed to analyse the factors influencing AP ＞ 24 h after pancreatic surgery.

Results Among 1073 patients, 12.58% (135/1073) patients were administered AP > 24 h after pancreatic surgery. The mean of the cumulative days of postoperative AP use was 6.24 ± 4.09. Pancreatic surgery performed in nonpancreatic centres was an independent risk factor for AP >24 h after surgery (OR=2.61, 95%CI=1.04-6.54). The rate of AP >24h after pancreatic surgery operated in nonpancreatic centres (37.73%, 29/73) was much greater than that in pancreatic centres (10.60%, 106/1000).

Conclusion A relatively high proportion of patients were administered AP >24h after pancreatic surgery (12.58%). Pancreatic surgery performed in nonpancreatic centres was indentified as an independent risk factor for AP administration >24 h after surgery. Therefore, relevant measures need to be taken to further standardize the management of antibacterial drug treatment in medical institutions.

头孢菌素类注射剂皮试的规范化管理及分析

贺钰茹[1]、李小丝[1]、谢沂宏[1]、姜怡雯[1]、钟燕[1]、黄璐瑶[1]、张家兴[2]
1. 西藏自治区人民政府驻成都办事处医院
2. 贵州省人民医院

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。

基于 CiteSpace 的 CRE 医院感染防控可视化研究

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目的 分析 2010-2024 年 CRE 的研究现状、热点及变化趋势，探索其发展方向。

方法 检索中国知网 (CNKI) 2010 年 1 月 1 日至 2024 年 2 月 27 日的核心期刊文献，利用 Origin pro 软件进行文献增长规律及来源期刊分析；利用 CiteSpace 6.1.R6 软件通过文献关键词共现、聚类及热点突变等网络分析方法识别 CRE 医院感染防控研究热点和趋势；通过文献被引频次分析反映该领域的关键点和学科前沿。

结果 共纳入文献 278 篇，发文量逐年增加，国内发文最多的机构是复旦大学附属儿科医院临床检验中心细菌室，其次是上海交通大学医学院附属上海儿童医学中心检验科，排名第三是上海交通大学医学院附属上海儿童医学中心感染科。发文最多的期刊包括中华医院感染学杂志、中国感染控制杂志、中国消毒学杂志。数据库形成聚类标签，高频关键词主要有医院感染、危险因素、耐药性、细菌、感染、病原菌、定植、主动筛查、药敏试验等。

结论 CRE 医院感染防控可视化研究是医院感染管理中的重要组成部分，是未来研究的热点和重点，本次分析为今后相关研究提供借鉴与参考。

基于 PDCA 理论在 ICU CRE 感染防控中的精准管理实践

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目的 本次研究选取三级甲等综合性医院的 ICU 重症监护室，探究 ICU CRE 院内感染管理中施行计划一实施一检查一处理（PDCA) 循环法的效果，评价其有形成果以及无形成果，提高 ICU CRE 感染防控措施落实率。

方法 于 2023 年 7 月起开始采用 PDCA 循环管理多维策略防控 ICU CRE 感染，纳入 ICU 患者例数 90 例（均自愿参与），比较观察 PDCA 模式应用前（2023 年 1 月 -2023 年 6 月）与应用后（2023 年 7 月 -2023 年 12 月），对比干预前后抽取时间段 ICU CRE 感染预防与控制措施落实率，评价管理效果包 ICU CRE 感染防控措施落实率、无形成果得分。

结果 PDCA 干预前后 ICU CRE 感染预防与控制措施落实率由 49.29% 提高至 83.10%，ICU CRE 各项防控措施的落实率较多维感染防控措施干预前显著提升。无形成果得分均明显更高，对比干预活动前，$P < 0.05$，组间的数据对比有统计学意义。

结论 PDCA 模式的应用可以精准管理 ICU CRE 医院感染防控，提升 ICU CRE 医院感染防控质量，进一步防控多重耐药菌院内传播与交叉感染。

Implications of deduplication on the detection rates of multidrug-resistant organism (MDRO) in various specimens: insights from the hospital infection surveillance program

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Abstract Content Abstract

Background Currently, diferent guidelines recommend using diferent methods to determine whether deduplication is necessary when determining the detection rates of multidrug-resistant organisms (MDROs). However, few studies have investigated the efect of deduplication on MDRO monitoring data. In this study, we aimed to investigate the infuence of deduplication on the detection rates of MDROs in diferent specimens to assess its impact on infec_x0002_tion surveillance outcomes.

Methods Samples were collected from hospitalized patients admitted between January 2022 and December 2022; four types of specimens were collected from key monitored MDROs, including sputum samples, urine samples, blood samples, and bronchoalveolar lavage fuid (BALF) samples. In this study, we compared and analysed the detection rates of carbapenem-resistant Klebsiella pneumoniae (CRKP), carbapenem-resistant Escherichia coli (CRECO), carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Pseudomonas aeruginosa (CRPA), and methicil_x0002_lin-resistant Staphylococcus aureus (MRSA) under two conditions: with and without deduplication.

Results When all specimens were included, the detection rates of CRKP, CRAB, CRPA, and MRSA without deduplication (33.52%, 77.24%, 44.56%, and 56.58%, respectively) were signifcantly greater than those with deduplication (24.78%, 66.25%, 36.24%, and 50.83%, respectively) (all $P<0.05$). The detection rates in sputum samples were signifcantly diferent between samples without duplication (28.39%, 76.19%, 46.95%, and 70.43%) and those with dedupli_x0002_cation (19.99%, 63.00%, 38.05%, and 64.50%) (all $P<0.05$). When deduplication was not performed, the rate of detection of CRKP in urine samples reached 30.05%, surpassing the rate observed with deduplication (21.56%) ($P<0.05$). In BALF specimens, the detection rates of CRKP and CRPA without deduplication (39.78% and 53.23%, respectively) were greater than those with deduplication (31.62% and 42.20%, respectively) ($P<0.05$). In blood samples, deduplication did not have a signifcant impact on the detection rates of MDROs.

Conclusion Deduplication had a signifcant efect on the detection rates of MDROs in sputum, urine, and BALF samples. Based on these data, we call for the Infection Prevention and Control Organization to align its analysis rules with those of the Bacterial Resistance Surveillance Organization when monitoring MDRO detection rates.

2014–2023 年术后肺炎临床分布特点及变化趋势

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目的 分析术后肺炎临床分布特点及变化趋势，为术后肺炎的进一步监测和管理提供依据。

方法 收集 2014 年—2023 年术后肺炎患者的临床资料，回顾性分析术后肺炎发生率、VAP 占比变化趋势、各科室术后肺炎发生率、术后肺炎感染病原体和术后肺炎时间分布。

结果 2014 年—2023 年共发生术后肺炎 2934 例次，平均年龄为（59.76±16.53）岁，男性占比 68.6%。术后肺炎发生率为 0.434%（1.998%~0.095%），呈逐年下降趋势，其中 VAP 占比呈上升趋势，差异有统计学意义（均 $P < 0.001$）。术后肺炎发生率排名前三的科室分别为心脏大血管外科（5.277%）、神经外科（2.114%）和胸外科（1.130%）。术后肺炎感染病原体以革兰阴性（G-）菌（77.58%）为主。术后肺炎发生时间 65.81% 发生在术后 7 天内，78.8% 发生在手术后 10 天内，4.36% 发生在术后 30 天后。

结论 术后肺炎发生率呈下降趋势，其中 VAP 应作为后续改进工作的重点关注对象，心脏血管外科、神经外科和胸外科则是术后肺炎的重点关注科室，手术后 10 天内应作为术后肺炎的重点关注时间段。

脊柱手术围手术期抗菌药物预防性使用合理性分析

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目的 旨在了解我院骨科在脊柱手术围手术期，抗菌药物预防性应用的现状，并对其应用的合理性进行评估，以期提高抗菌药物的合理使用。

方法 随机选取 2016 年 1 月至 2022 年 12 月期间，在我院骨科接受脊柱手术的 796 名患者，对其围手术期的抗菌药物预防性应用情况进行回顾性调查和分析。

结果 在 796 例脊柱手术患者中，792 例患者预防性应用抗菌药物，使用的药品主要为头孢唑林、头孢呋辛、克林霉素、（去甲）万古霉素。不合理用药主要表现在更换抗菌药物不合理、给药时机不适宜及预防用药疗程过长。

结论 医院脊柱手术围手术期抗菌药物预防性应用基本合理，但在药物选择、给药时机、应用疗程等方面存在一定不合理现象，应积极采取有效措施，加强质量监控，规范用药行为，提高医疗质量，确保用药安全、有效。

Association between TLR2 +2477G/A polymorphism and bacterial meningitis: a meta-analysis

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Abstract Content Background Toll-like receptor 2 (TLR2) is a key member of TLRs, which is crucial in the initial inflammatory response against bacteria. TLR2 is also the initial barrier against bacterial infection and plays an important role in recognizing a variety of bacterial lipoproteins. Several studies have been performed to investigate the TLR2+2477G/A polymorphism and bacterial meningitis susceptibility. Unfortunately, the results of previous studies were controversial. Therefore, we performed a meta-analysis to derive a more precise estimation of the association.

Methods The association between the TLR2+ 2477G/A polymorphism and bacterial meningitis susceptibility was assessed by odds ratios together with their 95% confidence intervals (CI). Six studies were enrolled in the present meta-analysis.

Results Overall, no significant association between TLR2+ 2477G/A polymorphism and bacterial meningitis risk were found under allele contrast (A vs. G: OR=1.15, 95% CI =0.93–1.43, P=0.202), recessive genetic model (AA vs.AG/GG: OR=1.12, 95% CI = 0.90–1.41, P =0.313). The significant association was found between TLR2+ 2477G/A polymorphism and pneumococcal meningitis risk under allele contrast (A vs. G: OR= 1.54, 95% CI =1.01–2.36, P=0.046), recessive genetic model (AA vs. AG/GG: OR= 1.63, 95% CI= 1.03–2.57, P =0.035).

Conclusion We conclude that TLR2 +2477G/A polymorphism is not associated with meningococcal meningitis risk but contributes an increased risk of pneumococcal meningitis.

我院抗菌药物处方点评制度与成效对比

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目的 介绍抗菌药物处方点评制度、实施方法、工作流程和效果评价

方法 对 2012 年 1 月至 6 月与 2013 年 1 月至 6 月的抗菌药物处方点评数据成效进行对比

结果 结果显示，与 2012 年 1 月至 6 月相比， 2013 年 1 月至 6 月门急诊合理处方比例、门诊患者抗菌药物处方比例、抗菌药物使用强度、抗菌药物费 用占药费百分率变化幅度分别为 2.5%、-4.7l%、-1.22、-0.37%。其中门诊患者抗菌药物处方比例最显著。

结论 制度化、规范化且卓有成效的处方点评模式已经建立。

基于信息化监测的维持性血透患者中心静脉导管相关血流感染危险因素分析及预测模型构建与验证

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目的 基于信息化监测手段，进一步分析维持性血液透析（MHD）患者中心静脉导管相关血流感染（CLABSI）危险因素，构建风险预测模型并进行验证。

方法 选自某三甲医院门诊血液净化中心自 2020 年 1 月 -2023 年 12 月期间 MHD 中心静脉导管置管患者共 300 例，收集基线资料，了解 CLABSI 病原菌分布状况，并以 7:3 分随机为训练集和验证集，以训练集分析确定 CLABSI 危险因素，构建风险预测模型，验证集进行内部验证。

结果 CLABSI 患者 32 例，感染率为 10.19%，结果显示置管时间、非首次置管、既往存在导管感染史及糖尿病是 MHD 患者 CLABSI 的危险因素（P < 0.05），基于 Logistic 回归方程模型：Logit(P)= － 5.661 +0.024* 置管时间（周）+3.391* 糖尿病 +2.037* 非首次置管 +1.546* 既往存在导管感染史。训练集 AUC 值 0.916（95%CI：0.837-0.994），灵敏度 87%、特异度 86.6%、约登指数 0.736，验证集 AUC 值 0.797（95% CI：0.632-0.962），灵敏度 77.8%、特异度 82.7%、约登指数 0.605，MHD 患者 CLABSI 实际发生概率与预测概率差异无显著意义（P > 0.05），模型区分度和准确性良好，CLABSI 病原菌金黄色葡萄球菌最多见。

结论 早期识别、预防对 HD 患者控制 CLABSI 至关重要，基于以上因素构建的 Logistic 回归方程预测模型整体效能较好，临床实用性较高，可对 MHD 患者 CLABSI 早期筛查及感染预防提供参考依据。

来源于不同菌群的 10 个耐药基因及其突变导致耐多粘菌素肺炎克雷伯菌的传播

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目的 分析多粘菌素耐药肺炎克雷伯菌的耐药机制、引起多粘菌素耐药的靶基因和传播链，向临床诊疗和预防提供参考。

方法 通过细菌培养、鉴定、药敏等常规方法，筛选广东省人民医院在 2022 年 6 月 -10 月在多个 ICU 病区爆发多粘菌素耐药肺炎克雷伯菌，通过 SNPs 和进化树分析了耐药菌株的传播链。

结果 多粘菌素耐药肺炎克雷伯菌主要分布于 ICU 病区，标本来源主要为痰液，以丝氨酸碳青霉烯酶为主要表型，发现 10 个与多粘菌素耐药相关的基因，导致其产生耐药的机制可能为：基因改变细胞壁的电荷、通过分子旁路产生抗生素耐药性的蛋白质和药物外排泵。共有 18 株菌存在同源一致性，表现为产碳青霉烯酶、含 KPC-2 基因，且 10 个多粘菌素耐药相关基因序列完全一致。此外，本研究发现多粘菌素耐药肺炎克雷伯菌存在获得性耐药，从其他菌群中获得 MCR-3、basS-1、basS-2、basR、arnA-1、arnA-2、PmrE、PmrF、PmrC、vanRF 基因，因此导致多粘菌素耐药肺炎克雷伯菌的耐药严重，无法治愈。

结论 多粘菌素耐药肺炎克雷伯菌存在局部爆发性传播，除与多粘菌素产生耐药高度相关的 MCR-3 基因以外，还存在多个耐药基因的共同作用。同时，本研究发现多粘菌素耐药肺炎克雷伯菌的获得性耐药为进一步研究耐药机制及传播提供理论基础。

TEM-135 型产青霉素酶淋球菌的突变分析及进化趋势

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目的 探讨亚洲型、非洲型产青霉素酶淋球菌（PPNG）的流行性、耐药性及突变情况，分析TEM-135 型 PPNG 的基因特征及进化趋势。

方法 以 2017-2022 年广东省人民医院保留的 433 株淋球菌菌株为研究对象，采用琼脂稀释法测定淋球菌的最小抑菌浓度（MIC）；通过纸片酸度法和多重 PCR 及琼脂糖凝胶电泳鉴定 PPNG 的型别，并使用质粒提取试剂盒获得其天然质粒 pJD4，以进行测序。通过 SnapGene 比对进行突变分析，经 mega11 绘制进化树分析流行性及进化历程。

结果 433 株淋球菌的 PPNG 阳性率为 15.24%（66/433），其中 PPNG 测出有 3 种型别：亚洲型（38 株）、非洲型（26 株）、多伦多型（2 株）。测序结果显示，C3867T，T3872G（20%）及 A5902G（80%）两种突变将亚洲型 PPNG 分为两群亚类，G1265A（50%）以及 A4230/4232G（50%）两种突变将非洲型 PPNG 分为两群亚类；84.21% 的亚洲型 PPNG 含 TEM-135 基因，且均存在额外的 A5902G 单碱基突变；所有的非洲型 PPNG 均为 TEM-1 基因；亚洲型 PPNG 对头孢曲松的耐药性相对于非洲型 PPNG 有显著差异（P=0.019），对临床经验用药有很强的指导作用。在亚洲型 PPNG 中，A5902G 突变始终与 TEM135 的出现保持一致，是含 TEM-135 基因的 PPNG 的第二特征，可作为 TEM-135 型菌株出现的佐证。

结论 PPNG 以亚洲型、非洲型为主要型别，其中亚洲型以含 TEM-135 基因为主（84.21%），非洲型均含 TEM-1 基因，两者存在耐药差异。亚洲型和非洲型 PPNG 存在不同的突变聚集，从而引起不同的进化特征。TEM-135 基因的播散，或是多重耐药淋球菌播散的潜在原因，TEM-135 型 PPNG 或可为评估淋病流行状况和防治措施提供参考价值。

间歇性次氯酸消毒对供水管路消毒效果及宏基因组测序分析

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目的 探讨间歇性次氯酸灌注消毒对供水管路的消毒效果。

方法 基线采取消毒供应中心 6 个固定出水口的水样，进行微生物培养。微酸性次氯酸发生机引入后，以 10 天为一个周期进行采样：其中第 1-3 天使用次氯酸进行持续性消毒，第 4-10 天停用次氯酸消毒，每个周期的第 1、4、7、10 天对 6 个固定出水口进行采样，共进行 3 个周期。对腔镜清洗槽出水口的所有水样同时进行微生物培养和宏基因组测序分析。

结果 水路消毒前共采集 18 瓶水样，10 瓶（55.55%）水样的细菌数集中在 102 ~ 104 CFU/mL，主要为粘连鞘氨醇单胞菌和蜡样芽胞杆菌；消毒后 72 瓶水样中仅有 2 瓶（2.78%）水样细菌超标。宏基因组测序分析显示，消毒前的 3 个水样最主要优势菌属为鞘氨醇单胞菌属和甲基杆菌属，SMRN 值在 10000~100000；消毒后水样最主要优势菌属为叶杆菌属、罗尔斯顿菌属、不动杆菌属、慢生根瘤菌属。PCoA 分析显示消毒前后的水样样本 β 多样性差异具有统计学意义（$P < 0.05$）。

结论 间歇性次氯酸灌注消毒可以有效清除水管路种细菌生物膜，但暂停消毒间期细菌生物膜存在恢复生长的风险，今后应加强医疗用水的监测与管理。

四川地区 2017–2023 年呼吸道病毒感染的流行病学特征分析

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目的 本研究旨在回顾分析 2017 年至 2023 年间四川地区呼吸道病毒感染情况，探究不同病毒的检出率及其在不同时期和不同年龄段的变化特征。

方法 研究共纳入 41516 例急性呼吸道感染患者，回顾临床实验室检测结果以统计不同病毒检出率，并对新冠疫情前后、混合感染、不同季节和不同年龄段的情况进行分析。

结果 本研究中呼吸道病毒整体检出率为 23.35%，甲型流感病毒（8.47%）、鼻病毒（7.13%）、乙型流感病毒（2.04%）居前三位。覆盖了从 7 日龄至 102 岁的全年龄段患者，其中 0–14 岁少年儿童的阳性检出率最高（48.62%），青年、中年和老年阶段的检出率大致相同（20.33% ~ 22.06%）。新冠疫情防控期间甲型流感病毒检出率降至 1.35%，疫情后回升至 13.05%。偏肺病毒、乙型流感病毒、冠状病毒和呼吸道合胞病毒中也观察到类似的模式。此外，腺病毒、博卡病毒、鼻病毒在三个阶段的检出率逐渐下降，副流感病毒则保持稳定，显示新冠疫情对这些病毒流行的影响不大。季节性分析显示秋冬季整体检出率高（28.90% 和 26.52%），春夏季低（17.61% 和 18.96%），表明季节变化对呼吸道病毒检出率有显著影响。在春季，甲型流感病毒、鼻病毒和腺病毒的检出率较高；而在冬季，甲型流感病毒、鼻病毒和乙型流感病毒成为主要病原。本研究共检出单病毒感染 8666 例，双重混合感染 948 例，三重感染 77 例，以及 5 例四重感染。双重感染中以博卡病毒与鼻病毒的组合最常见，占双重感染的 17.41%。三重感染中腺病毒 – 博卡病毒 – 鼻病毒和冠状病毒 – 博卡病毒 – 鼻病毒的组合最常见。

结论 呼吸道病毒检出率在秋冬季节高于春夏季节。新冠疫情防控期间多数病毒检出率降低，而疫情后又有所回升，这可能与防疫措施的变化有关。混合感染的结果提示公共卫生干预需考虑多病原同时流行的现实。本研究为未来预防策略的制定提供了重要的流行病学信息，特别是在呼吸道病毒高发季节及疫情爆发期间。

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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目的 分析经内镜逆行胰胆管造影 (ERCP) 与腹腔镜胆总管探查术 (LCBDE) 治疗胆总管（CBD）结石 (CBDS) 患者的医院感染相关因素，为胆总管结石患者选择治疗方案及制订院感防控措施提供依据。

方法 收集江苏省人民医院 2020 年 1 月至 2023 年 7 月胆总管结石患者 2629 例，最终纳入 ERCP 组 242 例和 LCBDE 组 160 例，对两组患者基本资料、住院时间、住院费用、围手术期感染相关指标及发生医院感染相关因素进行对比研究。

结果 两组患者之间年龄、性别无统计学差异 (P > 0.05)，在吸烟、饮酒、有胆囊切除 / 胆道手术史、胆囊炎疾病史、结石部位、合并胆囊结石、结石数目、结石最大直径、胆总管直径、住院总时间和总费用等方面差异有统计学意义 (P < 0.01)。术前两组感染指标及肝功能指标间比较均无统计学差异 (P > 0.05)；术后 ERCP 组 WBC、NEUT、AST 水平低于 LCBDE 组 (P<0.01)。采集胆汁样本送测 179 例，在分离的样本中共鉴定出病原菌 137 株 (ERCP 组 78 株；LCBDE 组 59 株)，其中革兰阴性菌 ERCP 组 42 株 (53.83%)、LCBDE 组 33 株 (55.93%)，革兰阳性菌 ERCP 组 34 株 (45.59%)、LCBDE 组 26 株 (44.07%)，真菌 ERCP 组 2 株 (2.56%)。402 例胆总管结石患者术后发生医院感染例次 38 例，感染例次率为 9.45%，其中 ERCP 组为 11.98%，LCBDE 组为 5.63%，差异有统计学意义（P < 0.05），主要感染部位为血流感染、肺部感染和腹盆腔感染。

结论 ERCP 和 LCBDE 术后医院感染病原菌均以革兰阴性菌为主，ERCP 相较 LCBDE 手术对患者的炎性指标、病原菌分布、住院时间及费用影响更小，ERCP 术后医院感染发生率高于 LCBDE。

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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目的 调查江苏省医院感控专职人员岗位胜任力现状及其影响因素。

方法 2023 年 3 月启动江苏省各级医疗机构感控专职人员岗位胜任力问卷调查，调查内容包括一般资料（医院性质、类型、等级；职务、专业背景、感控工作年限、职称）、岗位胜任力（进行医院感染病例监测与分析、识别和调查院感暴发检查、指导规章制度落实、指导职业防护、管理与沟通、实施院感培训、指导清洁、消毒灭菌与隔离、指导无菌操作技术、指导医疗废物管理、指导传染病防控、参与抗菌药物管理、审核消毒产品相关证明、开展院感相关科研工作）及环境支持满意度（接受培训情况、职业发展、职称晋升和岗位待遇）三部分，采用多元逐步线性回归分析感控专职人员岗位胜任力影响因素。

结果 397 人参加此次调查，从事感染管理工作以年限 2-5 年、护理专业、中级职称占比高；多元逐步线性回归分析结果显示，医院等级、专业背景、感控工作年限及职称是感控专职人员岗位胜任力的影响因素（$P < 0.05$）；院感工作年限、职称及职务在医院环境支持满意度方面具有统计学差异（$P < 0.05$）。

结论 江苏省不同级别医疗机构感控专职人员岗位胜任力差异较大，尤其是二级以下医院应加强教育培训，合理配置人力资源，增加医院环境支持力度，提升感控专职人员岗位胜任力，推动我省各级医疗机构卫生事业高质量发展。

Increased Transmission of Pseudomonas aeruginosa in ICU Settings During the COVID-19 Pandemic

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Abstract Content The transmission of Pseudomonas aeruginosa between the hospital environment and patients pose a serious threat to clinical treatment. Covid-19 pandemic potentially impact bacterial transmission in intensive care unit (ICU). We conducted the research to investigate the temporal and spatial spread of P. aeruginosa before and during Covid-19 pandemic.

Methods We routinely screened for P. aeruginosa in both the environment and patients in a newly-opened 21-room tertiary teaching hospital ICU in Hangzhou, Zhejiang during October 2022 – April 2023. Whole genome sequencing and antibiotic susceptibility test were performed on all non-repetitive P. aeruginosa samples.

Results Among 1694 environmental samples, 263 (15.53%) were positive for P. aeruginosa, and 40 (2.36%) were carbapenem-resistant Pseudomonas aeruginosa (CRPA). In 1575 oral and rectal samples (from 353 patients), 229 (14.54%) were positive for P. aeruginosa and 113 (7.17%) were CRPA. ST463 was highly prevalent in both patients (1st) and the environment (4th). Combined spatiotemporal distribution and genomic data, revealed no patients-related transmission before Covid-19 pandemic but detected multi-clonal patients-related transmission including high-risk ST463 clones during Covid-19 pandemic. Additionally, two independent blaKPC evolution events (from blaKPC-2 to blaKPC-71) were observed, leading in gastrointestinal and respiratory CRPA colonization in one patient.

Conclusion Our prospective study demonstrates that Covid-19 pandemic is associated to increased P. aeruginosa transmission. These finding provide insights for nosocomial infection management during future public health crisis.

Discovery of novel BfmR inhibitors restoring carbapenem susceptibility against carbapenem-resistant Acinetobacter baumannii by structure-based virtual screening and biological evaluation

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Abstract Content The emergence and spread of Acinetobacter baumannii pose a severe threat to public health, highlighting the urgent need for the next generation of therapeutics due to its increasing resistance to existing antibiotics. BfmR, a response regulator modulating virulence and antimicrobial resistance, shows a promising potential as a novel antimicrobial target. Developing BfmR inhibitors may propel a new therapeutic direction for intractable infection of resistant strains.

Methods In this study, we conducted a structure-based hierarchical virtual screening pipeline combining molecular docking, molecular dynamics simulation and MM/GBSA calculation to sift Specs chemical library and finally discover three novel potential BfmR inhibitors.

Results The three hits can reduce the MIC of meropenem for the carbapenem-resistant Acinetobacter baumannii (CRAB) strain ZJ06. Similar to the BfmR knockout strain, Cmp-98 was demonstrated to downregulate the expression of K locus genes, indicating it as a BfmR inhibitor. Bacteria underwent harmful morphological changes after treatment with these inhibitors. Molecular dynamics simulations found that all the hits tend to dynamically bind to different positions of the phosphorylation site of BfmR. Wherein we identified a potential inhibitory binding cleft, beside a possible activated binding cleft at the edge of the phosphorylation site. Restraining the ligand binding poses may help exerting inhibitory effects.

Conclusion This study reports a group of new-scaffold BfmR inhibitors, offering new insights for novel antibiotic therapeutics against CRAB.

Knowledge, Attitudes, and Practices of Chinese Residents Regarding Antibiotics and Antibiotic Resistance

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Abstract Content The World Health Organization (WHO) has listed antibiotic resistance as one of the most serious global public health threats this century. Between 2000 and 2018, the global rate of antibiotic consumption had increased by 46%, especially in low- and middle-income countries (LMICs). China, being a substantial consumer of antibiotics, is grappling with a more severe antimicrobial resistance (AMR) situation. It is estimated that China accounts for 600,000 deaths related to bacterial resistance, representing 12.2% of the total global deaths related to AMR. The causes of the irrational use of antibiotics are highly complex, encompassing issues such as the inappropriate prescription of antibiotics, insufficient awareness among residents about antibiotics and antibiotic resistance, and inadequate supervision of antibiotic circulation. Raising public awareness of antibiotics and antibiotic resistance is an effective means of mitigating the irrational utilization of antibiotics.Therefore, this study will report the knowledge, attitude, practices (KAP) of antibiotics and antibiotic resistance among respondents with different education attainments, and to explore factors associated with them.

Methods This cross-sectional study was conducted in China from November 2020 to April 2021. Knowledge, attitude and practices of antibiotics and antibiotic resistance were assessed using a self-administered questionnaire. The questionnaire included sociodemographic characteristics, KAP for antibiotics and antibiotic resistance. Linear regression analysis and machine learning models were employed to identify factors associated with KAP of antibiotics and antibiotic resistance.

Results A total of 3,135 respondents completed the questionnaire, of which there were slightly more respondents with a college degree and above (1697, 54.1%) than those with a below college degree (1438, 45.9%). Respondents' knowledge, attitude, and practices concerning antibiotics and antibiotic resistance remained at a moderate level. Both linear regression analysis and machine learning models revealed that education attainment was significantly associated with KAP of respondents. Respondents with higher

education attainment exhibited better knowledge, a more positive attitude, and more rational practices regarding antibiotics and antibiotic resistance.

Conclusion The insufficient KAP of the public towards antibiotics and antibiotic resistance may lead to an increase in irrational antibiotic use. It is necessary to enhance public education on antibiotics and antibiotic resistance by diversifying the forms of education.

重症监护病区（ICU）抗生素耐药性防控策略研究进展

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目的 2019 年中国共有 60 万例死亡与细菌 AMR 有关，占全球 AMR 相关死亡总数 (495 万) 的 12.2%，即每 10 万人中有 42.4 例死亡归因于 AMR。重症监护病区 (ICU) 是重症患者集中的特殊场所，是医院感染的高发科室，已成为医院耐药细菌感染预防控制的重要枢纽。并且 ICU 患者由于病情较重、免疫功能低下且合并多种基础疾病，侵入性检查和治疗等操作较多，感染发生的风险较高。针对我国医疗机构重症科室面临的抗生素耐药性防控压力，本研究旨在总结国内外有效的院内感染控制和抗生素耐药性防控的策略 , 指导重症科室有效进行耐药性预防与管理。

方法 通过质性研究方法、文献研究法及内容分析法等方法对国内外重症科室抗生素耐药性防控策略进行研究，总结院内感染控制和抗生素耐药性防控的策略、特点及实施内容。

结果 ICU 耐药性防控策略主要有以下几个方面：在规范 ICU 抗生素使用方面，实施抗生素降阶使用是保持抗生素治疗有效性的策略之一；在临床指标监测辅助诊疗方面，加强临床监测指标指导临床诊疗，如通过监测与细菌感染相关的生物标志物，指导医生调整抗生素使用的持续时间；并且部分医院尝试运用 AI 和机器学习算法快速确认病原体及其易感性特征，为抗感染诊疗提供依据。在多学科协作方面，多学科协作不仅能够优化 ICU 患者的抗生素使用提供指导，并且 MDT 感染管理团队具有分工明确、定期监督、跟踪反馈等特点，能在预防、发现、控制多重耐药菌感染问题中发挥优势，有效降低多重耐药菌感染发生率、提高感染防控措施的依从率。在院内感染控制方面，加强重症科室重点人群及重点菌群的防控是降低医院感染的关键，不仅要增强感染防控的意识，还应关注老年人、儿童等重点人群，强化监测，提高 ICU 感染管理水平，降低医院感染发生风险

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、评价监督等全过程防控工作，减少重症科室耐药细菌的产生和传播。

江苏省某大型三甲医院静脉药物调配中心 2019 年—2023 年环境卫生学监测结果分析

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目的 分析江苏省某大型三甲医院静脉药物调配中心（PIVAS）2019 年—2023 环境卫生学监测数据，探讨 PIVAS 医院感染管理模式。

方法 根据《静脉用药调配中心建设与管理指南（试行）》、《医院消毒卫生标准》GB15982 等的要求每季度对 PIVAS 空气、物表、工作人员手、超净台以及生物安全柜空气细菌菌落数进行监测，物表、手采样使用涂抹法，空气监测采用沉降法，采样后样品送至实验室 36℃孵化 48h，计数菌落总数。

结果 2022 年 -2023 年累计监测物表份 292 份，合格 289 份，合格率 98.97%，不合格标本为营养间手套（5.6cfu/ 皿）、抗生素间三层车（7.4cfu/ 皿）；累计监测消毒手 18 份，合格 16 份，合格率 88.89%，不合格样本菌落数为 12.3-25.2cfu/ 皿；2019 年—2023 年对 PIVAS 内部不同洁净度的区域监测 485 次、洁净工作台及生物安全柜监测 680 次，合格率均 100%。

结论 PIVAS 环境监测结果合理率高，物表、手清洁消毒是管理薄弱环节，输液相关医院感染风险极低，不建议纳入医院感染管理重点部门。

《粒缺伴发热患者血培养病原菌分布及耐药性：一项为期 10 年的单中心回顾性研究》

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目的 分析中性粒细胞缺乏（粒缺）伴发热患者血培养病原菌分布及耐药情况，为经验性抗菌药物治疗及多重耐药菌传播的精准防控提供依据。

方法 选择上海市某三甲医院 2014 年 1 月 -2023 年 12 月期间血液科收治的粒缺伴发热患者为研究对象，回顾性收集患者血培养结果及病原菌药敏信息，分析病原菌构成、耐药菌检出率以及历年变化趋势。

结果 共计获得 678 株分离菌株，其中以革兰阴性（G-）菌为主，占 68.29%，革兰阳性（G+）菌占 26.99%，真菌占 4.72%。G+ 菌以凝固酶阴性葡萄球菌居多，占 8.11%，依次为草绿色链球菌（7.67%）、屎肠球菌（2.51%）、革兰阳性需氧芽孢杆菌（1.92%）。凝固酶阴性葡萄球菌的苯唑西林耐药率为 78.18%，对利奈唑胺的耐药率较低，为 3.70%，未检出万古霉素耐药菌株；屎肠球菌对万古霉素、利奈唑胺均敏感；金黄色葡萄球菌的苯唑西林耐药率为 40.00%。G- 菌以大肠埃希菌为主，占 28.61%，其次为肺炎克雷伯菌（16.96%）、铜绿假单胞菌（8.41%）。大肠埃希菌对碳青霉烯类抗菌药物耐药率为 6.38%；肺炎克雷伯菌对碳青霉烯类抗菌药物耐药率为 15.91%；铜绿假单胞菌对碳青霉烯类抗菌药物耐药率为 12.73%。真菌以热带念珠菌居多，占 4.28%。2014 年 -2023 年，历年主要病原菌构成比及常见多重耐药菌检出率比较无统计学差异（$P > 0.05$）。

结论 近 10 年，本研究医疗机构历年血液科粒缺伴发热患者血培养主要病原菌构成及耐药性无显著变化。占比接近 50% 的检出病原菌为大肠埃希菌、肺炎克雷伯菌等肠杆菌科细菌，应为经验性抗菌药物治疗覆盖菌群，除此之外，草绿色链球菌、革兰阳性需氧芽孢杆菌等机会致病菌的防控不容忽视，怀疑真菌感染时，应首先考虑念珠菌，特别是热带念珠菌。粒缺伴发热患者血培养 MRSA 检出率较高，CREC、CRKP、CRPA 所致感染也应给予足够重视。

Establishment and validation of a nomogram based predictive model for Carbapenem-resistant organism infection

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Abstract Content Background Carbapenem-resistant bacteria (CRO) are defined as gram-negative bacteria, mainly including carbapenem-resistant Klebsiella pneumoniae (CRKP), Acinetobacter baumannii (CRAB), Pseudomonas aeruginosa(CRPA) and Enterobacteriaceae (CRE). The lack of safe and effective antibiotics has led to an increase in incidence rate. The purpose of this study is to establish and determine a risk nomogram to predict CRO infection in hospitalized patients.

Methods Hospitalized patients' information were collected from the electronic medical record system of hospital between January 2019 and December 2023. Based on the inclusion and exclusion criteria, we identified 131390 inpatients who met the criteria for this study. The patients were randomly divided into the training cohort (n =91973) and the validation cohort (n=39417),with a ratio of 7:3. We use data from the training cohort to create a nomogram and validate the nomogram with data from the validation cohort.

Results We constructed a nomogram based on the risk factor analysis for CRO infection. For the training cohort, the area under the curves (AUC) for predicting the CRO infection was 0.935. For the validation cohort, the AUC for predicting the CRO infection was 0.937. The results indicate that the nomogram has good discrimination ability. The calibration curve shows good consistency between the model prediction and actual observation of CRO infection in the training and validation cohort.

Conclusion We have developed the first novel nomogram to predict CRO infection in hospitalized patients, which is reliable and high-performance. The nomogram performs well among hospitalized patients and has good predictive ability.

Global, regional, and national time trends in incidence for tuberculosis, 1990− 2019: An age-period-cohort analysis for the Global Burden of Disease 2019 study

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Abstract Content This study presents the trend in TB incidence across 204 countries and regions over a 30-year period.

Methods The study utilises data sourced from the Global Burden of Disease (GBD) database. The age cohort model and gender subgroup analysis were employed to estimate the net drift (overall annual percentage change), local drift (age annual percentage change), longitudinal age curve (expected age ratio), and cycle and cohort effect (relative risk of cycle and birth cohort) of TB incidence from 1990 to 2019. This approach facilitates the examination and differentiation of age, period, and cohort effects in TB incidence trends, potentially identifying disparities in TB prevention across different countries.

Results Over the past three decades, a general downward trend in TB incidence has been observed in most countries. However, in 15 of the 204 countries, the overall incidence rate is still on the rise (net drift 0.0 %) or stagnant decline (⩾ –0.5 %). From 1990 to 2019, the net drift of tuberculosis mortality ranged from –2.2 % [95 % confidence interval (CI): –2.33, –2.05] in high Socio-demographic Index (SDI) countries to –1.7 % [95 % CI: –1.81, –1.62] in low SDI countries. In some below-average SDI countries,men in the birth cohort are at a disadvantage and at risk of deterioration, necessitating comprehensive TB prevention and treatment.

Conclusion While the global incidence of TB has declined, adverse period and cohort effects have been identified in numerous countries, raising questions about the adequacy of TB healthcare provision across all age groups. Furthermore, this study reveals gender disparities in TB incidence.



感染

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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目的 了解细菌性肝脓肿合并感染性心内膜炎的临床特征及诊治方案。

方法 1 例肺炎克雷伯菌所致肝脓肿合并感染性心内膜炎的病例资料进行分析。以“肝脓肿”、“感染性心内膜炎”为主题词检索万方、维普和中国知网数据库，以“liver Abscess”、“infective endocarditis”为主题词检索 Pubmed 数据库，检索国内外报道的细菌性肝脓肿（pyogenic liver abscess，PLA）合并感染性心内膜炎（Infective endocarditis，IE）的病例，筛选并总结分析病例资料。

结果 本院报道的病例合并 2 型糖尿病，初始诊断为肝脓肿，经验性给予头孢曲松治疗，并行肝脓肿穿刺引流。血培养提示肺炎克雷伯菌，对第三代头孢菌素敏感。补充诊断感染性心内膜炎后，给予头孢曲松联合阿米卡星治疗 1 周，停用阿米卡星，单用头孢曲松完成 6 周疗程，患者最后痊愈。文献检索到 14 例病例报道，包括本院报道的病例共 15 例。9 例患者合并基础疾病，7 例患者合并其他部位感染。5 例患者的病原菌为肺炎克雷伯菌，4 例患者的病原菌为厌氧菌（3 例坏死梭形杆菌、1 例核梭形杆菌）；3 例患者的病原菌为 β 溶血性链球菌（2 例咽峡链球菌、1 例星座链球菌）；3 例患者的病原菌分别为 HACEK（啮蚀艾肯菌）、紫色色杆菌、白色念珠菌。2 例患者死亡，13 例患者痊愈。5 例肺炎克雷伯菌所致 PLA 合并 IE 的案例，感染部位均为二尖瓣，只有 1 例患者进行换瓣手术，均进行肝脓肿引流，并选用 β 内酰胺类联合氨基糖苷类药物抗感染治疗，5 例患者最终均治愈。

结论 合并糖尿病的 PLA 患者，肺炎克雷伯菌的分离率较高，并且是肝外播散性感染的危险因素。肺炎克雷伯菌所致 PLA 可成为 IE 潜在的感染源。口腔菌群的血行播散可导致 IE 及 PLA。第三代头孢菌素联合氨基糖苷类可作为肺炎克雷伯菌所致 PLA 合并 IE 的经验性抗感染治疗方案。

P2X7 和 TRAF1/C5 基因多态性与结核病易感关联性的家庭病例对照研究

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目的 研究 P2X7 rs2230911 和 TRAF1/C5 rs10818488 位点基因多态性对结核病 (tuberculosis，TB) 易感性的影响，并分析基因与基因、基因与环境之间的交互作用在结核病发病中的影响。

方法 采用以家庭为单位的病例对照研究，选取结核病多发家庭中结核病确诊患者作为病例（TB）组，与病例组有血缘关系且未患病者组成家庭密切接触者（healthy household contacts，HHC）组，当地健康居民家庭中选取研究对象组成健康对照（healthy controls，HC）组。logistic 回归分析一般人口学特征、行为和环境因素与结核病的关联， GMDR 分析基因 - 基因、基因 - 环境交互作用对结核病患病的影响。

结果 P2X7 基因 rs2230911 位点中，CG 基因型和 CG-GG 基因型；TRAF1/C5 基因 rs10818488 位点中，AG 基因型、GG 基因型以及 AG-GG 基因型，均会增加健康对照人群患结核病的风险。而 TRAF1/C5 基因 rs10818488 位点的 AG 基因型、GG 基因型和 AG-GG 基因型均会增加家庭密切接触健康人群患结核病的风险。GMDR 分析结果显示，基因 - 环境交互作用在 TB 组和 HHC 组间，四因子作用模型（吸烟、每周锻炼、rs2230911、rs10818488）是最佳模型。而在 TB 组和 HC 组间，九因子作用模型（人均住房面积、居住地、BMI、文化程度、吸烟、每周锻炼、室内环境卫生、rs2230911、rs10818488）是最佳模型。

结论 P2X7 基因 rs2230911 位点和 TRAF1/C5 基因 rs10818488 位点的基因多态性与结核病患病风险相关，结核病易感性受基因 - 环境的相互作用的影响。

DRESS syndrome caused by comprehensive effects of multiple drugs-a case report

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Abstract Content We report a case of drugs-induced hypersensitivity syndrome (DRESS syndrome) caused by comprehensive effects of multiple drugs, including vancomycin, levofloxacin, rifampicin, celecoxib in a patient with left hip joint infection with sinus formation. The patient was successively treated with Meropenem, Vancomycin, Rifampicin, and Celecoxib, then was exposed to the sun for a long time after taking Levofloxacin, which led to the progression from mild rashes to erythema multiforme of the whole body. This case is a rare DRESS syndrome caused by multiple drugs, which deserves clinical attention and vigilance.

Methods A case report

Results A 50 years old chinese with 30+ years history of left hip joint infection was admitted for controlling infection. The patient reported a long-term fluid outflow with significant pain in the left hip. On the 19th day of Vancomycin treatment, the infection and pain of the wound were controlled, but mild local rashes were occurred around the wound. The patient was advised to stay for the treatment of rashes, but the patient refused. After discharge, the patient took rifampin, celecoxib, levofloxacin orally, and was exposed to sunlight during transportation, after which a large area erythema multiforme throughout her body with knife pain and itching. After stopping the above drugs, the patient took antihistamine drugs, full dose glucocorticoids and recovered after 11 days.

Conclusion In this case, the local allergic reaction caused by Vancomycin may ease or worsen, the direction of development is unpredictable. However, the patient took celecoxib, levofloxacin orally and was exposed to sunlight, the rash progressed rapidly within 2 hours, which definitely promote the development of erythra. This case reminds the clinicians that when encountering such situations, the patients need to stay in hospital for observation, the local rash should be treated in time, and the delayed allergic reaction caused by vancomycin should be vigilant. Try to avoid using drugs that aggravate the risk of rashes, such as rifampin, celecoxib. For drugs that are prone to photosensitive reactions, patients should be advised to avoid exposure to sunlight after taking the medication.

头孢他啶阿维巴坦用于儿童术后产超广谱 β 内酰胺酶大肠埃希菌脑膜炎和脑脓肿的病例报道

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Abstract Content CAZ-AVI therapeutic drug monitoring was performed to evaluate its efffcacy and effective drug distribution in the CNS.

Methods We measured CAZ and AVI in cerebrospinal fluid (CSF) samples obtained 3, 5, and 7 h after the administration of the 15th CAZ-AVI dose (2.5 g, q8h, iv), respectively. We also measured CAZ and AVI in serum samples obtained 3 and 5 h after the administration, respectively.

Results The respective serum concentrations 3 and 5 h after administration were 57.0 and 25.8 μg/mL for CAZ and 11.3 and 4.5 μg/mL for AVI. The respective CSF concentrations 3, 5, and 7 h after administration were 15.6, 7.1, and 3.5 μg/mL for CAZ and 4.0, 2.1, and 1.2 μg/mL for AVI.

Conclusion CAZ-AVI achieved CSF levels higher than the MIC throughout the dosing interval.

MRSA 菌血症患者万古霉素个体化治疗方案分析

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目的 为患者制定万古霉素个体化给药方案

方法 运用经典药动学软件万古霉素计算器（Vancomycin Calculator）对一例 MRSA 菌血症患者制定万古霉素给药方案，并进行血药浓度监

结果 患者在给予万古霉素 0.5g q8h 微泵静滴（约为 4-6 小时）治疗后，测得谷浓度均在 15-20mg/L 的范围内，AUC/MIC 约为 463，患者治疗成功，未发生万古霉素相关的 AKI

结论 运用万古霉素计算器（Vancomycin Calculator）设计万古霉素给药方案是可行的，可作为临床万古霉素个体化给药和优化的重要工具。

马尔尼菲青霉菌病 1 例

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目的 马尔尼菲青霉菌（PM）是青霉菌中唯一的呈温度双相型的致病菌，是一罕见的致病菌。可发生于健康者，但更多见于免疫缺陷或免疫功能抑制者。主要累及单核－巨噬细胞系统，常播散全身，累及肺、肝、皮肤、骨骼、淋巴等多种组织和器官，病死率高，是一种严重的深部真菌病。结合我院近期收住一肺部感染病患，入院后经常规抗感染等治疗后，病灶反复，并呈迁徙性改变，短期内出现肋骨、胸骨、腰椎等破坏，后经病损穿刺送检病理及病原微生物高通量基因检测最终诊断为马尔尼菲青霉菌病（PsM），特将诊治过程及经验体会汇报如下，以期加深对这种疾病的认识，早期诊断、早期干预。

方法 结合我院近期收住一肺部感染病患，入院后经常规抗感染等治疗后，病灶反复，并呈迁徙性改变，短期内出现肋骨、胸骨、腰椎等破坏

结果 经病损穿刺送检病理及病原微生物高通量基因检测最终诊断为马尔尼菲青霉菌病（PsM）

结论 PM 为深部条件致病菌，具有侵袭性、致病力强等特点，如不能早期治疗病死率很高。PsM 多见 AIDS 等免疫功能受损患者，但健康者感染也时有发生。临床表现无特征性，可引起肺部、肝脏、皮肤、软组织、关节、骨、血液、纵膈等多脏器损害。因此对于用结缔组织病及普通化脓性感染等无法解释的多系统损害，又有 PsM 流行区生活史的患者，应高度怀疑 PM 感染，及早进行病原学检查，以便能及时诊断、及时治疗，防止病情加重、降低病死率。

肺结核合并噬血细胞综合征 1 例

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目的 噬血细胞综合征（HPS）是又称噬血细胞性淋巴组织细胞增多症（HLH），是一种免疫介导的危及生命的疾病。HLH 可以影响各个年龄人群，不仅发生在先天性遗传易感性免疫缺陷患者，也在越来越多的自身免疫性疾病、持续性感染、恶性肿瘤或免疫抑制的患者中发现，因此涉及多学科交叉。结合我院近期收治一肺结核病患，入院后出现持续发热、肝功能损害、三系减少，后经骨穿、血清铁蛋白、血 NK、sCD25 等最终诊断为噬血细胞综合征，结合文献复习，特将诊治过程及经验体会汇报如下，以期加深对这种疾病的认识，早期诊断、早期干预、早期治疗。

方法 结合我院近期收治一肺结核病患，入院后出现持续发热、肝功能损害、三系减少。

结果 经骨穿、血清铁蛋白、血 NK、sCD25 等最终诊断为噬血细胞综合征

结论 噬血细胞综合征是少见疾病，但病情进展迅速、病情凶险，应及时诊断及鉴别，采取有效治疗措施以挽救患者生命。部分患者以肝损害为明显表现，当合并有发热、肝脾肿大、血细胞下降、凝血功能异常等、常见肝病等病因不能解释病情时应当及时排除噬血细胞综合征的可能，并及时完善铁蛋白、骨穿、完善 NK 细胞活性、可溶性 CD25 等检查，以协助下一步有效的诊治。

感染

Adoptive transfer of CMV-specific TCR-T cells for the treatment of CMV infection after haploidentical hematopoietic stem cell transplantation

chao ma
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Abstract Content CMV reactivation after unmanipulated haploidentical stem cell transplantation (SCT) frequently occurs, causing life-threatening morbidities and transplantation failure. Preemptive therapy upon the detection of CMV viremia using antiviral agents is currently the standard of care but it was associated with significant toxicity. The CMV antigen-specific cytotoxic T lymphocytes (CTLs) therapy was limited by the time-consuming manufacture process and relatively low success rate. More effective and safer approaches for the treatment of CMV reactivation after haploidentical SCT are in urgent need.

Methods A single-arm, open-label Phase I clinical trial evaluating the safety and efficacy of CMV-targeting TCR-T (CMV-TCR-T) cell therapy as the first-line preemptive therapy for patients with CMV reactivation post haploidentical PBSCT was conducted in the Chinese PLA General Hospital (ClinicalTrials.gov Identifier: NCT05140187). Six patients with CMV reactivation after haploidentical SCT were adoptively transferred by 1 to 3 doses of SCT donors-derived CMV-TCR-T cells. This trial was a dose-escalation study with doses ranging from 1×103 CMV-TCR-T cells/kg body weight per dose to 5×105 CMV-TCR-T cells/kg per dose

Results Except for the Grade 1 CRS observed in one patient and mild fever in 2 patients, no other adverse events were observed. Four patients had response within a month after CMV-TCR-T cells infusion without the administration of any antiviral agents. The other two patients who initially didn't respond to CMV-TCR-T cell therapy had salvage ganciclovir and foscarnet administration and then had rapid CMV clearance. The CMV-TCR-T cells displayed overall robust expansion and persistence in the peripheral blood after infusion. The CMV-TCR-T cells were firstly detected in the peripheral blood of these patients 3 to 7 days after the 1st dose of CMV-TCR-T infusion, rapidly expanded and persisted for at least 1-4 months, providing long-term protections against CMV reactivation. In one patient, the CMV-TCR-T cells started to expand even when the anti-GvHD reagents were still being used , further indicating the proliferation potential of CMV-TCR-T cells.

Conclusion Our study firstly showed CMV-targeting TCR-T cell as a highly feasible, safe and effective first-line preemptive treatment for CMV reactivation after haploidentical PBSCT.

225 株鲍曼不动杆菌的耐药性分析与 OXA-23 型碳青霉烯酶检测在神经重症中应用

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目的 了解南昌大学附属第一医院神经外科 2021 年至 2022 年鲍曼不动杆菌的分布特点和耐药状况，为临床合理使用抗生素提供依据，同时研究江西地区碳青霉烯耐药鲍曼不动杆菌中 OXA-23 型碳青霉烯酶的分子流行病学特征，探讨其耐药性与治疗策略。

方法 利用梅里埃 VITEK-2 Compact 微生物分析仪鉴定细菌，K-B 法进行药敏试验，采用 WHONET 5.6 软件统计分析药敏结果，PCR 检测 OXA-23 型碳青霉烯酶的编码基因。

结果 2021 年至 2022 年临床分离出 225 株鲍曼不动杆菌，标本类型以痰液为主 (195 株，占 87%)，其次脑脊液（28 株，12.4%），鲍曼不动杆菌对 12 种抗生素的耐药率总体呈逐年上升趋势，对碳青霉烯类抗生素的耐药上升到 84.0%，在 225 株碳青霉烯类抗生素耐药鲍曼不动杆菌中 PCR 检出 200 株 OXA-23 型碳青霉烯酶阳性菌株。

结论 ICU 耐碳青霉烯鲍曼不动杆菌广泛携带 OXA 型耐药基因，OXA-23 型碳青霉烯酶检测易于操作，时间短，能快速有效检测鲍曼不动杆菌可能感染、指导临床治疗。

心脏外科手术围术期抗菌药物的使用与术后切口感染发生率的研究

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目的 研究心脏外科手术围术期预防使用抗菌药物对患者术后切口感染发生率的影响，为临床合理使用抗菌药物提供可靠的依据。

方法 回顾性分析 2021 年 1 月至 2022 年 12 月期间东南大学附属中大医院收治的行心脏手术的 187 例患者的临床资料，根据围术期使用抗菌药物品种的不同分为主要覆盖革兰阳性菌组和加强覆盖革兰阴性菌组；比较两组患者术后切口感染以及其他部位感染发生情况，统计两组住院时间及住院费用，并且对可能导致术后切口感染的危险因素进行 Logistic 回归分析。

结果 相较于主要覆盖阳性菌的抗菌药物，围术期预防使用加强覆盖阴性菌的抗菌药物组的患者术后浅表切口感染的发生率更高（0.8% vs 7.4%，P=0.046）。而两组其他部位感染发生率，包括肺部感染、血流感染、尿路感染，均无统计学差异；使用加强覆盖阴性菌的抗菌药物组的患者 ICU 住院时间、总住院时间延长，住院总费用增加，差异均有统计学意义（$P < 0.05$）；另外，Logistic 回归分析结果表明，手术时长 > 5h 和 SOFA 评分 > 5 分是心脏外科术后患者发生切口感染的独立危险因素（$P < 0.05$）。

结论 对于心脏外科手术围术期预防使用抗菌药物品种的选择，相较于主要覆盖阳性菌的抗菌药物，使用加强覆盖阴性菌的抗菌药物的患者术后浅表切口感染发生率更高，且不降低其他部位感染的发生率，同时导致患者住院时间和住院费用显著增加。

一例肺组织胞浆菌患者的诊疗

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目的 分享一例肺组织胞浆菌患者的诊疗过程。

方法 收集资料如下：邓某，55 岁男性。因间断发热、咳嗽、咳痰 4 月入院。既往有先天性主动脉瓣畸形及主动脉瓣关闭不全。4 月前患者无诱因发热，Tmax 37.8℃，伴咳嗽、咳黄痰。胸部 CT（图 1）示双肺多发异常密度影，抗细菌治疗 3 周。3 月前胸部 CT（图 2）示右肺上叶斑片影较前增大。右肺组织穿刺活检病理示胞浆菌感染可能，PAS +，六胺银 +。诊断为肺组织胞浆菌病（弥漫性），静滴氟康唑 1 周后改为伊曲康唑口服液口服，2 月后因肝功异常停药。停药 1 周后再次发热伴咯血、咳嗽、咳白色粘痰，胸部 CT（图 3）示右肺上叶病变较前增大，结合实验室检查及组织病理考虑组织胞浆菌合并细菌感染可能。予以哌拉西林他唑巴坦钠抗细菌、两性霉素 B 胆固醇硫酸酯复合物抗真菌治疗，1 周后复查胸部 CT（图 4），继续抗真菌治疗直至 1 月后肝功异常停药。调整为伏立康唑口服 2 月。

结果 症状减轻，复查胸部 CT（图 5）病灶吸收好转。

结论 对免疫功能正常者规治疗组织胞浆菌感染可选择两性霉素 B、伊曲康唑等三唑类，如出现不能耐受的副作用时，可尝试伏立康唑治疗。

分享 1 例妊娠中期重度支原体肺炎的诊治

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目的 分享 1 例妊娠中期支原体感染致重症肺炎患者的救治过程。

方法 收集病史如下：36 岁女，孕 25w，汉族。因咳嗽、咳痰、发热 8 天入院。患者于 8 天前受凉后出现咳嗽、咳黄粘痰，伴发热、畏寒、寒战，Tmax 39.0℃。经阿奇霉素口服 3 天联合头孢类抗生素静滴抗感染 1 周，症状加重，并出现阴道少量出血，遂以“肺炎 呼吸衰竭；中期妊娠；先兆流产”来院。既往有不明原因贫血多年。2 周前接触支原体感染患儿。孕 2 产 1 男；本次怀孕为试管婴儿，试管前曾口服甲泼尼龙 4mg/ 日 ×1 月。查体：生命体征平稳。贫血面容，胸部双侧语颤减弱、叩诊实音，双下肺呼吸音减，未闻及干、湿性啰音。心脏（－）。腹膨隆，双下肢无水肿。痰肺炎支原体核酸检测 3.07E+8 拷贝 /ml。胸腔超声示右侧极少量胸腔积液。胎儿超声示单胎，右骶后位，存活；胎盘功能 I 级，羊水适中。胸部核磁示双肺多叶感染（图 1）。入院后紧急 MDT，予阿奇霉素静滴 0.5g/ 日 ×10d 联合口服甲泼尼龙 12mg/ 日 ×5d，辅以化痰、抗凝、加强营养、氧疗支持等。

结果 症状好转，胸部核磁示双肺感染吸收好转（图 2），顺利出院。

结论 妊娠期支原体感染亦可进展为重症，预后凶险；及时获取可靠的病原学依据是精准治疗的前提；对该类特殊人群，静脉用阿奇霉素联合小剂量激素足疗程治疗疗效显著。

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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Abstract Content 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.

b-Hydroxyisovalerylshikonin regulates macrophage polarization via the AMPK/ Nrf2 pathway and ameliorates sepsis in mice

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Abstract Content Context The potential anti-inflammatory bioactivities of β-hydroxyisovalerylshikonin (β-HIVS) remain largely unknown.

Objective: This study investigated the anti-inflammatory effects and underlying mechanisms of β-HIVS.

Methods RAW 264.7 cells stimulated with LPS (100 ng/mL) for 24 h were treated with the non-cytotoxic doses of β-HIVS (0.5 or 1 μM, determined by MTT and Trypan blue staining), qRT-PCR and FCM assay were used to examine macrophage polarization transitions. Western blotting was used to evaluate the activation of the AMPK/Nrf2 pathway. In vivo, C57BL/6 mice were randomly divided into vehicle control, LPS (10 mg/kg), and β-HIVS (2.5 mg/kg) combined with LPS (10 mg/kg) groups, blood samples, BALF, and lung tissues of mice were subjected to ELISA, qRT-PCR, FCM, and H&E staining.

Results β-HIVS (1 μM) inhibited LPS-induced expression of M1 macrophage markers (TNF-α: 0.29-fold, IL-1β: 0.32-fold), romoted the expression of M2 macrophage markers (CD206: 3.14-fold, Arginase-1: 3.98-fold) in RAW 264.7 cells; mechanistic studies showed that β-HIVS increased the expression of nuclear Nrf2 (2.04-fold) and p-AMPK (3.65-fold) compared with LPS group ($p< 0.05$). In vivo, β-HIVS decreased the levels of pro-inflammatory cytokines (TNF-α: 1130.41 vs. 334.88 pg/mL, IL-1β: 601.89 vs. 258.21 pg/mL in serum; TNF-α: 893.07 vs. 418.21 pg/mL, IL-1β: 475.22 vs. 298.54 pg/mL in BALF), decreased the proportion of M1 macrophages (77.83 vs. 68.53%) and increased the proportion of M2 macrophages (13.55 vs. 19.56%) in BALF, and reduced lung tissue damage and septic mice survival ($p< 0.05$).

Conclusion These results indicate that β-HIVS may be a new potential anti-inflammatory agent.

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，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，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，入院时诊断为感染的比例和血尿素氮水平更高，血红蛋白水平更低，住院时间和气管插管、导尿管、深静脉置管时间更长，碳青霉烯类药物和多黏菌素 B 使用时间更长，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。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。

高龄尿路感染患者的病原学特征分析

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目的 分析高龄尿路感染住院患者的病原学分布特征。

方法 回顾性分析中国医科大 学附属第一医院 2019 年 1 月至 2023 年 1 月收治的 809 例年龄≥ 60 岁尿路感染患者的临床资料和病原菌检出情况，比较年龄≥ 80 岁与 60 ~ 79 岁患者的病原学分布。统计学比较采用 χ^2 检验，多因素 logistic 回归分析细菌产超广谱 β 内酰胺酶的危险因素。

结果 809 例尿路感染患者中共分离出 914 株病原体，584 株分离自 60 ~ 79 岁患者，330 株分离自年龄≥ 80 岁患者，62 例患者存在细菌和真菌混合感 染。年龄≥ 80 岁组中，检出革兰阴性菌 144 株，肠杆菌科细菌以大肠埃希菌、肺炎克雷伯菌和奇异变形杆菌为主，非发酵菌以铜 绿假单胞菌和鲍曼不动杆菌为主；检出革兰阳性菌 104 株， 以屎肠球菌为主；检出真菌 63 株，以白念珠菌为主。 与 60 ~ 79 岁组相比，年龄≥ 80 岁组的大肠埃希菌检出率较低（χ^2 = 35.78，P < 0.001），而屎肠球菌（χ^2 = 4.91，P = 0.027）和真菌（χ^2 = 10.03，P = 0.002）检出率较高，差异均有统计学意义。375 株肠杆菌科细 菌中 ESBL 阳性株 190 株（50.67%） 多因素 logistic 回归分析提示住院前有抗菌药物使用史、合并肺部感染是细菌产 ESBL 的独立危险因素。

结论 年龄≥ 80 岁的高龄尿路感染患者的病原体以革兰阴性菌为主，肠球菌 和真菌的检出率也较高，且有相当数量患者存在细菌、真菌混合感染。住院前抗菌药物使用史和合并肺 部感染是细菌产 ESBL 的独立危险因素。

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治疗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 感染的患者的临床信息，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存活的重要治疗手段。

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。

肺炎克雷伯菌尿路感染 167 例碳青霉烯耐药风险列线图 预测模型的构建

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目的 构建肺炎克雷伯菌尿路感染碳青霉烯耐药风险列线图预测模型。

方法 回顾性分析 2018 年 1 月至 2020 年 12 月 在秦皇岛市第一医院确诊为肺炎克雷伯菌尿路感染的成人住院病人 167 例临床资料，将尿液标本中检出耐碳青霉烯类肺炎克 雷伯菌（CRKP）的 62 例病人设为 CRKP 组，非 CRKP 的 105 例病人设为非 CRKP 组。采用 logistic 回归分析发生 CRKP 尿路感染 的独立危险因素，并将 167 例病人按照分层随机抽样以 7 ： 3 比例分为训练集（118 例）和验证集（49 例），然后使用训练集根据独 立危险因素建立 CRKP 尿路感染列线图风险预测模型。采用校准曲线和受试者操作特征曲线（ROC 曲线）评估列线图预测模 型的准确度和区分度。

结果 CRKP 组肺炎克雷伯菌对头孢呋辛、哌拉西林 / 他唑巴坦、美罗培南、阿米卡星耐药性分别为 100%（62/62）、100%（62/62）、98.4%（61/62）、51.6%（32/62），明显高于非 CRKP 组的 42.9%（45/105）、8.6%（9/105）、1.0%（1/105）、 3.8%（4/105）。多因素 logistic 回归分析显示，入住重症监护室、两周内使用碳青霉烯和酶抑制剂为 CRKP 尿路感染的独立危险 因素（OR=8.95、5.52、6.12，P<0.05）。训练集、验证集一致性指数（C-index）分别为 0.88，0.90。ROC 曲线下面积为 0.88。校准曲 线和 ROC 曲线提示模型准确度、区分度良好。

结论 通过分析 CRKP 尿路感染的危险因素构建风险列线图预测模型，模型具 有良好的准确度和区分度，可有效预测肺炎克雷伯菌尿路感染碳青霉烯耐药发生风险，并可依此实施更有针对性的防护措施 和制定合理的药物治疗方案。

CRISPR/Cas13a 技术助力戊型肝炎病毒 RNA 准确、便携式检测

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目的 戊型肝炎病毒（HEV）对公共卫生和动物食品安全构成严重威胁，在很大程度上被公众所忽视，而且 HEV RNA 的检测率还不足以满足临床需求。因此，本研究旨在利用 CRISPR/Cas13a 技术开发一种准确、便携、高灵敏度和特异性的 HEV RNA 检测方法。

方法 该研究建立、评估并优化 CRISPR/Cas13a 技术结合反转录 - 聚合酶链反应（RT-PCR）技术（提高 HEV 感染实验室诊断的准确性）以及结合反转录 - 重组酶介导等温核酸扩增（RT-RAA）技术（构建快速诊断便携式试剂盒）检测 HEV RNA 的方法。此外，该研究还利用 154 例 HEV 感染患者和 74 例 HEV 感染动物的样本进行了临床应用验证。

结果 该研究建立、评估、优化并验证了检测 HEV RNA（基因型：HEV-1、HEV-3 和 HEV-4）的 RT-PCR/RT-RAA-CRISPR/Cas13a 检测方法，其检测下限 (LoD) 为 1 拷贝 / μL，特异性为 100%。在 HEV 感染应用验证中（以 ddPCR 检测为金标准），RT-qPCR、RT-PCR-CRISPR 和 RT-RAA-CRISPR 方法患者阳性检出率分别为 70.8%、98.6% 和 79.2%，HEV 感染动物阳性检出率分别为 75.8%、95.2% 和 87.1%，且该检测系统在准确性、敏感性、阳性预测值（PPA）和阴性预测值（NPA）方面都优于目前临床常用的 HEV 核酸检测方法。此外，5 分钟快速裂解处理样本（血清和粪便）大大缩短了 RT-RAA-CRISPR 试纸条检测的操作时间，表明了基于 CRISPR 的即时检测（POCT）的可行性。

结论 该研究利用 CRISPR/Cas13a 技术开发了准确、灵敏、便携的 HEV RNA 检测方法，适用于检测 HEV 感染。这种新方法对扩大 HEV 感染患者以及动物 HEV 感染的诊断筛查能力和低成本监测治疗具有全球意义。

马尔尼菲篮状菌持续成为福建省艾滋病患者血流感染的压倒性病原体

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目的 艾滋病患者的血流感染率及病原菌分布因不同地理环境及不同时间周期存在较大差异。目前福建省无大样本的艾滋病患者血流感染流行率及病原学的研究。本研究探讨过去 6 年福建省艾滋病住院患者血流感染流行率及病原谱。

方法 回顾性分析 2015 年 9 月 ~2021 年 8 月于福建医科大学孟超肝胆医院住院的艾滋病患者血流感染情况。收集患者人口学资料如性别、年龄及实验室检查包括血常规、生化、CD4 计数、CD8 计数、HIV-RNA 载量、血培养病原学、降钙素原及 C 反应蛋白。计量资料采用中位数（全距）表示，用 Kruskal-Wallis 或 Mann-Whitney test 分析组间差异。计数资料以样本量（率）表示，采用 Pearson’s chi- squared test 分析组间差异。

结果 共有 3681 位艾滋病住院患者进行了血培养，646 位患者共分离 683 株病原菌纳入分析。患者中位数年龄为 38 岁，86.84% 为男性。血流感染总体流行率为 18.55%（过去 6 年介于 12.01% ~ 22.36% 之间）。马尔尼菲篮状菌总体分离率为 12.42%（过去 6 年介于 8.3% ~ 15.00% 之间）。从 2015 年 ~2021 年，马尔尼菲篮状菌持续成为最主要的病原体（过去 6 年占比介于 63.04% ~ 71.43% 之间），其次是新生隐球菌（占比介于 10.00% ~ 20.83% 之间）。与其他病原体血流感染组患者相比，马尔尼菲篮状菌病血流感染患者年龄更小、CD4 计数、白细胞计数、血红蛋白及 C- 反应蛋白均更低，而 HIV-RNA 载量更高。

结论 即使在抗逆转录病毒治疗时代，血流感染仍然是福建省艾滋病患者面临的重要挑战，马尔尼菲篮状菌是最主要的病原体，对于免疫力低下的患者，临床医师应及时识别机会性感染以避免发展为血流感染。

耐甲氧西林金黄色葡萄球菌致 5 例 PICC 导管相关性血流感染的血液肿瘤患者的护理分析

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目的 总结耐甲氧西林金黄色葡萄球菌（methicillin-resistantstaphylococcus aureus,MRSA）致 5 例 PICC 导管相关性血流感染的血液肿瘤患者护理经验。

方法 回顾性分析耐甲氧西林金黄色葡萄球菌所致的 5 例 PICC 导管相关性血流感染的血液肿瘤患者诊治和护理的全过程。建立 MDT 团队，临床药师运用临床药学理论知识，结合血管内导管相关感染的预防与治疗指南原则，对 5 例 PICC 导管感染患者进行全程药学监护，制订个体化给药方案；护理重点包括选择注射用盐酸万古霉素药物和准确配制抗生素锁溶液，严格控制抗生素锁治疗药物留置时间；精确封管；关注潜在风险；观察抗生素锁治疗终止时机；进行导管补救后的监测。

结果 5 例 PICC 置管感染的血液肿瘤患者，PICC 导管感染得到控制，导管留置时间延长以及功能良好，未发生并发症。

结论 肿瘤患者 PICC 置管感染的药学监护模式保障了患者用药的安全性和有效性，结合抗生素封锁治疗提高了肿瘤患者 PICC 导管感染的治愈率，值得推广。

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检出耶氏肺孢子菌并临床诊断为耶氏肺孢子菌肺炎的 CKD 患者进行回顾性分析。

结果 2019 年 10 月 -2023 年 10 月共 22 例 CKD 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，平均年龄为 57 岁。肾病患者发生 PJP 中位时间为肾病确诊后 3 个月。16 例（72.7%）患者发生Ⅰ型呼吸衰竭。所有患者在感染前 3 个月内使用免疫抑制剂。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 232.0 μmol/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。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。SMZ/TMP 平均剂量为 11.0 mg · kg-1 · d-1。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、需要机械通气可能是 PJP 患者预后不佳的危险因素。

伏立康唑治疗肝衰竭合并侵袭性肺曲霉病的临床研究

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目的 回顾性分析标准谷浓度的伏立康唑在肝衰竭合并侵袭性肺曲霉病（invasive pulmonary aspergillosis，IPA）患者中使用的安全性和有效性。

方法 收集2016年12月-2023年3月在树兰（杭州）医院住院治疗的肝衰竭合并IPA患者，将其分为两组，分别是无效监测组：使用伏立康唑治疗但无有效监测血药谷浓度，共计22例；有效监测组：使用伏立康唑治疗并有效监测血药谷浓度，共计20例；对照组：肝衰竭未合并IPA组，共计46例；比较三组患者的存活率，并通过Logistic回归分析肝衰竭合并IPA患者预后的高危因素。

结果 合并IPA的肝衰竭患者存活率显著低于未合并IPA者（21/42 VS 35/46）。其中，合并IPA的肝衰竭患者中，有效检测组存活率高于无有效监测组（55% VS 45.55），两组差异具有统计学意义（11/20 VS 10/22）(P=0.036)；有效监测组和对照组的存活率无统计学意义。通过单因素logistic回归分析筛选影响肝衰竭合并IPA患者预后的影响因素，其中有Cr（OR=0.981，95%CI：0.962-1，P=0.048）、GEF-Cr（OR=1.020，95%CI：1.001-1.039，P=0.042）；多因素logistic回归分析，Cr（P=0.376 > 0.05）和GEF-Cr（P=0.133 > 0.05）无统计学差异，未筛选出肝衰竭合并IPA患者预后的影响因素。

结论 在使用伏立康唑治疗肝衰竭合并IPA患者中，有效血药浓度的监测可以提高患者存活率，但预后相关影响因素还需进一步明确。

Infection with Carbapenem-resistant Hypervirulent Klebsiella Pneumoniae: clinical, virulence and molecular epidemiological characteristics

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Abstract Content Background: 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.

代谢途径中的磷酸烯醇丙酮酸（PEP）在肿瘤免疫微环境中作用

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目的 肿瘤是一种复杂的异质性疾病，其发生发展受到多种因素的影响，包括遗传、环境、生活方式，以及机体免疫系统对肿瘤的作用。肿瘤免疫是指机体免疫系统对肿瘤细胞的识别和清除的过程，是一种重要的抗肿瘤机制。然而，肿瘤细胞可以通过多种方式逃避免疫系统的监视和攻击，形成免疫耐受和免疫抑制的肿瘤微环境，从而促进肿瘤的生长和转移。

方法 肿瘤是一种复杂的异质性疾病，其发生发展受到多种因素的影响，包括遗传、环境、生活方式，以及机体免疫系统对肿瘤的作用。肿瘤免疫是指机体免疫系统对肿瘤细胞的识别和清除的过程，是一种重要的抗肿瘤机制。然而，肿瘤细胞可以通过多种方式逃避免疫系统的监视和攻击，形成免疫耐受和免疫抑制的肿瘤微环境，从而促进肿瘤的生长和转移。

结果 近年来，越来越多的研究表明，PEP 不仅是一种能量分子，还是一种重要的免疫调节剂，能够影响肿瘤微环境中的免疫细胞的功能和极化。

结论 磷酸烯醇丙酮酸（PEP）是一种存在于细胞内的代谢物，是糖酵解的最后一个中间产物，也是三羧酸循环的入口分子。PEP 的主要功能是提供能量和碳骨架，参与葡萄糖、脂肪和氨基酸的代谢。然而，PEP 不仅是一种能量分子，还是一种重要的免疫调节剂，能够影响肿瘤微环境中的免疫细胞的功能和极化。本文着眼于 PEP 在肿瘤免疫中的作用和机制，对近期的相关研究进展进行归纳和总结，以期为 PEP 作为一种潜在的抗肿瘤免疫治疗靶点的研究，提供新的视角和思路。

The first case report: diagnosis and management of necrotizing fusobacterium lung abscess via BALF next generation sequencing

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Abstract Content AbstractBackground Fusobacterium necrophorum (F. necrophorum)-induced necrotizing pneumonia is a rare but severe pulmonary infection. Insufficient microbiological detection methods can lead to diagnostic difficulties.Methods We report a case of F. necrophorum lung abscess diagnosed by next-generation sequencing (NGS) of bronchoalveolar lavage fluid (BALF).Results BALF-NGS detected F. necrophorum, guiding subsequent targeted antibiotic therapy. With active drainage and metronidazole treatment, the patient's condition was effectively treated.Conclusion BALF-NGS is a valuable tool for the rapid diagnosis of infections caused by difficult-to-culture bacteria. It played a decisive role in the early identification of F. necrophorum, enabling timely and targeted antibiotic intervention. Early diagnosis and appropriate treatment are crucial for the management of F. necrophorumpneumonia. Keywords Fusobacterium necrophorum, Lung abscess, Bronchoalveolar lavage fluid, Next-generation sequencing, Targeted antibiotic therapy liuyang, Shaoxing City Keqiao District Hospital of Traditional Chinese Medicine, 312030 Shaoxing, China

Methods We report a case of F. necrophorum lung abscess diagnosed by next-generation sequencing (NGS) of bronchoalveolar lavage fluid (BALF).

Results BALF-NGS detected F. necrophorum, guiding subsequent targeted antibiotic therapy. With active drainage and metronidazole treatment, the patient's condition was effectively treated.

Conclusion BALF-NGS is a valuable tool for the rapid diagnosis of infections caused by difficult-to-culture bacteria. It played a decisive role in the early identification of F. necrophorum, enabling timely and targeted antibiotic intervention. Early diagnosis and appropriate treatment are crucial for the management of F. necrophorumpneumonia.

大肠埃希菌感染引起肝脓肿、肠系膜脓肿合并肝假性动脉瘤一例

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目的 报告一例大肠埃希菌感染引起肝脓肿、肠系膜脓肿合并肝假性动脉瘤。

方法 通过检索数据库等总结病例，为以后的临床病例提供思路。

结果 患者 1 月前（2024.1.5）因“腹痛、发热、黄疸”就诊外院查 MRCP 提示“胆总管上段结石，肝内胆管及胆总管炎性病变并肝内多发小脓肿可能”。转至我院消化科，诊断“胆总管结石伴急性化脓性胆管炎”行 ERCP 取石术。术后予亚胺培南西司他丁抗感染，复查腹部增强 CT 提示“多发小片状肝脓肿，门静脉血栓”。胆汁培养提示大肠埃希菌（对头孢曲松、哌拉西林他唑巴坦、头孢哌酮舒巴坦耐药、碳青霉烯敏感、左氧氟沙星中介）。后降级为左氧氟沙星出院。因门静脉血栓出院时口服利伐沙班 10mg bid。18 天前（2024.02.05）患者再次发热，就诊当地医院，行 CT 提示“肝脓肿，胆系炎性病变并胆道出血”。予美罗培南抗感染治疗，体温好转。6 天前（2024-02-15）复查腹腔增强 CT 见“肝脓肿范围较前扩大”，患者为进一步诊治转至我院。入院后回顾患者既往影像学及病原学，考虑“大肠埃希菌菌血症、肝脓肿、肠系膜脓肿、门脉血栓、动脉瘤”。继续美罗培南抗感染治疗，介入行肝动脉造影提示肝右动脉假性动脉瘤，予栓塞治疗。病情稳定予调整为厄他培南抗感染出院。

结论 大肠埃希菌引起肠系膜脓肿及肝假性动脉瘤较为罕见，汇报病例希望在以后临床工作中为大家提出更多思路。

社区获得性耐甲氧西林金黄色葡萄球菌致感染性心内膜炎合并肺脓肿病例报道及文献复习

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目的 耐甲氧西林金黄色葡萄球菌是社区获得性感染和医院感染的主要致病菌，也是菌血症、心内膜炎、皮肤和软组织感染、骨骼和关节感染等的主要原因，尽管 MRSA 的发病率在一些地区有所下降，但它的患病率和死亡率一直居高不下，仍然构成了巨大的临床威胁。本文通过病例报道及文献复习，希望能在 CA-MRSA 感染方面为大家提供一些参考及帮助。

方法 本文通过报道 1 例社区获得性耐甲氧西林金黄色葡萄球菌致感染性心内膜炎合并肺脓肿病例，通过分析其起病经过、诊断技术、治疗过程等，并结合既往文献进行复习，诊治过程中引进了最新的数字 PCR 技术。

结果 患者中年男性，社区起病，既往糖尿病病史，为社区获得性金黄色葡萄球菌感染的高发人群，影像学上符合金黄色葡萄球菌感染的特点。入院行胸腔穿刺置管引流术，外送胸腔积液数字 PCR 技术，检测回报金黄色葡萄球菌（mecA 阳性），后续血培养及痰培养结果回报均为 MRSA 且药敏结果基本一致。我们在病程早期将胸腔积液标本送检了数字 PCR 技术，快速明确了感染病原体并在 24 小时内应用了万古霉素覆盖 CA-MRSA 抗菌治疗，应用抗菌治疗时机较早，预后良好。

结论 金黄色葡萄球菌感染是菌血症的主要原因之一，菌血症患者极易并发感染性心内膜炎，治疗不充分可危及生命。本文报道了 1 例社区获得性耐甲氧西林金黄色葡萄球菌致感染性心内膜炎合并肺脓肿的病例，并引进了数字 PCR 技术，以帮助早期识别感染病原体及其耐药性，尽早、有效的应用抗生素，以减少血流感染并发症的发生并降低死亡率。

中国不同城市 61 例鹦鹉热衣原体肺炎病例分析

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Abstract Content Chlamydia psittaci pneumonia can quickly progress to severe pneumonia, leading to respiratory failure. Therefore, we should improve our diagnostic and treatment capabilities for this disease.

Methods This article retrospectively studied 61 cases of Chlamydia psittaci pneumonia from 12 different provinces in China, and classified them into severe pneumonia and non severe pneumonia. Divided into two groups, with 23 cases of severe pneumonia and 38 cases of non severe pneumonia.

Results There are significant regional differences in the distribution of Chlamydia psittaci pneumonia. There are many differences between non severe Chlamydia psittaci pneumonia and severe Chlamydia psittaci pneumonia.

Conclusion The imaging manifestations of Chlamydia psittaci pneumonia do not have fixed characteristics.

Maraviroc, an inhibitor of chemokine receptor type 5, alleviates Sepsis associated liver injury via regulating MAPK/NF-κB signaling

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Abstract Content Sepsis is one of the most intractable problems in intensive care units. Sepsis-related liver injury(SALI) often leads to poor clinical outcomes due to its complex physiological mechanism. In previous studies, chemokine receptor 5(CCR5) inhibitors have shown their unique anti-inflammatory ability. The therapeutic effect of Maraviroc (MVC) on SALI is still unclear. We established a SALI model through CLP and injected 20mg/kg dose of MVC intraperitoneally two hours after CLP. The results showed that MVC could significantly improve liver injury after CLP. Further,we demonstrated that MVC reduce inflammatory infiltration, reduce apoptosis after SALI. In addition, we found that MVC exerted anti-inflammatory effects by inhibiting NF-κB and MVC signaling pathways. Finally,JNK agonist AN was chosen for reverse research. The results showed that the protective effect of MVC disappeared after AN treatment, indicating that MVC exerted anti-inflammatory and anti-apoptotic effects through JNK. As a mature drug for treating HIV, the safety of MVC has been widely recognized. Based on our research results, we guess that MVC has great potential to become a clinical drug for SALI in the future.

Methods We established a model of SALI by cecal ligation and puncture (CLP) and intraperitoneally injected 20 mg/kg MVC two hours after CLP.

Results The results showed that MVC could significantly ameliorate liver injury after CLP. Furthermore, we demonstrated that MVC reduced inflammatory infiltration and apoptosis after SALI. In addition, we found that the function of MVC in reducing inflammatory was obtained through the inhibition of the two inflammatory signaling pathways mentioned above. Finally, the JNK agonist AN was chosen for reverse research. As shown by the results, the therapeutic effects of MVC disappeared after AN treatment, indicating that MVC exerted anti-inflammatory and antiapoptotic effects through JNK.

Conclusion Our study revealed that MVC could reduce liver injury after SALI by inhibiting liver inflammation and hepatocyte apoptosis induced by CLP and that MVC exerted diminish inflammatory effects by inhibiting theNF-κB and MAPK signaling pathways.

于临床宏基因组测序技术快速预测中枢神经系统感染耐多药细菌表型研究

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目的 探讨基于宏基因组测序技术快速预测临床常见耐多药细菌表型对于治疗中枢神经系统感染的应用价值。

方法 选取航空总医院脑脊液病神经外科 2020 年 1 月至 2023 年 12 月收治的中枢神经系统感染患者 80 例，其中鲍曼不动杆菌感染 23 例，肺炎克雷伯菌感染 25 例，铜绿假单胞菌感 12 染例，金黄色葡萄球菌感染 20 例。所有患者在留取脑脊液细菌培养及药敏鉴定的同时进行脑脊液宏基因组检测，并采用 GenseqAMR3.0 平台对细菌表型进行预测。收集常规培养组药敏时间、mNGS 组预测表型时间进行对比，同时统计药敏结果与预测表型结果的一致性比例。所有患者在预测表型结果后第一时间进行抗感染治疗，同时部分患者在常规药敏结果后进行抗菌素调整。

结果 临床治愈率 98.75%（79/80），死亡 1 例。常规细菌培养及药敏鉴定平均时间为 68.75h，快速预测表型时间平均为 19.32h。预测表型结果一致性 92.46%。

结论 基于临床宏基因组测序技术快速预测临床常见耐多药表型对于治疗中枢神经系统感染具有更好的时效性，可作为治疗中枢神经系统感染的重要辅助检测方法。但此类检测方法与常规培养及药敏鉴定结果存在一定误差，后续仍需进一步研究以提高准确性。

血药浓度监测下伏立康唑致肝酶升高及视觉异常的药学监护

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目的 探讨临床药师参与 1 例中年免疫力低下肺曲霉菌病患者使用伏立康唑治疗的药学监护，以及在抗感染药物治疗过程中防治该类不良反应的作用，临床药师适时提出干预意见并参与给药方案制订等药学监护措施。

方法 伏立康唑血药谷浓度在安全范围内的 1 例中年男性患者发生肝酶升高及视觉异常的不良反应，临床药师充分利用专业优势，查阅相关文献资料，分析导致肝酶升高及视觉异常的原因、处理措施，以及临床药师实施个体化药学监护的切入点。

结果 通过 RUCAM 评分分析，该患者出现肝酶升高及视觉为伏立康唑所致。

结论 临床药师在参与临床治疗过程中，需密切关注用药安全，注意药物之间相互作用，有条件的医疗机构需进行血药浓度监测。

PIRO（易感因素、损害、反应、器官功能障碍）评分与其他六个临床预测评分对 COVID-19 患者预后预测的比较：一项基于急诊科数据的研究

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目的 本研究旨在评估和比较 PIRO 评分与其他六种常用评分：快速序贯器官功能衰竭评分（qSOFA）、CURB-65 评分、肺炎严重指数（PSI）、新冠危重症评分（COVID-GRAM）、急性生理评分（RAPS）和国家早期预警评分 2（NEWS2）在预测新冠患者预后方面的预测价值。

方法 对入住北京佑安医院急诊科的 506 名 COVID-19 患者进行了筛查。收集了患者的人口统计学数据、临床治疗信息，并评估了包括 PIRO 在内的七项临床预测评分。使用受试者工作特征曲线（ROC 曲线）评估不同评分系统对 COVID-19 患者 28 天死亡的预测性能。使用 DeLong 检验比较不同临床评分系统预测 28 天死亡的曲线下面积（AUC）是否存在统计学差异。

结果 最终有 374 名患者符合进一步分析的标准，其中 120 名患者（32.1%）在入院 28 天内死亡。我们发现入院后 28 天内存活组和 28 天内死亡组的年龄、实验室指标和临床预测评分方面存在显著差异。我们还观察到随着临床评分的增加，28 天内死亡的患者比例也增加。PIRO 评分对患者预后的预测价值最高，曲线下面积（AUC）为 0.898（95% CI：0.866 - 0.929）。qSOFA 评分紧随其后，AUC 为 0.882（95% CI：0.849 - 0.914）。COVID-GRAM 和 NEWS2 评分的 AUC 均超过 0.85。DeLong 检验发现 PIRO 的 AUC 与 CURB-65、PSI、COVID-GRAM、RAPS 和 NEWS2 的 AUC 存在统计学差异（所有 p 值 <0.05）。

结论 我们发现 PIRO 评分是预测急诊科 COVID-19 患者的 28 天死亡的有效评分模型，有助于预后评估。在未来，我们期待进行更大规模的多中心研究来验证这一评分系统对于 COVID-19 患者预后的预测价值。

Presepsin 作为 COVID-19 患者预后预测的生物标志物：结合临床评分系统和实验室炎症指标的预测研究

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目的 本研究旨在评估入院时 Presepsin、临床评分系统和炎症标志物以及联合这些指标对于 COVID-19 患者疾病严重程度和预后的预测价值。主要结局指标是住院 28 天内的死亡。

方法 筛选了 2022 年 5 月至 11 月期间入住北京佑安医院急诊科的 226 名 COVID-19 患者。收集入院时的人口统计学信息、实验室指标结果。收集患者入院时的血浆并检测 Presepsin 水平。分析 Presepsin、临床评分系统和炎症标志物对于患者 28 天死亡的预测价值。

结果 最终 190 名患者纳入了分析，其中 83 例为轻型，61 例为中型，46 例为重症 / 危重症患者。有 23 例在入院 28 天内死亡。重症 / 危重症患者的 Presepsin 水平升高，三个组别患者血浆中的 Presepsin 水平存在显著差异（$p<0.0001$）。Presepsin 对 COVID-19 患者的 28 天死亡率预测具有显著的预测价值，受试者工作特征曲线下面积（AUC）为 0.828（95% CI: 0.737-0.920）。临床评分系统和炎症标志物在预测 28 天预后方面也有重要作用。经多因素 Cox 回归校正后，Presepsin、快速序贯器官功能衰竭评分（qSOFA）、国家早期预警评分 2（NEWS2）、肺炎严重指数（PSI）、CURB-65 评分、C- 反应蛋白（CRP）、中性粒细胞与淋巴细胞比值（NLR）、C- 反应蛋白与白蛋白比值（CAR）和淋巴细胞与 C- 反应蛋白比值（LCR）被确定为 COVID-19 患者 28 天死亡的危险预测因子（所有 p 值 <0.05）。将 Presepsin 与临床评分系统和炎症标志物结合可以进一步提高对患者预后的预测价值。

结论 Presepsin 是预测 COVID-19 患者预后的有用指标，与临床评分系统和炎症标志物的结合可以进一步提高预后预测价值。未来，我们期待进行大规模多中心研究以验证我们的研究结果。

中国西部地区 HIV 阴性结核性脑膜炎发生矛盾反应的临床特征研究

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目的 提高人们对矛盾反应（Paradoxical reaction, PR）的认识，减少误诊率。

方法 选择 2016 年 1 月至 2021 年 12 月在喀什地区第一人民医院就诊的结核性脑膜炎（Tuberculous meningitis, TBM）患者，根据 PR 定义，将患者分为 PR 组和非 PR 组，对两组患者的基本信息、临床表现、辅助检查及治疗方案等相关资料进行对比分析。

结果 本研究共纳入 130 例人类免疫缺陷病毒（Human immunodeficiency virus, HIV）阴性的 TBM 患者。其中，PR 组 15 例（11.5%），女性患者 9 例，男性患者 6 例；非 PR 组 115 例（88.5%），女性 45 例，男性 70 例，两组性别差异无统计学意义。PR 组的住院时间中位数为 27 天，明显长于非 PR 组（P=0.001）。PR 的发生时间中位数为 30 天（4-151 天），好转时间为 12 天（6-30 天），主要临床表现为头痛（86.7%），影像学表现为基底膜强化（60%）。当出现 PR 时，外周血淋巴细胞的绝对值和百分比分别为 1.81 和 24.5%，高于入院时的 0.96 和 9.7%，两者之间均存在统计学差异（$P < 0.05$）。PR 组预后不良患者 0 人，非 PR 组 21 人（18%），两组之间无明显统计学差异。

结论 PR 发生率为 11.5%，基线血低淋巴细胞经抗结核治疗后明显升高可能预示着 PR 的发生。PR 对短期预后无明显影响，但可延长住院时间。糖皮质激素能有效治疗 PR，但不能完全预防 PR 发生。

Quality assessment of therapeutic drug monitoring guidelines for voriconazole using AGREE II instrument

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Abstract Content The quality of therapeutic drug monitoring (TDM) guidelines of voriconazole was appraised for quality improvement.

Methods PubMed was systematically searched to obtain the recommendations on TDM of voriconazole by October 2023. Four reviewers assessed the guidelines that met the standard using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument independently.

Results Out of 564 identified guidelines, 5 from UK, Canada, Australia, China and Japan met the standard and were assessed. The guidelines from China, Japan, and Canada could be 'recommended for immediate use', and the guidelines from UK and Australia was 'recommended with modifications'.

Conclusion Our analysis of TDM guidelines for voriconazole suggested that the methodological quality of guidelines was reliable.

化学发光法检测胃功能的方法学评价

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目的 对诺曼 NORMAN-CL 5 全自动化学发光免疫分析仪化学发光法检测胃功能的方法学进行评价。

方法 参照美国临床和实验室标准协会（CLSI）的 EP 文件要求，对诺曼 NORMAN-CL 5 全自动化学发光免疫分析仪检测血清胃蛋白酶原Ⅰ（PG Ⅰ）、胃蛋白酶原Ⅱ（PG Ⅱ）、胃泌素 17（G17）3 项的精密度、正确度、临床样本比对、分析测量范围、可报告范围、参考区间等进行验证和评价。

结果 胃蛋白酶原Ⅰ（PG Ⅰ）、胃蛋白酶原Ⅱ（PG Ⅱ）、胃泌素 17（G17）的低、高值质控品和临床标本的批内精密度变异系数（CV）为 2.42% ~ 4.52%、1.46% ~ 1.81%，均小于 CLIA’88 认可的 1/4TEa；批间精密度变异系数（CV）为 3.37% ~ 5.10%、2.73% ~ 4.35% 均小于 CLIA’88 认可的 1/3Tea；正确度允许偏倚均小于 CLIA’88 认可的 1/2TEa；临床样本比对数据相关性评估 r 在 0.997 ~ 0.998，认为数据相关性评估为接受；实验方法系统误差评估 SE< 判断允许误差（允许误差为 1/2TEa）判断通过；PG Ⅰ、PG Ⅱ、G17 的线性回归方程斜率在 0.9980 ~ 0.9991，$R^2 \geqslant 0.95$，表明线性良好，与厂家声明一致；健康人群的 20 例样本结果，95% 的健康者检测结果在厂家标注的生物参考区间范围内。

结论 诺曼 NORMAN-CL 5 全自动化学发光免疫分析仪检测胃功能项目的主要分析性能符合厂家声称的性能指标或公认的质量目标和要求，能够保证临床检验结果的真实性、准确性和可靠性，能满足临床需要。

PDCA 循环模式在干眼理疗眼部感染发生率中的应用

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目的 探讨应用 PDCA 循环模式科学的质量管理程序降低干眼理疗眼部感染发生率，规范干眼理疗标准化服务流程及设备清洗消毒灭菌，从而有效地降低干眼理疗后眼部感染的发生。

方法 应用 PDCA 循环模式中的计划、实施、检查、处理四个步骤对导致眼部感染进行分析，找出要因，并根据要因，制定改进措施，并组织实施，检查计划实施的结果，比较应用 PDCA 前后眼部炎症发生率，建立干眼理疗的标准化服务流程。

结果 应用 PDCA 循环模式科学的质量管理程序后半年眼部感染发生率为 0 人，$P < 0.05$，差异有统计学意义。

结论 运用 PDCA 循环模式科学的质量管理程序对眼部感染（结膜炎、睑腺炎）的发生率是行之有效的，值得临床上推广应用。

基于 COM-B 理论模型的口腔卫生管理对造血干细胞移植后患者口腔感染的影响

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目的 探讨基于 COM-B 理论模型的口腔卫生管理对造血干细胞移植后患者口腔感染状况的影响。

方法 选取 2022 年 1 月—2023 年 6 月我科收治的 200 例行造血干细胞移植的患者，采用随机数字表法将其分为试验组和对照组，各 100 例。对照组实施常规口腔卫生教育及管理，试验组在对照组的基础上实施基于 COM-B 理论模型的卫生教育管理，分别在基线时、干预后 6 个月评定两组口腔溃疡率、牙龈红肿数、口腔出血数和口腔相关生活质量。

结果 干预后，试验组口腔溃疡率、牙龈红肿数、口腔出血率、均低于对照组，差异有统计学意义（P<0.001）；干预后，试验组口腔相关生活质量得分低于对照组（P<0.001）。

结论 基于 COM-B 理论模型的口腔卫生管理能有效改善血液病造血干细胞移植后患者的口腔感染率和提高生活质量。

药师参与 1 例啮蚀艾肯菌致腰大肌脓肿患者的药物治疗实践

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目的 为临床药师开展苛养菌感染患者的药学服务提供参考。

方法 药师参与一例啮蚀艾肯菌致腰大肌脓肿患者的诊疗，通过查阅文献，结合病例，充分考虑患者的病史和临床症状，对该患者药物治疗过程进行分析，并总结其治疗过程中的药学监护重点。

结果 对该例感染患者的监护重点包括多种抗感染药物选择；根据患者肾功能对多种抗感染药物剂量进行调整；药物不良反应等方面。通过本例病例报道和文献复习可知，啮蚀艾肯菌具有较强的致病力，可导致免疫功能正常人群的感染，而伴随有严重基础疾病或创伤的免疫力低下人群感染程度通常更重。

结论 临床药师参与临床抗感染方案制订，通过结合致病菌本身特点、抗菌药物特性、相关指南以及患者实际情况，给出了合理的抗感染治疗方 案，提高了患者的治愈率及临床合理用药水平。

肺部混合感染并抗合成酶抗体综合征活动 1 例

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目的 提高对肺部萜烯诺卡菌合并耶氏肺孢子菌混合感染及抗合成酶抗体综合征临床特征、影像学表现及治疗的认识。

方法 回顾性分析 2023 年 3 月广西医科大学附属武鸣医院收治的 1 例肺部混合感染治疗后抗合成酶抗体综合征活动患者的临床资料。

结果 该患者以发热、气喘、咳嗽、咳痰为首发表现，既往长期使用激素及免疫抑制剂，肺部 CT 以双肺多发渗出、实变影、结节和肿块影伴内部空洞为主要特点，肺泡灌洗液 mNGS 见萜烯诺卡菌、耶氏肺孢子菌序列，予复方磺胺甲噁唑抗感染、糖皮质激素抗炎后症状改善。激素减量后再次发热、新发颈胸部皮疹，自身抗体检测见抗 Jo-1 抗体、抗 Ro-52 抗体阳性，肌电图提示四肢肌肉肌源性损害，肺部 CT 见肺部新发条索影，最终确诊抗合成酶抗体综合征，予加用免疫球蛋白、甲泼尼龙、环孢素联合治疗，患者病情好转出院，出院后规律口服甲泼尼龙 + 环孢素，随访至今病情稳定，复查肺部病灶吸收。

结论 免疫缺陷患者易并发各种机会性感染，mNGS 对临床诊疗有较好指导意义，其肺诺卡菌、耶氏肺孢子菌感染影像表现可无特异性，但仍有其特点。在积极有效抗感染治疗后再次出现发热、皮损，要高度重视非感染因素，详细询问病史，及时完善肌炎自身抗体检测显得尤为重要。

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 % vs32%，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。

大浪淘沙，寻因高热肺脓肿

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目的 回顾性分析 1 例的肺脓肿的免疫抑制患者的诊治过程。患者病程迁延痰及 BALF 培养回报 CRPA，经抗感染治疗体温控制不加，多次气管镜检查及病理后诊断为肺癌。

方法 患者某男，70 岁，主因发热伴咳嗽 1 个月余收住入院，既往支气管哮喘，肾病综合征、膜性肾病、糖尿病。青霉素类药物可疑过敏史，吸烟史 30 余年，平均 3 支 / 天，家族性低钾血症病史。入院后完善相关辅助检查，考虑肺脓肿诊断明确，且完善痰培养提示铜绿假单胞菌，予亚胺培南 / 西司他丁静点。但患者仍有间断发热，后呼吸道病原核酸提示呼吸道合胞病毒阳性。完善支气管镜检查，灌洗液培养提示 CRPA，调整治疗为特治星 + 阿米卡星雾化治疗。但患者仍有发热，其后复查胸部 CT 示肺脓肿较前变化不著，需警惕肿瘤可能，其后予支气管镜间断吸痰引流。但患者仍有发热。经多学科 MDT 讨论，改为特治星 + 多黏菌素 B 雾化治疗。并继续予支气管镜吸痰引流。其后患者热退，炎症指标较前好转。但支气管镜活检回报肺腺癌。

结果 患者病情稳定后，带药回当地医院近一步诊治，门诊随访肺脓肿较前好转吸收，外院肺腺癌继续治疗

结论 患者发热病情不缓解时，应警惕其他原因导致的发热可能。

宏基因组二代测序和血培养在血液病粒缺患者革兰阴性杆菌感染中的对比研究

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目的 通过宏基因组二代测序（mNGS）与血培养检出病原结果进行对比分析，探讨 mNGS 在血液病粒缺患者革兰阴性杆菌感染中的检出优势、诊断价值及预后影响。

方法 回顾性分析 2019 年 4 月至 2023 年 8 月在解放军总医院第一医学中心血液科住院期间出现粒缺发热的血液病患者的病历资料，纳入同时送检外周血 mNGS 和血培养的患者，分析外周血 mNGS 与血培养方法在革兰阴性杆菌感染中的病原检出率、检测周期及对预后影响的差异。

结果 共 170 例血液病粒缺发热患者同时进行外周血 mNGS 和血培养，其中男性 118 例（69.4%），中位年龄 49.5（10-78）岁，最常见疾病是急性髓系白血病占 49.4%（84/170）。mNGS 对细菌的检出率为 17.6%（30/170），其中革兰阴性杆菌占 86.7%（26/30），革兰阳性球菌占 13.3%（4/30）。血培养的细菌检出率为 15.3%（26/170），其中革兰阳性球菌占 57.7%（15/26），革兰阴性杆菌占 38.5%（10/26）。共发生 21 例革兰阴性杆菌感染和 7 例混合感染（含革兰阴性杆菌），其中 8 例革兰阴性杆菌感染被 mNGS 和血培养同时诊断，18 例仅被 mNGS 诊断，2 例仅被血培养诊断，mNGS 对革兰阴性杆菌检出率明显高于血培养（15.3% vs 5.9%, P=0.003）。共有 6 例耐碳青霉烯革兰阴性杆菌（CRE）感染被 mNGS 和血培养同时诊断，共有 3 例 CRE 仅被 mNGS 诊断，mNGS 和血培养的 CRE 检出率分别为 5.3% 和 3.5%。mNGS 检测时间为（1.21±0.48）天，血培养检测时间为（2.60±0.27）天，差异有统计学意义（P<0.001）。mNGS 与血培养方法对调整抗生素后的 30 天内感染死亡率无统计学差异（P>0.05）。

结论 mNGS 相较于血培养方法在血液病粒缺患者革兰阴性杆菌感染，尤其是 CRE 感染中具有检出率高、检测周期短的优势。

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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目的 分析新冠患者继发真菌感染的临床特征及预后影响因素。

方法 纳入 2022 年 9 月至 2023 年 9 月深圳市第二人民医院收治的新冠后继发真菌感染患者，分析其临床特征及预后。新冠患者继发真菌感染预后的影响因素采用单因素方差分析，多重共线性分析，多因素 Logistic 回归分析。采用 ROC 分析检验影响因素对预后不良预测的准确率。

结果 共纳入 295 例患者，单因素分析结果证实，年龄、基础疾病、免疫抑制、住院时间、真菌治疗时间、为新冠患者继发真菌感染预后不良的危险因素，且各因素间不存在多重共线性。多因素分析结果证实，年龄、免疫抑制状态、住院时间、真菌治疗时间、为新冠患者继发真菌感染预后不良的独立危险因素。ROC 分析证实联合多因素（年龄、基础疾病、免疫抑制状态、住院时间，抗真菌治疗时间）对新冠患者继发真菌感染预后不良有较好的预测价值。

结论 年龄越大、存在基础疾病、存在免疫抑制状态、住院时间越长、真菌治疗时间越长的新冠后继发真菌感染的患者越容易出现预后不良。

临床药师参与 1 例铅黄肠球菌血流感染的体外膜肺氧合患者抗感染治疗的药学监护

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目的 分析铅黄肠球菌血流感染患者在体外膜肺氧合状态下抗感染治疗的药学监护过程，为该类患者的救治提供参考。

方法 临床药师参与 1 例急性心肌炎患者在静脉 - 动脉体外膜肺氧合（VA-ECMO）支持治疗下并发血流感染患者的多学科讨论，结合药物药代动力学特点建议初始经验治疗使用美罗培南联用替考拉宁抗感染；第 4 天根据患者宏基因二代测序（mNGS）报告修正诊断为“血流感染（铅黄肠球菌）”，临床药师根据替考拉宁血药浓度建议增加替考拉宁给药剂量至 600mg，给药间隔不变；第 7 天患者感染未见好转，临床药师根据循证医学证据建议将替考拉宁调整为达托霉素；第 9 日患者生命体征平稳，顺利撤除 ECMO，停用美罗培南；第 15 日患者病情好转，停用达托霉素转当地医院继续治疗；临床药师还参与了评估、预防治疗过程中的药物不良反应。

结果 医师采纳了临床药师的建议，经过 2 次调整治疗方案，患者抗感染治疗 2 周病情得到良好控制，未发生严重不良反应。

结论 临床药师参与 1 例铅黄肠球菌血流感染的 ECMO 患者诊疗过程，为其制订了个体化的抗感染治疗方案并取得了良好的效果；临床药师将药学理论与临床实践相结合，从临床诊断、药物合理选择及治疗方案调整等方面提出合理建议，使患者感染得到控制；临床药师的参与，促进了临床合理用药，对患者治疗起到了积极作用。

二代测序技术在皮肌炎并发肺部感染患者中的作用：1 例报告

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目的 本研究旨在评估支气管肺泡灌洗液二代测序技术在皮肌炎并发肺部感染中的诊断效能。我们着重探讨该技术在诊断上的准确性和应用价值，特别关注其在致病菌鉴定方面的作用，并探讨其在临床实践中的潜在应用。

方法 对一例皮肌炎合并肺部感染患者的支气管肺泡灌洗液样本进行二代测序分析，确定致病菌，并评估其与临床表现的关联。

结果 一位 24 岁的年轻男性因呼吸困难已持续一周，并在最近一天情况加重而入院。 患者既往皮肌炎病史 1+ 年，长期口服“硫唑嘌呤 + 硫酸羟氯喹 + 甲泼尼龙 + 托法替布”。入院时，胸部 CT 检查显示双肺散在的斑点、结节和片絮状密度增高影，部分表现为实变影，并伴有部分呈现“树芽征”，且胸膜邻近区域出现增厚，初步考虑为多系感染性病变。血液常规检查显示白细胞计数（主要为中性粒细胞）、CRP 和 ESR 均明显升高。经过经验性的头孢哌酮舒巴坦联合伏立康唑治疗后，患者治疗反应不佳。我们采集了肺泡灌洗液（BALF）进行细菌、真菌培养及药敏、tNGS 检查、结核杆菌 DNA 检查、G 试验以及 GM 试验。微生物培养结果、结核杆菌 DNA 检查、G 试验以及 GM 试验均呈阴性，然而，tNGS 检测却发现了 4973 条耶氏肺孢子菌序列。鉴于此结果，我们修订诊断为耶氏肺孢子菌肺炎，并调整了治疗方案，口服复方磺胺甲噁唑片 0.96g tid 并且首剂加倍抗感染治疗。治疗 8 天后再次复查 CT 发现病灶明显吸收，患者症状基本改善。

结论 本病例凸显了支气管肺泡灌洗液二代测序技术在皮肌炎并发肺部感染诊断中的关键作用，尤其在不常见病原体鉴定方面。二代测序技术为临床提供了更精准的诊断工具，为患者个体化治疗和管理带来新的机遇。

宜春市人民医院感染 CRKP 患者的预后数据分析

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目的 通过对宜春市人民医院 CRKP 定植 / 感染患者的各项因素分析，及其感染患者的死亡因素分析。以减少抗生素的滥用，并对患者做出较准确的预后评估。

方法 采用回顾性病例对照研究 , 收集 CRKP 患者的临床信息，（1）一般资料：性别、年龄、住院时间、APACHE Ⅱ评分、查尔顿共病指数评分、SOFA 评分、D- 二聚体、皮特评分等。（2）可能易感染因素统计：喹诺酮类、碳青霉烯类、第三代头孢菌素等药物的使用、肠外营养 > 48 h、免疫抑制 / 类固醇类的使用、既往一年内 KP 定植 / 感染、既往一年与其他多耐药定植 / 感染等。

结果 经过病例回顾性查找分析，共找到感染或者定植 KP 患者 409 例。 经筛选排除后，确定感染 / 定植 CRKP 患者共 48 例，其中感染患者 26 例，定植患者 22 例。通过独立样本 T 检验对年龄≥ 60 岁等 22 项 CRKP 可能易感危险因素进行研究分析。结果显示：使用碳青霉烯类药物等 10 项为我院 CRKP 易感危险因素。感染患者中死亡患者 16 例，存活患者 10 例。对死亡因素进行分析，结果显示：免疫抑制或类固醇类使用等 3 项内容是医院导致 CRKP 感染患者死亡的危险因素。

结论 医务人员应减少对患者进行有创操作，必须严格执行无菌操作；对入院患者根据病情进行准确快速评估预测，减少盲目性的经验用药，实现抗菌药物的针对性治疗，及时调整抗菌药物种类，减少患者入院时长以及抗生素等药物的使用时长，从而降低 CRKP 的感染率和病死率。

感染

临床药师参与 1 例毗邻颗粒链菌菌血症合并化脓性脑膜炎患者抗感染治疗的药学实践

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目的 探讨临床药师在毗邻颗粒链菌菌血症合并化脓性脑膜炎患者抗感染治疗和监护中的作用。

方法 临床药师以患者的临床疗效和安全性为切入点，结合患者的病情和抗菌药物药代动力学 / 药效学特点协助医师制定合理的抗感染治疗方案及药学监护。

结果 在临床药师与医师共同协作下，患者得到了有效治疗，及时发现并处理了相关不良反应。

结论 临床药师通过发挥自己的专长，协助医师优化抗感染治疗方案，促进了临床合理用药，保障了患者安全。

耶氏肺孢子菌肺炎诱发哮喘急性发作 1 例

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目的 报道非 HIV 免疫功能正常宿主感染耶氏肺孢子菌肺炎（PJP）可诱发支气管哮喘的罕见病例以提高对肺部感染疾病的诊治准确性。

方法 回顾分析一位 20 岁非 HIV 免疫功能正常的宿主确诊感染耶氏肺孢子菌肺炎经规范治疗后诱发哮喘急性发作的临床资料。

结果 患者系 20 岁男性因发热、咳嗽咳痰、呼吸困难及皮疹 1 月入院，无支气管哮喘史。外院多种抗生素治疗无效，入院后 CT 示两肺见小斑片状毛磨玻璃影。对症平喘，抗炎抗过敏，万古霉素抗感染治疗后临床症状缓解，但胸部 CT 复查示两肺下叶磨玻璃影增多。GM 试验、曲霉菌抗体、念珠菌检测均阴性，支气管灌洗 mNGS 检测发现耶氏肺孢子菌序列，最终确诊为 PJP。规范使用磺胺甲噁唑，泼尼松治疗后症状明显改善，但出院后因受凉再次出现气促呼吸困难，血嗜酸性粒细胞增高，CT 示肺部病灶吸收，支气管舒张试验阳性。诊断支气管哮喘，予甲泼尼龙、布地奈德联合治疗，复查 mNGS 未见耶氏肺孢子菌，患者病情好转出院，随访半年无哮喘再发。

结论 非 HIV 免疫功能正常宿主出现咳嗽呼吸困难，但胸部 CT 表现轻时应警惕 PJP，早期 mNGS 检测助于早期诊断。若规范治疗 PJP 出现哮喘症状及血嗜酸性粒细胞增高，应排除其它嗜酸性粒细胞相关肺病，重视 PJP 诱发支气管哮喘的可能。

Mycobacterium paragordonae pulmonary disease with rapidly growing solitary lesions: a case report and literature review

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Abstract Content Mycobacterium paragordonae (MPG) is a novel and uncommon nontuberculous mycobacterium (NTM). We describe a case of MPG pulmonary disease (MPGPD) with a single pulmonary mass growing rapidly, which has rarely been reported.

Methods A routine chest CT scan of a 66-year-old woman revealed a rapidly growing solitary mass-like lesion in the upper lobe of the right lung, which was not seen in the previous chest CT scan six months ago. H&E staining of the CT-guided percutaneous lung tissue biopsy showed chronic inflammatory changes with epithelioid granulomas. MPG was identified in a lung tissue biopsy by metagenomic next-generation sequencing (mNGS), with a sequence number of 1617 and a confidence level of 99%. Because the following MPG droplet digital PCR (MPG-ddPCR) test result of the lung tissue biopsy was positive, the patient was eventually diagnosed with MPGPD. The patient was administered clarithromycin, levofloxacin, rifampicin, and ethambutol in a quadruple oral regimen according to the ATS/IDSA protocol for Mycobacterium gordonae (MG) infection.

Results The chest CT scans showed that the lesion was significantly reduced one month after the treatment and almost completely disappeared four months later.

Conclusion MPGPD is a rare NTM infection. The imaging manifestation of MPGPD is diverse, even in rapid development, and it should draw clinical attention. mNGS of a tissue biopsy can quickly diagnose MPG infection and is a good alternative to routine NTM microbial testing. The ATS/IDSA protocol for MG infection also applies to the feasible and effective treatment for MPG infection.

硫酸黏菌素不同给药方式治疗碳青霉烯类耐药革兰阴性菌所致肺部感染的临床应用分析

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目的 多黏菌素类药物是治疗碳青霉烯类耐药革兰阴性菌（CR-GNB）感染的重要选择，CR-GNB 引起的肺部感染给医疗带来巨大挑战，硫酸黏菌素临床应用尤其是在治疗肺部感染的循证数据有限，本研究旨在比较硫酸黏菌素不同给药方式治疗 CR-GNB 所致肺部感染的有效性和安全性。

方法 运用医疗信息管理系统，回顾收集 2022 年 1 月 -2023 年 12 月住院并首次应用硫酸黏菌素患者的基本信息和各项医疗指标。主要结局是抗感染疗效、微生物根除率及不良反应发生率，次要结局是 30 天全因死亡率及肺部感染相关死亡率。

结果 共纳入 176 名患者，其中静脉滴注（IV）组 61 例；雾化吸入（IH）组 59 例；联合（IV+IH）组 56 例，三组患者基线水平无明显差异。在有效性方面，三组患者抗感染疗效无显著差异（P=0.555），但在微生物根除率方面 IV+IH 组明显高于 IV 组（P=0.016）。次要结局中三组患者的 30 天全因死亡率相似（P=0.598），但在肺部感染相关死亡率方面 IV+IH 组显著低于两单药组（P=0.032）；在不良反应方面，三组患者的急性肾损伤发生率无显著差异（P=0.489）。

结论 虽然在抗感染疗效及全因死亡率方面三组结果相似，但 IV+IH 组在微生物根除率及肺部感染相关死亡率方面具有明显优势，并未增加急性肾损伤的风险。

基于 FAERS 数据库万古霉素在老年患者中的不良事件信号挖掘

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目的 通过分析美国食品药品监督管理局不良事件报告系统（FAERS）数据库，挖掘万古霉素在老年患者的不良 事件（ADE），为临床用药监护提供参考。

方法 收集 FAERS 数据库从 2004 年至 2022 年第 1 季度的 ADE 报告，使用 OpenVigil 2.1 数据平台，对 65 岁以上患者使用万古霉素的 ADE 进行预处理。采用报告比值比（ROR）法和比例报告比值 比（PRR）法对 ADE 进行挖掘与分析，获得发生频次及信号强度前 10 位的 ADE，并分析前 10 位的联合用药情况。

结果 以万古霉素为首要怀疑药品在 65 岁以上人群中的 ADE 报告共 2 221 份，检测到 ADE 信号 2 194 个，其中 445 个属于药物的不 良反应。按照发生频次排序，ADE 分别为药物超敏反应（313 例）、急性肾损伤（301 例）及发热（296 例）等。按照信号 强度排序，ADE 分别为禽流感（ROR = 4 312.79）、细菌性心包炎（ROR = 2 985.78）及假丝酵母菌脑膜炎（ROR = 1 658.77）。联合用 药中，前 3 位的药物分别为哌拉西林 / 他唑巴坦 151 例，庆大霉素 119 例及美罗培南 112 例。

结论 万古霉素在老年人应用时， 应警惕肾毒性、超敏反应及谷浓度，同时应注意联合用药对万古霉素不良反应发生的影响。

miR-223 Regulates FOXO1 Expression, Autophagy, and Im-mune Function in CD4+ T lymphocytes during Sepsis: ex-hibiting a potential application of small RNA (miR-223) in solving the immune imbalance during sepsis

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Abstract Content Immunosuppression is the main cause of the high mortality rate in patients with sepsis. The decrease in the number and dysfunction of CD4+ T lymphocytes play a pivotal role in the immunosuppressed state of sepsis, in turn affecting the development and prognosis of sepsis. With advances in sepsis research, autophagy has been shown to play an important role in the immune imbalance exhibited during sepsis and the immune function of T lymphocytes. In our previous work, we demonstrated the positive clinical value of circulating micro RNA (miR)-223 in the serum of patients with sepsis and its function as an early biomarker of sepsis.

Methods In this study, we modulate the expression of miR-223 in CD4+ T, via the transfection of a mimic or an inhibitor of miR-223 to establish cell models of miR-223 overexpression and knockdown, respectively. Levels of autophagy were monitored using a double-labeled lentivirus (mRFP-GFP-LC3) and electron microscopy, and western blot analysis was used to estimate the levels of autophagy-related proteins and FOXO1 in the two cell models after co-treatment with lipopolysaccharide (LPS) and siRNA against FOXO1.

Results We found that when the expression of miR-223 increased, FOXO1 expression decreased and autophagy increased; whereas, when FOXO1 expression was inhibited, autophagy decreased significantly in different cell models after LPS induction.

Conclusion Thus, this study proved that miR-223 participate in the regulation of LPS-induced autophagy via the regulation of FOXO1 expression in CD4+ T lymphocytes which shed a new light for the diagnosis and treatment of sepsis.

Efficacy and Safety of Eravacycline (ERV) in Treating Infections Caused by Gram-Negative Pathogens: A Systematic Review and Meta-Analysis

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Abstract Content Background Eravacycline (ERV) is a novel synthetic fluorocycline antibiotic with broad-spectrum antibacterial efficacy against Gram-negative pathogens (GNPs). This study sought to investigate ERV's effectiveness and safety in treating GNP infections.

Methods We conducted a comprehensive search of PubMed, Cochrane Library, Embase, Web of Science, and ClinicalTrials.gov up to September 2023. Included in the review were studies assessing the efficacy or safety of ERV in treating GNP infections. Efficacy outcomes encompassed clinical cure and microbiologic eradication, while safety outcomes included adverse events (AEs) and 30-day all-cause mortality.

Results This systematic review incorporated data from 1,597 patients across four controlled studies [three randomized controlled trials (RCTs) and one cohort study], six single-arm cohort studies, and two case reports. Meta-analysis outcomes demonstrated that there was no statistically significant difference between ERV and comparators in clinical cure (OR=0.84, 95% CI=0.59-1.19, P=0.43, I^2=0%), microbiologic eradication (OR=0.69, 95% CI=0.36-1.33, P=0.09, I^2=53%), and mortality (OR=1.66, 95% CI=0.81-3.41, P=0.21, I^2=34%). However, a significantly higher rate of AEs with ERV was observed compared to the control group (OR=1.55, 95% CI=1.21-1.99, P=0.41, I^2=0%). Additionally, cohort studies reported a clinical cure rate of 73.2% (88.8% in RCTs), an AE rate of 4.5% (38.3% in RCTs), and mortality of 16.2% (1.5% in RCTs). Patients in RCTs received ERV monotherapy, whereas almost half of the patients in cohort studies were treated with ERV in combination with other antibiotics. The outcome of treatment was related to the severity of the patient's illness.

Conclusion ERV exhibited promising safety and efficacy in patients with GNP infections. However, further studies are warranted to investigate the safety and efficacy of ERV monotherapy or combination therapy in critically ill patients.

咽峡炎后败血症（lemierre 综合征）个案报道并文献复习

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目的 探讨咽峡炎后败血症（Lemierre syndrome，LS 综合征）的诊断及治疗方法。

方法 报告 1 例 lemirre 综合征，并检索 2005~2020 年国内外相关文献，选取资料相对完整的文献 48 篇，对 lemirre 综合征患者的临床表现、实验室检查、辅助检查、治疗方式进行临床分析。

结果 本病例确诊为 Lemierre 综合征，采用静脉内抗菌治疗，患者恢复较好。

结论 临床医生在遇到不同症状的 Lemierre 综合征患者，需要及时准确的诊断这一综合征，以便迅速采取有效的治疗方法。

Clinical features and risk factors of Klebsiella pneumoniae infection in premature infants: a retrospective cohort study

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Abstract Content With the constantly advancing modern medical technology, the survival rate of premature infants has shown a significant increase. Klebsiella pneumoniae (K. pneumoniae) is one of the common pathogens causing neonatal infections. In particular, premature infants are at a serious risk of infection. We aimed to analysed the clinical characteristics, antibiotic susceptibility profiles, and treatment outcomes of K. pneumoniae infection in premature infants.

Methods We retrospectively compared cases of K. pneumoniae infection in premature and term infants admitted in a tertiary hospital from January 2017 to December 2022 in China. The clinical and microbiological characteristics were outlined. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS), with statistical significance defined as $P < 0.05$.

Results We enrolled 166 premature infants and 68 term infants. In premature infants, fetal distress, patent ductus arteriosus, acleistocardia, enteritis, anemia, hypoproteinemia, bacteremia, abdominal infection, mechanical ventilation, nasogastric feeding, drainage tube, parenteral nutrition, and prior exposure to carbapenem antibiotics were identified as the factors most significantly associated with K. pneumoniae infections through univariate analysis. Additionally, univariate analysis revealed that septic shock, bacteremia, abdominal infection, indwelling catheters, drainage tubes, parenteral nutrition, and previous exposure to glycopeptide antibiotics were significantly correlated with negative outcomes. Importantly, the independent risk factors for K. pneumoniae infections in premature infants were fetal distress (OR: 3.702, [95% CI: 1.056-12.986], P = 0.041), enteritis (OR: 4.434, [95% CI: 1.066-18.451], P = 0.041), anemia (OR: 4.028, [95% CI: 1.550-10.466], P = 0.004), bacteremia (OR: 0.221, [95% CI: 0.061-0.802], P = 0.022), mechanical ventilation (OR: 4.974, [95% CI: 1.685-14.685], P = 0.004) and prior exposure to carbapenem antibiotic (OR: 14.738, [95% CI: 2.393-90.767], P = 0.004). Finally, septic shock (OR: 0.180, [95% CI: 0.046-0.709], P = 0.014), abdominal infection (OR: 0.116, [95% CI: 0.027-0.500], P = 0.004), and indwelling catheters (OR: 0.130, [95% CI: 0.017-1.002], P = 0.050) were identified as positive predictors of negative outcomes in premature infants infected with K. pneumonia.

Conclusion Premature neonates were more susceptible to K. pneumoniae, exhibited heightened antibacterial resistance, and experienced unfavorable treatment outcomes. A multitude of distinct risk factors are associated with K. pneumoniae infections and adverse treatment responses in premature neonates. More attention should be paid to K. pneumoniae infections in the premature neonates.

113 例艾滋病相关淋巴瘤患者的治疗结局及影响因素

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目的 探究艾滋病相关淋巴瘤（acquired immunodeficiency syndrome related lymphoma，ARL）患者的临床治疗结局及其影响因素。

方法 回顾性分析云南省某传染病医院感染科 2018 年至 2022 年收治的 113 例 ARL 住院患者的流行病学资料、临床症状及体征、辅助检查资料、治疗情况及临床转归等，采用 Kaplan-Meier 法进行生存分析，采用 Cox 比例风险回归模型进行单因素及多因素分析，筛选可能影响患者治疗结局的因素。

结果 总共纳入了 113 名患者。大多数患者患有弥漫性大 B 细胞淋巴瘤（87 例，77%）、伯基特淋巴瘤（11 例，9.7%）和浆母细胞淋巴瘤（8 例，7%）。男性占 85%（96/113），年龄（39.5±11.7）岁。中位随访 46 个月，总体 2 年 PFS 和 OS 率分别为 50.50% 和 66.18%。临床表现以体表肿物、发热和腹痛为主。根据单因素分析和多因素分析的结果显示：男性、年龄、体能状态 (performance status, PS）评分、国际淋巴瘤预后指标（international prognostic index, IPI）评分、基线 CD4+ 淋巴细胞、Ann Arbor 分期、β-2 微球蛋白水平、中枢神经系统（CNS）浸润、存在机会性感染均与较差无进展生存期（progression free survival，PFS）有关，接受 cART 联合化疗发生疾病进展的风险要低于未接受的患者。PS 评分，Ann Arbor 分期、存在机会性感染和中枢神经系统（CNS）浸润与较差总生存期（overall survival，OS）有关。

结论 本研究显示了 ARL 患者的临床特征和治疗结局，并得出影响 OS 和 PFS 的预后因素。接受 cART 联合化疗可以延缓 ARL 进展，改善 ARL 预后。

流感相关肺曲霉菌病与新冠相关肺曲霉菌病临床特征及预后分析：一项多中心回顾性研究

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目的 侵袭性肺曲霉菌病是一种好发于免疫缺陷人群且致死性率高的真菌性疾病，严重病毒感染已被多项研究证实为 IPA 发病的高危因素，其中尤以流感相关肺曲霉菌病及新冠相关肺曲霉菌为著，但相关研究缺乏，本回顾性研究旨在分析两组患者临床特征、预后及死亡高危因素的差异

方法 收集从 2018 年 1 月至 2024 年 3 月于浙江大学医学院附属第一医院及浙江省杭州市临平区中西医结合医院的 IAPA 及 CAPA 住院患者的临床资料，分析并比较两组患者之间的临床特征及预后差异，同时应用 Logistic 回归分析探究患者死亡的风险因素

结果 基线数据上 IAPA 较 CAPA 患者慢阻肺比例更高 , 有器官移植病史低（p <0.05），患者病毒感染到继发曲霉菌感染病程更短。辅助检查上 CAPA 较 IAPA 组白细胞计数、中性粒细胞计数、淋巴细胞低。总治疗病程中 CAPA 组抗病毒药物疗程、抗生素疗程、激素疗程、住院时间更长，激素使用比例及总量更高。并发症上 CAPA 相比 IAPA 组合并细菌感染、新发下肢深静脉血栓、消化道出血、心功能衰竭比例高。CAPA 组死亡率更高，中位生存时间为 108 天，IAPA 的生存曲线优于 CAPA，相较于好转组，在死亡高风险因素上，多因素 Logistic 回归分析发现基础 SOFA 评分高为 IAPA 死亡的危险因素（OR = 1.479；95%CI: 1.035-2.114；p = 0.032），确诊时呼吸衰竭为 CAPA 死亡的危险因素（OR = 4.942；95%CI: 1.305-18.713；p = 0.019）

结论 IAPA 组较 CAPA 组多合并基础肺病，起病急，确诊时 SOFA 评分高为 IAPA 患者死亡的危险因素，CAPA 相较 IAPA 患者多合并免疫功能不全，治疗时间长，易出现细菌感染、血栓形成、消化道出血等并发症，预后差，死亡风险高，确诊时存在呼吸衰竭为 CAPA 患者死亡的危险因素，1 周后 SOFA 评分变化可有助于预测 IAPA 及 CAPA 预后。

tNGS 对高毒力肺炎克雷伯杆菌感染的诊断价值分析

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目的 高毒力肺炎克雷伯菌（highly virulent Klebsiella pneumonia，hvKP），具有严重的侵袭性，可引起肝脓肿、眼内炎和骨髓炎等临床病症，且病情进展迅速凶险。近年来，hvKP 感染的发生率逐年上升，该型菌株属于临床高度关注的重点菌株。但目前耐药的 hvKP 在临床分布情况还不太明确，通过病原多重扩增靶向测序技术（tNGS）对临床感染样本 KP 类型进行相关分析。

方法 选取本单位 2023 年 6 月 -12 月检出 hvKP 的 76 例样本进行相关分析，分析其检出毒力基因类型，以及耐药基因检出情况。

结果 76 例检出 hvKP 的样本中肺泡灌洗液 63 例，痰液 13 例，其中毒力因子类型：ybt-64 例（84.21%），clb-17 例（22.37%），iroN-7 例（9.21%），all-7 例（9.21 %），fep-1 例（1.3%）。其中含 hvKP 的样本检出 48 例（63.16%）含超广谱 β 内酰胺酶（extended-spectrum β -lactamases, ESBLs）的耐药基因，具体分布情况如下：TEM-39 例（51.32%），SHV-25 例（32.89%），检出 OXA-20 例（26.32%），检出 CTX-M-9 例（11.84%）；hvKP 检出耐碳青霉烯的基因 KPC-27 例（35.53%）。其中检出含耐药基因的 hvKP 有 54 例（71.05%），检出 2 种以上耐药基因的 hvKP 有 42 例（55.26%）。

结论 从本次分析的数据来看 hvKP 中含有耐药基因的菌株占比达到 71.05%，高毒力且广谱耐药的出现会大大增加临床治疗难度，早期发现并干预将有助于临床诊疗。相比于传统检测方法 tNGS 对于临床 KP 耐药基因和毒力基因检测有一定优势，能够为 hvKP 的研究、监测以及临床诊疗提供及时、准确的病原学诊断依据。对于耐药和毒力基因的类型可能根据相应的检测范围会存在一定的偏向性，仍需要更全面、更深入的研究。

Optimizing Antimicrobial Strategies and Prognosis Prediction in Corticosteroid-Sensitive Diffuse Parenchymal Lung Diseases with Negative mNGS Results

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Abstract Content Background Timely adjustments of antibiotic and corticosteroid treatments are vital for patients with diffuse parenchymal lung diseases.

Methods A total of 41 DPLD patients with negative mNGS results who were responsive to corticosteroids were enrolled.

Results Among those patients, about 26.8% suffered from drug-induced DPLD, while 9.8% presented autoimmune-related DPLD. The complete antibiotics administration profiles of 34 patients before and after the negative mNGS results were compared and 79.4% patients (27/34) discontinued antibiotics. Moreover, 27 exhibited a reduction in the variety of antibiotics used, 4 remained unchanged, and 3 showed an increase. Negative mNGS results could contribute to the antibiotic de-escalation in the corticosteroid-responsive DPLD patients in one day. Besides, all the patients enrolled in our study timely commenced corticosteroid administration and increased the dosage of the medication following negative mNGS results. The high detection rate of Pseudomonas, Corynebacterium, Staphylococcus, and Stenotrophomonas as well as the low detection rate of Porphyromonas have been confirmed in patients with Oxygenation Index (OI, SpO_2/FiO_2) below 300 compared with patients with OI above 300. In addition, a higher abundance of Escherichia and Stenotrophomonas but a lower abundance of Streptococcus was observed in patients with pleural effusion as opposed to those without such a condition. Those differential microbiota results might be clinically meaningful in assessing the variation in OI and the emergence of pleural effusion.

Conclusion In summary, our findings demonstrated the clinical significance of mNGS in assisting the antibiotic and corticosteroid treatment adjustment in corticosteroid-responsive DPLD. Lung microbiota may imply the severity of the disease.

某院 360 例氨基糖苷类抗感染药物合理用药分析

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目的 分析某院氨基糖苷类抗感染药物在住院患者中的使用情况，促进临床合理用药。

方法 回顾性分析某院 2023 年 1 月 1 日 ~2023 年 6 月 1 日期间全身性使用氨基糖苷类抗感染药物的住院患者的人口学资料、给药情况、病原学检查、联合用药情况、用药不良反应等，并进行统计分析。

结果 该院共有 360 例患者在此期间全身性使用氨基糖苷类抗感染药物，包括阿米卡星、依替米星和庆大霉素。其中男 251 例，女 109 例，年龄平均 69.1 岁。该类药物主要用于治疗革兰阴性菌感染，且多与 β－内酰胺类药物合用（42.53%），治疗用药有效率为 91.09%。共有 25 例患者用药后血肌酐较前明显升高（6.94%）。

结论 该院对全身性使用氨基糖苷类抗感染药物的临床应用总体较为合理，但仍存在用药剂量不精确、联合用药不合理等问题，应当在 TDM 的指导下合理用药，并且在用药期间密切关注肾功能相关指标的变化。

类器官共培养模型的研究进展

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目的 类器官是源自干细胞的自组织三维培养物，可模拟器官的生理结构、细胞组成，并在一定程度上模拟其功能。

方法 然而，类器官有缺乏血管化结构、缺乏免疫细胞、器官系统化程度低等局限性，限制了类器官研究的进一步发展。共培养技术是将多种细胞共同培养于同一环境中，能更好地反映机体生理或病理真实状态，有助于突破类器官研究壁垒。

结果 目前，类器官共培养无论在技术和模型类型方面都有较大的研发进展，类器官与免疫细胞共培养、类器官血管化及多体系类器官共培养等共培养模型能突破传统模型瓶颈，为研究机体生理或疾病发生机制提供新的方向。

结论 本文主要对类器官的研究现状、类器官共培养模型及共培养技术等方面进行综述，为后续研究提供一定参考。

Optimizing Pharmacokinetics: Insights into Antimicrobial Agents in the Elderly Population

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Abstract Content The global elderly population is on the rise, and infections tend to have a higher mortality rate among older individuals.

Methods Aging is associated with the progressive impairment of multi-organ function, which can impact the pharmacokinetics of antimicrobials, potentially leading to the failure of anti-infective therapy.

Results With the increasing life expectancy, a significant growth in the elderly demographic, and the escalating costs of healthcare, gaining a thorough understanding of pharmacokinetic changes in the elderly holds crucial clinical significance.

Conclusion This review compiles findings from published studies, offering a comprehensive overview of the pharmacokinetics of various antimicrobials in both adults and the elderly. Furthermore, it delves into advancements in pharmacokinetic methods specific to the elderly population.

1 例慢性阻塞性肺疾病急性加重伴肺部感染患者药源性血小板减少症的药学监护

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目的 旨在通过分析临床药师参与的一例慢性阻塞性肺疾病急性加重伴肺部感染患者发生药源性血小板减少症的治疗过程，研究评价药物与血小板发生的关联性及治疗过程。

方法 通过对多个数据库的系统检索和广泛查找文献数据库，深入分析此病例中抗菌药物应用与发生药源性血小板减少的关联性及相关危险因素，为临床医生提供药学监护要点。

结果 结合患者的查体、检验检查、病史和症状等多方面信息，对该患者药源性血小板减少的个体化治疗方案进行了临床分析和制定整体药学监护计划。医生采纳临床药师的建议并付诸实践，患者药源性血小板减少得到改善。

结论 利奈唑胺联合头孢哌酮舒巴坦可共同致药源性血小板减少症，通过及时调整用药方案可明显的减轻和改善患者的症状和病情。在治疗过程中，临床药师的参与起到了积极的作用，协助医生制定了更加个体化的治疗方案，为患者的安全、有效和合理用药提供了有力的支持。

噬菌体与抗生素联合清除细菌生物膜的研究进展

付观双
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目的 随着多重耐药细菌引起的感染威胁的出现，噬菌体疗法已被重新考虑作为治疗由顽固病原体引起的感染的替代方法。噬菌体－抗生素协同治疗法发展尤为迅速。

方法 近年来，越来越多的研究者意识到细菌生物膜感染的危害和其给医疗领域带来的挑战，并为此做出了许多关于将噬菌体与抗生素联合治疗细菌生物膜感染的疗效、机制研究。

结果 本文综合评述了不同菌属的细菌生物膜感染对联合治疗响应的研究进展，包括治疗组合的选择和药物剂量的优化等。

结论 此外，文章还汇总了当前关于该联合疗法作用于各菌属生物膜感染的机制性见解，以期为未来相关领域的研究提供宝贵的信息，并促进新型治疗策略的开发。

亚胺培南 / 瑞来巴坦和 ceftolozane/tazobactam 对肠杆菌目细菌、铜绿假单胞菌的抗菌活性：SMART 2020~2021

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目的 亚胺培南 / 瑞来巴坦（IMI/REL）和 ceftolozane/tazobactam（C/T）是两种组合抗菌药物，主要用于治疗复杂性泌尿、腹部以及医院获得性肺炎感染。本研究旨在探讨 IMI/REL 和 C/T 对肠杆菌目细菌和铜绿假单胞菌（PA）及其耐药菌的体外抗菌活性。

方法 2020~2021 年，从中国 18 家医院收集临床分离的肠杆菌目细菌和 PA，标本来源包括腹腔、尿路、下呼吸道和血流。使用由 IHMA 自制的抗菌药物被板测定最低抑菌浓度，依据 CLSI M100 33th 进行药敏判定。产超广谱 β - 内酰胺酶肠杆目细菌（ESBL-E）定义是对头孢曲松不敏感且对碳青霉烯类均敏感。IMI-R 菌株定义是对 IMI 耐药的分离菌株。

结果 2020~2021 年共检出 5461 株非重复 GNB，其中大肠埃希菌（EC）、肺炎克雷伯菌（KP）、铜绿假单胞菌（PA）的检出率分别为 29.8%、26.7%、15.1%。ESBL-E 有 1290 株，IMI-R-E 有 632 株（图 1）。在所有菌株中，IMI/REL 是较 C/T 和 IMI 活跃的抗菌药物，对肠杆菌目细菌的敏感率为 91.3%。对 EC、KP 和阴沟肠杆菌均具有很高的抑制力（95.3%，87.8%，80.7%）。在 ESBL-E 中，C/T 对其抑制力为 84.7%（图 2A）。同样，IMI/REL 和 C/T 对 PA 均显示了 >75.7% 的抑制活性，而对特殊耐药 PA 的活性在 24.4%~72.1%（图 2B）。

结论 IMI/REL 对所有肠杆菌目细菌是一种很好的治疗选择，而 C/T 在针对 ESBL-E 感染时表现突出。两药对各 PA 活性良好且不存在完全的交叉耐药。故 IMI/REL 和 CT 可成为治疗 ESBL-E、IMI-R-E 及 PA 的潜在药物选择。

EBV-LPDs 患者免疫紊乱及早期诊断预测指标研究

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目的 EBV 相关淋巴组织增殖性疾病 (EBV-associated lymphoproliferative diseases，EBV-LPDs) 包括 B、T 和 NK 细胞来源的疾病，这些疾病预后差且早期诊断具有挑战性。本研究旨在通过比较 EBV 相关传染性单核细胞增多症（EBV-IM）和 EBV 相关淋巴组织增殖性疾病（EBV-LPDs）患者的血液学参数、淋巴细胞亚群、细胞因子和血浆病毒载量等水平，评估两组患者的免疫功能状态和炎症水平，探索可早期识别 EBV-LPDs 的生物标志物，并通过 ROC 曲线确定这些标志物的截断值，评估其在 EBV-LPDs 早期诊断中的价值。

方法 本研究对 EBV-IM 和 EBV-LPDs 患者的血液学参数、淋巴细胞亚群、细胞因子和血浆病毒载量进行了分析和比较，评估患者的免疫功能状态和炎症水平。使用 ROC 曲线确定生物标志物的截断值，并通过 Logistic 多因素分析评估这些标志物在 EBV-LPDs 早期诊断和预后中的作用。

结果 1. 免疫紊乱是 EBV 感染转化为恶性疾病的核心环节。

2. 慢性活动性 EBV 感染、EBV 相关噬血细胞综合征和 EBV 相关淋巴瘤等恶性淋巴增殖性疾病表现出高炎症水平、免疫失控以及固有免疫与适应免疫失衡的特征。

3. EBV-LPDs 患者的外周血 EBV 核酸载量通常更高，NLR、SII、CRP 等炎症标志物的升高在预测 EBV 感染向恶性疾病转化方面具有良好的诊断和预测效能。

4. Logistic 多因素分析表明，纤维蛋白原水平升高是成人 EBV-LPDs 患者短期死亡的独立危险因素。

结论 EBV-LPDs 患者表现出显著的免疫紊乱和高炎症水平。NLR、SII、CRP 等炎症标志物在诊断和预测 EBV 感染向恶性疾病转化中具有重要价值。纤维蛋白原水平升高是成人 EBV-LPDs 患者短期死亡的独立危险因素。这些发现为 EBV-LPDs 的早期诊断和预后评估提供了潜在的生物标志物。

持续炎症刺激下耐受型树突状细胞的细胞模型

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目的 本研究旨在开发一种新的体外细胞模型以模拟慢性炎症条件下产生的耐受型树突状细胞(tolerogenic DCs, tolDC)。

方法 我们通过将骨髓来源的树突状细胞暴露于亚致死脂多糖 (LPS, 100 ng/mL) 72 小时，同时细胞活力不受影响的情况下，成功构建了 tolDC (LPS-tolDCs) 模型。 IL-10 诱导的 tolDC（IL-10-tolDC）是既往研究中经典的 tolDC 模型，因此我们也比较了 LPS-tolDC 和 IL-10-tolDC 之间免疫耐受性的异同。

结果 我们的研究结果表明，LPS-tolDC 和 IL-10-tolDC 均表现出成熟标记物 MHC II, CD86 表达减少，而抑制标记物 PD-L1 水平升高。 此外，LPS-tolDC 和 IL-10-tolDC 的免疫调节活性是相当的。免疫功能障碍包括抗原呈递能力受损以及 T 细胞活化、增殖和分化受到抑制。与 IL-10-tolDC 相比，LPS-tolDC 在接受刺激后的成熟度和细胞因子产生方面表现出较低的反应，因此 LPS-tolDC 是一个较为理想的 tolDC 研究模型。

结论 总之，长期暴露于 LPS 可以有效诱导 tolDC 产生，使其无法获得进一步成熟、细胞因子产生和正常的抗原呈递能力。此外，两种细胞模型在刺激下诱导成熟和细胞因子分泌能力受损，LPS-tolDCs 可能是比 IL-10-tolDCs 更好的研究 tolDCs 的模型。 这些发现表明，靶向 LPS-tolDC 可能是逆转脓毒症引起的免疫抑制的一种有前途的治疗方法。

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相关因素，以此构建在线列线图预测模型并进行验证。

方法 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多因素 logistic 回归模型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，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。使用 SMOTE 算法进行过采样处理，使正负样本比例为 1 ： 1，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、血红蛋白、血尿素氮、脓肿大小和序贯性器官功能衰竭评分（ SOFA ）。多因素 logistic 回归模型结果显示，空腹血糖、血红蛋白、血尿素氮、脓肿直径、SOFA 评分为糖尿病合并肺炎克雷伯菌肝脓肿患者发生侵袭综合征的相关因素。训练集中 ROC 的曲线下面积为 0.966，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，灵敏度为 79.6%，特异度为 88.9%。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 IKPLAS 有较好的临床净收益。

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相关因素，基于此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。

奥马环素治疗急性细菌性皮肤和皮肤软组织感染的疗效和安全性：随机对照试验的系统评价和荟萃分析

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目的 依据现有临床研究，系统评价奥马环素治疗急性细菌性皮肤和皮肤结构感染（ABSSSIs）的疗效和安全性

方法 计算机检索 PubMed、Embase、Cochrane Library 和 Clinical Trials.gov 等，检索时限到 2023 年 6 月。仅纳入奥马环素与对照药物比较治疗成人 ABSSSIs 的随机对照研究（RCT），对符合纳入标准的临床研究进行资料提取和评估方法学质量后，采用 Rev Man 5.3 统计软件对结果进行分析

结果 共纳入 4 篇 RCT，合计 1742 例患者。在 mITT 和 CE 人群中，奥马环素组和利奈唑胺组的 ECR 相似。在 EOT 的 mITT 人群分析和在 PTE 的 CE 人群分析中，奥马环素的临床成功率高于利奈唑胺（$P < 0.05$）。在 PTE 的 mITT 人群分析和在 EOT 的 CE 人群分析中，奥马环素与利奈唑胺的临床成功率相当。在 PTE 的 micro-mITT 人群中的亚组分析显示，在金黄色葡萄球菌、MSSA、MRSA、化脓性链球菌和粪肠球菌引起的 ABSSSIs 患者中，奥马环素和利奈唑胺的临床成功率相当。在 EOT 的 ME 人群和 micro-mITT 人群以及在 PTE 的 micro-mITT 人群，奥马环素和利奈唑胺的微生物根除率相当。但在 PTE 的 ME 人群，奥马环素微生物根除率高于利奈唑胺（$P < 0.05$）。两组患者之间的不良反应相当。特别注意，奥马环素总的胃肠道反应的发生率高于利奈唑胺组（$P < 0.05$）。

结论 奥马环素治疗成人 ABSSSIs（包括 MRSA）患者的临床疗效和微生物反应略高于利奈唑胺，耐受良好。因此，奥达环素是成人 ABSSSIs 患者抗生素治疗的合适选择。

替考拉宁在老年人群中的血药谷浓度监测结果及影响因素探讨

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目的 通过监测老年患者替考拉宁血药谷浓度（Cmin）水平及达标情况，探讨老年患者 Cmin 达标影响因素，为老年患者合理使用替考拉宁提供参考

方法 回顾性收集 2017 年 11 月 -2022 年 7 月陆军军医大学第一附属医院使用替考拉宁治疗的老年感染患者。统计老年患者替考拉宁 Cmin 的分布情况。根据起始负荷剂量分为高剂量组（≥ 10mg/kg）和低剂量组（< 10mg/kg），根据肌酐清除率（Ccr）将患者分为 Ccr>80mL/min、Ccr 30~80mL/min 及 Ccr<30mL/min 3 组，分析不同起始负荷剂量和不同 Ccr 组对替考拉宁血药浓度水平及达标情况的影响，并利用多重线性回归分析进一步探讨影响替考拉宁血药浓度的相关因素

结果 83 例老年患者监测替考拉宁血药浓度共 129 例次，平均 Cmin 为（17.76 ± 9.59）mg/L，其中 88 例次达到目标浓度。高剂量组较低剂量组可提高平均 Cmin（P < 0.001）。Ccr>80mL/min 组替考拉宁平均 Cmin 和超标率低于 Ccr < 30mL/min 组患者，差异均有统计学意义。多重线性回归分析显示，性别（B=-3.130，95%CI=-6.219~-0.042，P=0.047）、起始负荷给药剂量（B=31.251，95%CI=23.868~38.634，P<0.001）、Ccr（B=-0.064，95%CI=-0.105~-0.023，P=0.002）和总胆红素（B=-0.045，95%CI= -0.081~-0.009，P=0.016）是影响老年患者替考拉宁血药谷浓度的主要相关因素

结论 老年患者替考拉宁血药谷浓度个体差异大，在优化替考拉宁给药方案时应考虑起始负荷给药剂量、Ccr 和总胆红素水平因素的影响

替考拉宁治疗脓毒症患者的血药谷浓度与临床疗效和安全性的相关性分析

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目的 探讨脓毒症患者使用替考拉宁血药谷浓度（Cmin）达标情况与疗效和安全性的相关性，为临床合理用药提供参考。

方法 回顾性收集 2017 年 11 月 -2022 年 7 月陆军军医大学第一附属医院脓毒症患者使用替考拉宁治疗后的血药谷浓度达标情况、临床疗效及安全性。

结果 116 例脓毒脓毒症患者共监测替考拉宁 Cmin 169 例次。第 4 剂前和第 6 剂前 Cmin 平均值分别为（16.35 ± 10.05）mg/L 和（20.46 ± 10.27）mg/L，差异有统计学意义（P < 0.05）。第 4 剂前和第 6 剂前 Cmin ≥ 15 mg/L 的达标率分别为 43.97%（51/116）和 62.26%（33/53），差异无统计学意义（P=0.226）。116 例患者临床有效率 85.34%，不良反应发生率 6.03%。75 例目标性治疗患者共检出 90 株 G+ 菌，临床总有效率 86.67%，细菌清除率 87.78%，不良反应发生率 6.67%。目标性治疗中按 Cmin 达标情况分为达标组和未达标组，两组的临床总有效率分别为 93.18%（41/44）和 77.42%（24/31），细菌总清除率分别为 92.98%（53/57）和 78.79%（26/33），差异均有统计学意义（P < 0.05）；不良反应发生率分别为 4.55%（2/44）和 9.68%（3/31），差异无统计学意义（P > 0.05）。按替考拉宁起始负荷剂量分为高剂量组和低剂量组，两组的临床总有效率分别为 97.06%（33/34）和 78.05%（32/41），细菌总清除率分别为 97.73%（43/44）和 78.79%（36/46），差异均有统计学意义（P < 0.05）；不良反应发生率分别为 5.88%（2/34）和 7.32%（3/41），差异无统计学意义（P > 0.05）。

结论 替考拉宁在治疗脓毒症 G+ 菌感染时疗效好，安全性较高。替考拉宁起始负荷剂量及 Cmin 与临床疗效呈正相关，且未导致不良反应增加。

3 例鹦鹉热衣原体重症肺炎临床特征及诊治特点

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目的 分析鹦鹉热衣原体重症肺炎患者的临床特征和诊治方法，提高对该病的认识。

方法 回顾性分析某院 2020 年 9 月 -2022 年 9 月经肺泡灌洗液宏基因组学二代测序技术（metagenomic next-generation sequencing, mNGS）诊断的 3 例鹦鹉热衣原体重症肺炎患者的临床资料，总结该病的临床特征及诊治要点。

结果 3 例患者中男性 1 名，女性 2 名，平均年龄 70 岁，平均住院时间 33 天，均以高热起病，伴有不同程度的咳嗽、咳痰、喘息、肌肉酸痛及意识障碍表现，其中 2 例患者有鸽子接触史。实验室检查 2 例患者血象 WBC 计数正常，3 例患者炎症指标 CRP、PCT 及铁蛋白水平均显著升高，2 例患者出现不同程度的肝肾功能损害，2 例患者出现意识改变，3 例患者凝血功能均有不同改变，3 例患者肺泡灌洗液 mNGS 检测，均检测出鹦鹉热衣原体，肺部影像病变以单侧肺部病变为主，均表现为肺斑片状实变影伴支气管充气征改变，3 例患者均出现不同程度的呼吸衰竭，氧合指数为 51-62mmHg，需行气管插管机械通气，给予多西环素、替加环素等治疗后，所有患者均治疗好转出院。

结论 鹦鹉热衣原体重症肺炎通常表现为严重呼吸衰竭，伴多脏器功能障碍，对患者支气管肺泡灌洗液进行 mNGS 检测能快速准确诊断。早期给予多西环素等四环素类药物治疗效果明显。

不同乳杆菌对脓毒血症保护作用

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目的 脓毒血症是由宿主对感染反应失调引起的危及生命的器官功能障碍炎症性疾病，导致全球每年 500 万人死于该病，是全球重症监护病房主要的死亡原因。虽然抗感染、器官保护和液体复苏等治疗方法用于改善脓毒症，然而疗效有限， 所以迫切需要获得脓毒症治疗的新见解。肠道微生物群可作为人体的第一道防线抵抗外来病原体的入侵，不仅与消化吸收密切相关，还起着重要的免疫调节作用。肠道微生物疾病与许多疾病密切相关，如溃疡性结肠炎、炎症性肠病、自身免疫性疾病、脓毒血症等。在脓毒血症期间，致病微生物的过度生长，肠道菌群紊乱，破坏菌群平衡，进而恶化脓毒症的发展。有很多方法恢复肠道微生物平衡，而益生菌被广泛使用。益生菌是一种活的微生物，通常定植于在人或动物的肠道中，可以与宿主细胞或肠道菌群相互作用，调节人体免疫反应，有益于人体健康。据报道，补充益生菌后可重建肠道菌群，恢复菌群平衡，可减轻肺部、肾脏等炎症。我们从酸菜中分离了乳杆菌，本研究旨在探讨不同乳杆菌（腐败乳杆菌、植物乳杆菌、短乳杆菌）对脓毒血症小鼠的治疗作用。

方法 我们予以 6 周龄 C57 小鼠行不同乳杆菌和 PBS 各 120ul 灌胃 14 天，送检粪便行 16sRNA 测序和代谢组，后行盲肠结扎穿刺构建小鼠脓毒血症模型，72 小时通过组织学染色评价肝、肾、脾、小肠及结肠等脏器损伤，检测血清 IL-1β、IL-6、TNF-a、GSH、MDA、TEAC 水平，检测结肠壁通透性及 claudin1、occludin、ZO-1 水平。

结果 研究结果表明乳杆菌可增加肠道菌群丰富度和厚壁菌门 / 拟杆菌门比值，显著降低败血症的死亡率，减轻脓毒血症小鼠的炎症反应和氧化应激水平，保护脓毒血症引起的器官损伤。降低肠壁通透性，上调 claudin1、occludin 连接蛋白表达。

结论 因此，饮食中补充乳杆菌，可以减轻脓毒血症症引起的器官损害，且腐败乳杆菌和植物乳杆菌效果优于短乳杆菌。

Polymyxin B resistance rates in carbapenem-resistant Pseudomonas aeruginosa isolates and a comparison between Etest ® and broth microdilution methods of antimicrobial susceptibility testing

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Abstract Content Background Polymyxin B has been considered to be the last line of defense for life-threatening infections caused by multiple drug resistant gram-negative pathogens, including carbapenem-resistant Pseudomonas aeruginosa (CRPA).

Methods Objective and methods The present study analyzed CRPA resistance to polymyxin B in the Suzhou district of China. Additionally, polymyxin B resistance rates were compared in different parts of the world to determine global trends. The present study also assessed the reliability and effectiveness of the Etest ® in a clinical setting, as laboratories lack a reliable and efficient susceptibility test for polymyxin B.

Results The susceptibility rate of polymyxin B reached 96.0%, which is in accordance with results obtained from the United States of America, Europe, Africa and the majority of Asian countries. However, the rate of polymyxin B non-susceptibility (resistant or intermediate) in Singapore is 0.53 (95% confidence interval, 0.12-0.93). In addition, the susceptibility rate of polymyxin B determined via Etest ® was not significantly increased compared with that determined via broth microdilution (98.0 vs. 96.0%; P=0.558). Essential and categorical agreement rates reached 98.0%.

Conclusion In conclusion, the polymyxin B resistance rate of CRPA isolates is relatively low in the majority of countries, with the exception of Singapore. Furthermore, Etest ® may be a reliable clinical method for the measurement of polymyxin B resistance in CRPA isolates.

新型冠状病毒感染患者炎症指标及细胞因子检测的临床价值

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目的 自 SARS-CoV-19 感染以来，已经开发了各种用于诊断 COVID-19 的检测试剂盒和测试，然而，上述方法只适合用于诊断。本文旨在通过观察及分析患者多种血液学指标的变化，为临床早期识别危重症患者提供依据。

方法 选取 2022 年 12 月 ~ 2023 年 02 月江苏大学附属人民医院收治的 74 例 COVID-19 患者，确诊病例及分类标准均符合国家卫生健康委员会发布的《新型冠状病毒感染诊疗方案（试行第十版）》，对入院 24 小时内空腹状态下采集的静脉血进行检测，检测指标包括炎症指标、细胞因子等，采用 IBMSPSS26.0 软件，通过 Mann-Whitney 检验分析，分析其与临床特征的相关性。

结果 结果发现普通组患者的 PCT、IL-6、中性粒细胞计数水平明显低于重症组，淋巴细胞计数、CD4+T、CD8+T 计数明显高于重症组，差异均有统计学意义。建立 logistic 回归分析及该指标对患者的受试者工作特征曲线（ROC），表明中性粒细胞、IL-6、D- 二聚体及中性粒细胞 / 淋巴细胞对重症组患者均有诊断价值，且联合诊断的价值最高。

结论 综上所述，IL-6、中性粒细胞、D- 二聚体及中性粒细胞 / 淋巴细胞在 COVID-19 患者的病情评估中都发挥了一定作用，根据联合诊断模型数据分析，对患者进行疾病严重程度评估时，对多项指标的数值变化综合分析，能更加合理且准确的预测，并制定更为规范且个体化的诊疗方案。

鄞州地区结核患者营养风险和营养指标调查分析

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目的 评估鄞州地区结核患者营养状况，为后续营养干预提供参考依据。

资料 选取 2023 年 5 月 -2024 年 4 月浙江省宁波市鄞州区传染病质控中心首次确诊肺结核患者 260 例。

方法 对肺结核患者的营养状况进行筛查、评估，并同时进行空腹血常规、血生化指标检测。

观察指标：①营养风险筛查评估表 (NRS-2002) 评分：NRS-2002 主要包括 3 个部分：疾病严重程度评分（0 ~ 3 分）、营养状态受损评分（0 ~ 3 分）、年龄评分（0 ~ 1 分）。②客观指标评价：包括体表指数（BMI）、前白蛋白、白蛋白、淋巴细胞计数、血红蛋白（Hb）。

结果 一、营养风险筛查：

本次调查对象中，NRS-2002 ＜ 3 分者 95 例，占比 36.54%；NRS-2002 ≥ 3 分者 165 例，占比 63.46%。疾病严重程度评分占比 23.08%（60/260）、营养状态受损评分占比 69.23%（180/260）、年龄评分占比 58.47%（152/260）。通过患者户籍追踪进一步分析，发生营养不良风险人群来自广西及云南、贵州山区居多。

二、客观指标评价：

本次调查对象中，白蛋白下降占比 45.45%（75/165）、前白蛋白下降占比 77.58%（128/165）、淋巴细胞计数下降占比 41.21%（68/165）、血红蛋白下降占比 81.82%（135/165）。

结论 肺结核患者存在较高比例的营养风险和营养不足，从营养风险筛查来看，结核患者存在营养不良风险主要以年龄、营养状态受损为主；从实验室检查来看，存在营养不良风险的患者以前白蛋白、血红蛋白水平下降为主。

CD8+ 组织驻留记忆 T 细胞在新型冠状病毒感染中的研究进展

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目的 探讨组织驻留记忆 T 细胞（tissue-resident memory T cells，TRM）在新型冠状病毒（Severe Acute Respiratory Syndrome Coronavirus 2，SARS-CoV-2）感染中的免疫机制，探索新型冠状病毒疫苗及新冠后综合征防治思路。

方法 使用 Pubmed 检索相关研究，选择标题或摘要中包含以下关键字的文章：(CD8+ tissue-resident memory T cells) AND ((COVID-19) OR (SARS-COV-2))。

结果 组织驻留记忆 T 细胞因具有外周组织长期驻留和细胞毒性作用而得名，其中 CD8+ TRM 细胞功能相对明确，在肺和大脑等多处部位被研究，可增强外周组织的免疫反应；而 CD4+ 的 TRM 细胞特征和功能仍待探索。因高度异质，CD8+ TRM 细胞表型与其驻留部位有关，目前发现受多种趋化因子、黏附分子和细胞因子的调控。SARS-COV-2 初次感染时，在上呼吸道粘膜处由既往其他冠状病毒感染产生的非特异性 CD8+TRM 发挥交叉反应抗病毒作用；再次感染后，病毒特异 CD8+ TRM 细胞诱导固有免疫和细胞免疫，在短时间内识别 SARS-COV-2，产生穿孔素和颗粒酶 B 等细胞毒性分子，分泌 IFN-γ 和 TNF-α 等细胞因子，并招募其他的免疫细胞发挥 “警报”作用；呼吸道 CD8+ TRM 细胞限制病毒在人群中传播方面也有重要作用。但在衰老机体中发现 TRM 细胞有强大的致病潜能，提示该群细胞功能的两面性。在新冠后综合征防治中，开发粘膜免疫的疫苗，在呼吸道诱导特异性 CD8+TRM 的产生，其长期驻留和细胞毒性作为局部“哨兵”发挥持续清除病毒的可能作用。

结论 CD8+ TRM 细胞是适应性免疫的重要成员之一，全面了解 TRM 细胞与病原体之间的病理生理，对持续变异的病毒感染如 SARS-COV-2 等开发新型疫苗和治疗新策略有重要启发作用。

高黄芩素抑制鲍曼不动杆菌多聚磷酸盐激酶 PPK1 的作用及机制

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目的 鲍曼不动杆菌是临床常见的机会致病菌，在机体免疫力受损时可引发多种感染，其中以肺部感染及菌血症多见。随着抗生素的滥用，细菌在强大的选择压力下进化出了多重耐药机制，因此，寻求新的治疗靶点对抗鲍曼不动杆菌感染迫在眉睫。多聚磷酸盐激酶 PPK1 作为催化细菌 ATP 或 GTP 形成多聚磷酸盐 poly P 的关键酶，被证实与细菌的致病性与持留性均密切相关。因此，本研究以鲍曼不动杆菌 PPK1 的功能活性为靶标开展抑制剂的筛选，以期为有效遏制鲍曼不动杆菌感染提供潜在先导化合物和可行的防控策略。

方法 通过酶活性抑制试验筛选靶向 PPK1 的活性抑制剂，进一步应用细菌滑行运动试验、生物被膜形成试验、细菌在多种刺激下（致死剂量的抗生素、热刺激、液氮刺激、氧化应激刺激等）的持留性试验等验证活性抑制剂对 PPK1 调控的致病性与持留性的抑制效果。通过 SPR 分析、生物化学技术和分子生物学手段探究抑制剂拮抗 PPK1 的分子机制。通过大蜡螟感染模型和小鼠肺炎模型评价抑制剂对抗鲍曼不动杆菌感染的体内疗效。

结果 本研究通过 PPK1 酶活性抑制试验筛选出天然化合物高黄芩素为强效的 PPK1 抑制剂，可在体外抑制细菌的滑行运动，干扰细菌生物被膜的形成，同时减弱细菌面对不良刺激时的持留能力。机制探究表明，高黄芩素通过结合在 PPK1 的催化活性中心，改变其二级结构，进而发挥其酶活性抑制作用。体内试验证实，高黄芩素可有效降低鲍曼不动杆菌感染的死亡率，减轻靶器官的细菌载量和组织病理学损伤。

结论 本研究揭示了高黄芩素可通过抑制 PPK1 酶活性减轻鲍曼不动杆菌的致病性与持留性，为对抗鲍曼不动杆菌感染提供了有前景的治疗策略和潜在的先导化合物。

Copper metabolism-mediated virulence evolution of omadacycline in carbapenem-resistant Klebsiella pneumoniae ST11

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Abstract Content Klebsiella pneumoniae is a common clinical Gram-negative opportunistic pathogen that predisposes to a wide range of infectious diseases, including pneumonia, liver abscesses, urinary tract infections, and bloodstream infections. Carbapenem-resistant Klebsiella pneumoniae has posed a certain threat to global health due to its high morbidity as well as high morbidity and mortality after infection, especially the dominant strain ST11-CRKP in our country.Here, we report the virulence changes of the strain in two cases of CRKP of sputum origin treated with omadacycline, and reveal the copper metabolism mediated by omadacycline in the ST11-CRKP strain under clinical anti-infective treatment. possible evolutionary mechanisms of virulence.

Methods Strain identification and drug sensitivity test
Carbapenem resistance genotype testing and virulence testing
(1) Serum resistance test
(2) Biofilm formation assay
(3) Galleria mellonella infection model
(4) Carbapenem resistance genotype detection
Pulsed-field gel electrophoresis
Whole genome sequencing
Confirmation of copper-related associated genes

Results Resistance phenotype and virulence of CRKP isolates
PFGE analysis and carbapenem resistance genes
Genomic analysis
CopC, PcoB copper metabolism-related genes are the possible loci causing the effect of omadacycline on CRKP virulence

Conclusion In summary, omadacycline treatment may be able to affect the expression of virulence genes or genomic composition of Klebsiella pneumoniae for a certain period of time, but resistance usually develops gradually over a long period of antibiotic use. Therefore, it is further speculated that copper metabolism is a possible locus causing the effect of omadacycline on CRKP virulence, and CopC and PcoB mutations may be a potential locus for copper metabolism-mediated virulence evolution, and the specific mechanisms need to be further verified and analyzed in depth. Overall, these findings reveal the possibility of virulence evolution in CRKP due to omadacycline treatment stress and emphasize that Cu metabolism may be critical for virulence changes in this group of bacteria.

123 例免疫缺陷人群肺孢子菌肺炎合并急性呼吸衰竭临床特征分析

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目的 肺孢子菌肺炎（PJP）死亡率高，可达 40%。早期识别免疫缺陷人群 PJP 患者急性呼吸衰竭的危险因素，有望改善此类人群预后。

方法 回顾性收集 2021.01-2023.12 在福建医科大学孟超肝胆医院住院治疗的 PJP 患者临床资料。 纳入标准：1）年龄≥ 18 周岁。2) 符合免疫缺陷人群定义。3）为 PJP 确诊病例。4) 临床资料完整。排除标准：1）年龄小于 18 周岁。2）病例资料残缺。3）非免疫缺陷人群 PJP。4）标本检出 PJP，考虑为定植菌。

结果 1. 我院免疫缺陷人群 PJP 以 HIV 感染为主（77/123），46 例为非 HIV 感染人群，其中 15 例（15/46）为肾移植术后受者、13 例（13/46）为正接受化学 / 免疫治疗的恶性肿瘤患者、18 例（18/46）正在长期接受糖皮质激素治疗。其中 40 例合并呼吸衰竭（40/123），有 6 例出现死亡（6/123）。非 HIV PJP 组更易发生呼吸衰竭（P=0.007）、入住 ICU 概率更高（P=0.023）。

2.NLR 比值高（P=0.031，OR 0.935（0.880, 0.994））、非 HIV 感染人群（P=0.002，OR 0.115（0.029, 0.456））、合并其他病原学感染（P < 0.01，OR 17.267（4.38, 68.07））是免疫缺陷人群 PJP 发生呼吸衰竭的独立危险因素。绘制 ROC 曲线发现，非 HIV 感染的 ROC 曲线下面积为 0.686（0.584,0.789）、合并其他病原学感染的 ROC 曲线下面积为 0.731（0.637,0.826）、NLR 指标的 ROC 曲线下面积为 0.648（0.546,0.750）。

结论 免疫缺陷人群肺孢子菌肺炎易发生呼吸衰竭，临床上应当及时评估患者基础状况及病情，尽早治疗。

基于微信小程序的 OTO 药学服务在抗菌药物科学化管理中的应用

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目的 探索基于移动互联网大数据平台构建信息化、科学化、精准化抗菌药物管理模式，提升安全用药水平，创新药学服务模式，为临床精准用药提供新的途径和治疗策略。

方法 根据抗菌药物科学化管理要素为基本原则，设计开发抗感染方案速查微信小程序。同时通过 HIS 系统提取信息（微生物检验结果、抗菌药物使用数据等），嵌入微信小程序；临床药师定期点评（处方、住院病历）、监测和预警，对小程序后台进行功能维护和数据更新，再通过微信公众号，进行临床反馈和信息推送。

结果 通过抗感染速查微信小程序的临床使用及线下反馈沟通，解决了临床抗感染用药查找费时、药物使用偏差、临床反馈滞后、干预手段欠缺等问题，微信小程序使用覆盖了 80% 以上的临床科室，规范了临床用药，完善了抗菌药物管理体系。

结论 基于微信小程序 OTO（线上 – 线下）服务模式，实现精准的抗感染药物治疗，能有效提高临床抗菌药物使用的规范性和有效性，在抗菌药物全程化、科学化管理方面有较好的实践意义和科学价值。

影像类似肺水肿表现的常见疱疹病毒肺炎合并隐球菌、白色念珠菌感染 1 例

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目的 介绍影像类似肺水肿表现的常见疱疹病毒肺炎合并隐球菌、白色念珠菌感染 1 例，为临床上诊断该类疾病提供依据。

方法 个案报导。

结果 患者女性，62 岁，农民，主因“咳嗽、咳痰 1 月，加重伴胸闷、气促 1 周”。入院后查 CT：肺水肿可能。但 BNP 不高。血常规：中性粒细胞百分比 81.2 %，淋巴细胞百分比 16.0 %；真菌细胞壁（1,3）β-D 葡聚糖试 279.861 pg/ml；EB 病毒 DNA 定量 3.08E+04 IU/ml、巨细胞病毒 DNA 定量 6.31E+02 IU/ml；CD 系列细胞检测：CD3+ 细胞 875.7 个 /ul；痰白念珠菌、热带念珠菌、光滑念珠菌核酸检测 阳性。支气管肺泡灌洗液病原体靶向测序：1. 新型隐球菌均一化序列数 49、白念珠菌均一化序列数 12；2. 单纯疱疹病毒 1 型均一化序列数 1030；3. 巨细胞病毒均一化序列数 239；4.EB 病毒均一化序列数 462。给予抗病毒、抗真菌等治疗，病变明显吸收。

结论 临床发现类似肺水肿 CT 表现的，也要常规排除疱疹病毒感染的可能，以免误诊。

第三章基因二代测序（mNGS）在气管食管瘘病原学检测中的应用研究

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目的 分析宏基因二代测序技术（mNGS）在气管食管瘘（TEF）病原学感染诊断中的临床应用价值。

方法 收集 2020 年 1 月至 2022 年 12 月广东省人民医院呼吸与危重症医学科住院治疗的 8 例气管食管瘘患者数据，包括痰液、支气管肺泡灌洗液和组织样本，进行细菌培养及 NGS 检测。通过 DNA 提取、文库构建、测序以及数据处理与分析，探寻病原菌，并与细菌培养结果进行对比分析。

结果 8 例患者的痰液、支气管肺泡灌洗液及组织样本中，细菌培养阳性 10 例，阴性 5 例。NGS 检测结果显示，15 例患者的样本中均存在细菌，其中 10 例患者细菌菌属与细菌培养结果一致，9 例优势菌群（丰度最高）与细菌培养结果相符。在细菌培养阳性的 10 例标本中，NGS 检测到的细菌属种类（15 种）多于细菌培养检出的种类（10 种），差异具有统计学意义（P=0.042）。而细菌培养阴性的 5 例标本，NGS 均检测到细菌。

结论 NGS 检测作为一种快速、准确的气管食管瘘病原学感染诊断方法，能够检测到常规细菌培养难以发现的细菌，尤其在细菌培养阴性标本中具有较高的诊断价值。

Diagnostic sensitivity of immune-inflammatory cell proportion in early diagnosis of endometrial cancer

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Abstract Content Inflammation is closely linked to the occurrence and progression of cancer. Previous studies have demonstrated the role of immune-inflammatory cell proportions in cancer prognosis, but further research is needed to fully understand its predictive value. This study aims to examine the potential of immune-inflammatory cell proportions, such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), red blood cell distribution width to platelet ratio (RPR), and monocyte to lymphocyte ratio (MLR), in predicting endometrial cancer (EC).

Methods A total of 62 patients with endometrial cancer were included in the study. Receiver operating characteristic (ROC) curves for NLR, MLR, PLR, and RPR were plotted, and the area under the curve (AUC) was calculated. Binary logistic regression analysis was performed to create composite indicators. Subsequently, an ROC curve was generated for the combined indicators, and the corresponding AUC was calculated to evaluate the diagnostic efficacy of NLR, MLR, PLR, and RPR individually and in combination.

Results In the single-indicator ROC curve, NLR AUC baseline was 0.724 and $P<0.05$, with good predictive power and significance. In the two-indicator combined ROC curve, the baseline combined AUC of NLR and the other three indicators was greater than 0.724 and $P<0.05$. In the combined ROC curve of the three indicators, the baseline AUC of the combined indicator including NLR was greater than 0.766 and the P value was equal to 0.001.

Conclusion Taken together, we suggest that the immune-inflammatory cell ratio, especially NLR, has a good role in the prediction of EC. In addition, the combined predictive value of immune-inflammatory cell ratio is better than its individual application.

神经型布鲁菌病 20 例病例系列

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目的 总结我院 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 回顾性分析我院 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 患者中男女性 16 例（80%），女性 4 例（20%），中位年龄 44 岁（20-76 岁）。13 例（65%）患者报告有畜牧相关接触史。诊断脑膜炎 / 脑炎共 17 例（85%），脑脓肿 2 例（10%），脊髓炎 1 例（5%）。中枢神经系统受累表现包括：颈项强直（25%，5 例）、复视（25%，5 例）、肌力下降（20%，4 例）等。5 例（25%）以神经系统受累症状起病，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。所有患者的布鲁菌血清凝集试验阳性，3 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（序列数中位数：46；范围 5-8293）。14 例（70%）的患者存在影像学异常，脑叶异常信号 7 例（35%），脑室或脑室周围白质病变 5 例（25%），多发缺血灶 2 例（10%），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，选择性联合复方新诺明或左氧氟沙星。经治疗，19 例（95%）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。

Practice of standardization of CLSI M45 A3 antimicrobial susceptibility testing of Infrequently Isolated or Fastidious Bacteria strains isolated from blood specimens in Guangdong Province 2017 -2021

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Abstract Content Monitoring of bacterial resistance levels is considered as a necessary means to control the bacterial resistance. Reference standards are critical for antimicrobial susceptibility testing.

Methods CLSI M45 A3 standard defines pathogenic microorganisms that cause infections less frequently than those covered by CLSI M02, M07, and M100 as Infrequently Isolated or Fastidious Bacteria and specifies antimicrobial susceptibility testing methods. Our study investigated the epidemiology and antimicrobial susceptibility testing data of Infrequently Isolated or Fastidious Bacteria strains isolated from blood specimens in 70 hospitals in Guangdong Province between 2017 and 2021. We defined testing methods other than those specified in CLSI M45 A3 as "Non-Standardized."

Results The proportion of standardized antimicrobial susceptibility testing for penicillin increased significantly (Corynebacterium spp. 17.4% vs. 50.0% $p < 0.05$; Micrococcus spp. 50.0% vs. 77.8% $p < 0.05$; Abiotrophia spp. and Granulicatella spp. 21.4% vs. 90.9% $p < 0.001$), while for cefotaxime (Corynebacterium spp. 0.0% vs. 45.2% $p < 0.05$; Abiotrophia spp. and Granulicatella spp. 0.0% vs. 14.3% $p = 0.515$) and vancomycin increased finitely. Non-standardized methods were used for all other antimicrobials.

Conclusion Due to limitations in the economic and medical environment, some clinical laboratories are unable to fully comply with CLSI M45 A3 standard. We recommend that CLSI should add breakpoints for disk diffusion method to improve the standardization of antimicrobial susceptibility testing.

Association between serum vitamin E and bacterial vaginitis in women: a cross-sectional study

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Abstract Content Introduction Bacterial vaginitis (BV) is a common vaginal disease. Vitamin E has been shown to reduce BV by enhancing immune function, but no studies have analyzed the relationship between vitamin E and BV at different BMIs and ages.

Methods This study used 2242 participants from four cycles of NHANES 1999-2006 in American. Participants' vitamin E levels were divided into four groups, and analyses such as study population description, stratified analysis, multiple logistic regression analysis, and curve fitting were performed. To perform data processing, the researchers used the statistical package R (The R Foundation; http://www.r-project.org; version 3.6.3) and Empower Stats software (www.empowerstats.net, X&Y solutions, Inc. Boston, Massachusetts).

Results The concentrations of serum vitamin E were negatively correlated with the risk of BV, especially when vitamin E were at 1198-5459ug/dL with (OR=-0.443, 95%CI=0.447-0.923, P=0.032) or without (OR=-0.521, 95%CI=0.421-0.837, P=0.006) adjustment for variables. At the same time, at lower levels, there was no significant association. Vitamin E supplementation may significantly reduce the risk of BV($p<0.001$). In addition, the risk of having BV decreased and then increased with increasing vitamin E concentrations at high BMI levels ($p<0.01$).

Conclusion Vitamin E at moderate to high concentrations may significantly reduce BV risk, says the study, providing clinical evidence for the prevention and the treatment of BV.

广泛耐药鲍曼不动杆菌肺部感染的危险因素与抗菌药物治疗方案 分析

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目的 本研究主要针对广泛耐药鲍曼不动杆菌（Extensively Drug Resistant Acinetobacter baumanii, XDRAB）肺部感染的临床特征及危险因素进行分析研究，同时探讨 XDRAB 抗菌药物治疗方案与患者预后情况，为有效防控医院感染和临床诊治提供参考依据。

方法 收集我院 2021 年 1 月 -2022 年 12 月所有住院患者病例中下呼吸道标本（纤支镜冲洗液、肺泡灌洗液）分离出 XDRAB 的病例，剔除重复例数及定植菌株，采用病例回顾性分析的研究方法，对病例资料进行分析。

结果 我院共检出 210 株 XDRAB。临床科室的分布主要集中于危重病监护室，有 108 例（51.4%）。呼吸系统疾病（OR=2.294、95%CI: 1.018-5.170、P<0.05）、碳青霉烯类（OR=12.723，95%CI：4.585-35.306，P<0.05）、喹诺酮类（OR=10.100，95%CI：1.950-52.317，P<0.05）、β - 内酰胺抑制剂（OR=4.012，95%CI：1.659-9.702，P<0.05）是 XDRAB 感染的独立危险因素。临床治疗 XDRAB 感染使用最多的抗菌药物是替加环素联合舒巴坦合剂，有 27 例，好转率为 62.96%（17/27）。XDRAB 组的未好转率高于 NXDRAB 组（$\chi 2$=94.500，P<0.05）。

结论 由 XDRAB 菌株标本分离自危重病监护室的比例最高，呼吸系统疾病、抗菌药物（碳青霉烯类、β - 内酰胺抑制剂、喹诺酮类）是 XDRAB 感染的独立危险因素，替加环素联合舒巴坦合剂是临床治疗 XDRAB 感染使用最多的抗菌药物，XDRAB 感染预后较差。

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%）（X^2=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%）（X^2=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%）（X^2=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%）（X^2=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（X^2=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。

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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目的 探讨医院内耐碳青酶烯类肠杆菌科（Carbapenase-tolerant enterobacteriaceae,CRE）血流感染的临床特征以及死亡危险因素，为其感染控制提供依据。

方法 收集广东省人民医院 2013 年 1 月至 2022 年 12 月 CRE 血流感染患者 28d 内预后的临床资料，采用病例对照研究方法，运用单因素和多因素 logistics 回归分析 CRE 血流感染患者预后的临床危险因素。

结果 122 例 CRE 血流感染患者中，67 例存活，55 例死亡。共检出病原菌 122 例，前三位依次为肺炎克雷伯菌、大肠埃希菌、阴沟肠杆菌。单因素分析结果提示，年龄、患有基础疾病、侵入性操作、抗菌药物使用情况及 ICU 入住情况是导致 CRE 血流感染预后不良的重要危险因素。多因素 logistic 回归模型的深度分析则提示，感染性休克（OR=4.655、95%CI：1.118-19.385、P=0.035）是导致 CRE 血流感染患者 28d 内死亡的独立危险因素。

结论 伴有感染性休克的患者更容易发生 CRE 血流感染，临床应加强对此类患者的重视并进行及早筛查，有效控制血流感染的发生。

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 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。

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。

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。

孕妇尿路感染的病原菌分布及危险因素分析

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目的 探讨医院内孕妇尿路感染的病原菌分布特点及相关危险因素，为及时防控尿路感染提供科学指导。

方法 收集 2018 年 12 月至 2023 年 9 月广东省人民医院确诊的 299 例妊娠合并尿路感染孕妇为感染组，按照病例对照 1：1 原则，随机选取同期诊断 299 例无尿路感染孕妇为对照组，回顾性分析孕妇尿路感染的病原菌分布特点和危险因素。

结果 感染组中检出革兰阳性菌占 46.5%，革兰阴性菌占 45.5%，真菌占 8.0%；其中大肠埃希菌检出率最高（32.4%），其次为无乳链球菌（31.4%）和肺炎克雷伯菌（5.4%）。年龄、孕周、住院时间、流产史、个人尿路感染史和阴道炎是孕妇尿路感染的重要危险因素，孕周、流产史、个人尿路感染史和阴道炎是孕妇发生妊娠合并尿路感染的独立危险因素。

结论 孕妇尿路感染的因素相对较为复杂，孕周、流产史、个人尿路感染史和阴道炎是孕妇发生妊娠合并尿路感染的独立危险因素，临床可据此给予针对性的防治措施及抗菌治疗，以达到降低尿路感染风险的目的。

基于真实世界数据的集采注射用头孢唑林钠预防手术部位感染（SSI）的临床综合评价

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目的 本研究拟结合国家带量采购、国家临床综合评价政策，通过真实世界数据研究，评价关节置换术中不同注射用头孢唑林钠预防手术部位感染（SSI）的有效性、安全性和经济性，为围术期用药提供循证证据，完善此类药品评价体系，为相关政策提供一定依据。

方法 真实世界研究，回顾性收集医院 2019 年 1 月至 2023 年 12 月使用集采或非集采注射用头孢唑林钠的关节置换术患者临床数据。应用倾向性评分匹配法（PSM）、增量成本－效果分析等统计学方法开展药品临床综合评价。

结果 根据非劣效试验设计，纳入集采组 218 例、非集采组 51 例。PSM 后，每组 43 例患者匹配成功。

1. 有效性: 匹配前术后感染发生率(1.38% vs. 1.58%，P=0.952)，匹配后感染发生率(2.30% vs. 2.30%，P=1.000) 在集采组和非集采组间差异无统计学意义。体温及感染相关指标（WBC、NEUT%、LY%）在组间差异亦无统计学意义；集采组患者术后 72h CRP 均值高于非集采组。

2. 安全性：两组不良事件发生率均较低，组间差异无统计学意义；肝肾功能（ALT、AST、ALP、Cr、eGFR）在组间差异均无统计学意义且使用研究药物期间两组均未发生过敏反应。

3. 经济性：增量成本－效果比分析结果显示，集采组产生了负 ICER：获得 1% 的预防率增量需要减少 2086.095 元的花费。决策树模型分析结果显示集采组成本低于非集采组。单因素敏感性分析表明经济学评价结果具有稳健性。

结论 注射用头孢唑林钠集采品种的有效性不劣于非集采品种，两者安全性较高且无显著性差异；经济性方面，集采品种具有经济学优势。

Increased Co-Infection of Mycoplasma and Chlamydia Pneumoniae Among COVID-19-Positive Kidney Disease Patients

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Abstract Content The COVID-19 pandemic has disproportionately impacted immunocompromised individuals, including kidney transplant recipients (KTR). Limited research explores their susceptibility to concurrent infections with atypical pathogens. This study examines whether KTRs are more prone to SARS-CoV-2, Mycoplasma pneumoniae (MP) and Chlamydia pneumoniae (CP) co-infections.

Methods To achieve this, a retrospective analysis of MP and CP detection results spanning from 2017 to 2023 was undertaken. Disease diagnostic distributions, patient characteristics, laboratory tests and survival status were comprehensively evaluated.

Results Compared to the pre-COVID-19 era, MP and CP infection surged during the Omicron peak months in China. Remarkably, this rise in MP and CP infection did not align with the prevalence of H1N1 or other respiratory viruses. Further analysis revealed significantly higher co-infections specifically in patients with kidney disease. Notably, KTR represented a significant 70% of co-infections involving SARS-CoV-2, MP and CP, while their presence in the SARS-CoV-2-negative group remained below 20%. Subsequent stratified analysis unveiled a higher susceptibility of KTR (90.91%) to SARS-CoV-2 compared to CKD-5 patients (65.71%), accompanied by an elevated incidence of co-infections with MP or CP in SARS-CoV-2-positive KTR cases. Despite this increased propensity for co-infections among KTR, the impact on patient survival did not reach statistical significance.

Conclusion In conclusion, this study highlights the complex interplay between SARS-CoV-2 and MP/CP co-infections, underscoring the necessity for nuanced therapeutic strategies, particularly in vulnerable populations like KTR. However, given the limited inclusion of subjects in our study, further investigations are warranted to elucidate the impact of co-infections on the survival of KTR.

Oridonin protects LPS-induced acute lung injury by modulating Nrf2-mediated oxidative stress and Nrf2-independent NLRP3 and NF-κB pathways

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Abstract Content Oxidative stress and the resulting inflammation are essential pathological processes in acute lunginjury (ALI). Nuclear factor erythroid 2-related factor 2 (Nrf2), a vital transcriptional factor, possesses antioxidativepotential and has become a primary target to treat many diseases. Oridonin (Ori), isolated from the plant RabdosiaRrubescens, is a natural substance that possesses antioxidative and anti-inflammatory effects. Our aim was to studywhether the anti-inflammatory and antioxidant effects of Ori on LPS-induced ALI were mediated by Nrf2.

Methods MTT assays, Western blotting analysis, a mouse model, and hematoxylin-eosin (H & E) staining wereemployed to explore the mechanisms by which Ori exerts a protective effect on LPS-induced lung injury inRAW264.7 cells and in a mouse model.

Results Our results indicated that Ori increased the expression of Nrf2 and its downstream genes (HO-1, GCLM),which was mediated by the activation of Akt and MAPK. Additionally, Ori inhibited LPS-induced activation of thepro-inflammatory pathways NLRP3 inflammasome and NF-κB pathways. These two pathways were also proven tobe Nrf2-independent by the use of a Nrf2 inhibitor. In keeping with these findings, Ori alleviated LPS-inducedhistopathological changes, the enhanced production of myeloperoxidase and malondialdehyde, and the depletedexpression of GSH and superoxide dismutase in the lung tissue of mice. Furthermore, the expression of LPSinduced NLRP3 inflammasome and NF-κB pathways was more evident in Nrf2-deficient mice but could still bereversed by Ori.

Conclusion Our results demonstrated that Ori exerted protective effects on LPS-induced ALI via Nrf2-independentanti-inflammatory and Nrf2-dependent antioxidative activities.

Oridonin attenuates carrageenan-induced pleurisy via activation of the KEAP-1/Nrf2 pathway and inhibition of the TXNIP/NLRP3 and NF-κB pathway in mice

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Abstract Content The classic NLRP3 inflammasome and NF-κB molecular pathways are activated in many inflammatory-related diseases,such as pleurisy. Because oridonin (Ori) has been indicated as a covalent NLRP3 inhibitor with strong anti-inflammasome activity, we herein aimed to assess the effects of Ori in a mouse model of carrageenan (CAR)-induced pleurisy.

Methods Enzyme-linked immunosorbent assay, Western blotting analysis, and hematoxylin-eosin (H & E) staining wereemployed to explore the mechanisms by which Ori exerts a protective effect on carrageenan-induced pleurisy ina mouse model.

Results The results showed that CAR caused hemorrhaging and exudation of lung tissues and the release of inflammatory factors (TNF-α, IL-6 and IL-1β), effects that were significantly reduced by treatment with Ori. In addition, increased neutrophil infiltration, protein concentrations and volumes were found in the exudates of the CAR group, and these phenomena were suppressed by Ori treatment. Regarding cellular pathways, Ori could alleviate the CAR-activated NF-κB and TXNIP/NLRP3 pathways. Additionally, oxidative stress was shown to be involved in the pathogenesis of pleurisy, but possible mechanisms remain to be explored. Herein, Ori reversed the CAR-induced depletion of GSH and SOD and the CAR-induced increases in ROS, MPO and MDA levels. Furthermore, Ori inhibited NOX-4 levels, initiated the dissociation of KEAP-1 from Nrf2, activated the downstream genes HO-1 and exerted antioxidative effects on CAR-induced pleurisy.

Conclusion In conclusion, Ori conferred protection against CAR-induced pleurisy via Nrf2-dependent antioxidative and NLRP3-dependent anti-inflammatory properties.

肺泡灌洗液 mTGS 检测流程的优化和临床验证

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目的 在纳米孔宏基因组技术基础流程体系（Pre-mTGS）的基础上，优化相关技术要求及质控参数，形成相对标准化的 mTGS 质控流程及参数标准，合评估其与其他检测手段的临床诊断价值。

方法 先利用参考品及小量临床样本对 Pre-mTGS 基础流程体系中的破壁方法、片段筛选方法、人源处理操作及数据量参数进行优化，以形成相对标准化的 mTGS 质控流程及参数标准。再纳入疑似肺部感染的 168 例患者。收集患者的临床资料及肺泡灌洗液（BALF），评估肺泡灌洗液 mTGS 的临床诊断价值。

结果 在 Pre-mTGS 基础流程体系基础上，确定了破壁方法、片筛处理方法、不去人源处理及 800MB 数据量作为标准化 mTGS 检测的反应体系条件。mTGS 较 Pre-mTGS 对参考品中个别病原微生物的检测限提升 10 倍。

纳入的 156 例患者中，明确诊断的感染患者 135 例，最终共确认了 188 株病原体。与 CMTs 相比，mTGS 识别出更多的病原体（152vs.60），检测灵敏度提高 39.26%（82.96% vs.43.70%，P<0.01）。与优化前 Pre-mTGS 相比，mTGS 检测灵敏度提高 34.07%（82.96% vs.48.89%，P<0.01）。与 mNGS 相比，mTGS 在病原体检测性能上二者持相当水平（82.96%vs. 77.78%，P=0.21），均明显优于传统微生物检测。但两者在个别病原体检测上各有优劣，其中人型支原体、曲霉等，mNGS 检出率更高，结核分枝杆菌、新型隐球菌、铜绿假单胞菌，mTGS 检出率更高。综合来看，mTGS 与临床诊断的整体一致性达 81.50%。

结论 本研究初步形成相对标准化的 mTGS 流程体系及相关参数，且经验证 mTGS 较 Pre-mTGS 在肺部感染病原体检测方面性能显著提升，总体性能与 mNGS 持平，两者均明显优于 CMTs。优化后 mTGS 方法可作为肺部感染病原学检测的可靠手段。

发热半年的罪魁竟然是它?

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目的 本文以我病房收治的一例发热半年患者为例，探讨不明原因发热及肺部念珠菌病的临床诊治思考

方法 通过 1 例发热半年的患者临床诊治经过，结合相关诊治指南及病例文献进行回顾性分析。

结果 本例患者为 61 岁男性，既往 2 型糖尿病、淋巴瘤病史。本次病程以发热半年，咳嗽、咳痰、气短为主要不适诉求。病程中院外新冠病毒及甲、乙流病毒等核酸检验阴性，肺部影像提示多肺叶段淡片影、结节影。PET/CT 提示双肺野多发斑片状密度增高影，胸膜下区为著，代谢不均匀增高；视野内骨骼及骨髓代谢弥漫性增高。从长期发热鉴别诊断考虑中，本例患者除肺部病变外，其他器官系统活动性疾病诊断依据不足。临床考虑肺部感染可能性大。从感染责任病原体考虑，患者病程早期倾向于呼吸道病毒感染，在长期病程中仍需注意同一病原体反复感染及多种病原体继发 / 混合感染可能性。本例患者入院后经气管镜检查灌洗液 NGS 检验提示新型冠状病毒核酸阳性、近平滑念珠菌阳性。予莫诺拉韦 1 疗程、氟康唑抗感染治疗 1 周不适症状缓解，住院治疗 10 天续贯为氟康唑口服治疗出院。院外继续氟康唑治疗至总疗程 4 周，临床转归良好。

结论 免疫妥协人群患病临床表现常不典型，病程迁延，临床诊治过程需在充分评估基础疾病前提下，综合考虑制定临床诊治方案。另，对于鼻拭子新冠病毒核酸阴性但呼吸道症状持续存在者，可考虑多次送检或送检肺泡灌洗液核酸检测或宏基因二代测序。

外周血宏基因组二代测序诊断侵袭性曲霉菌病的价值：一项单中心回顾性研究

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目的 探讨外周血宏基因组二代测序（metagenomic Next Generation Sequencing，mNGS）在侵袭性曲霉菌病诊断中的价值。

方法 回顾性分析浙江大学医学院附属第一医院 2021 年 2 月至 2022 年 12 月共 167 例外周血 mNGS 检测出曲霉菌属核酸的患者临床资料，分析其曲霉感染的高危因素、临床表现、影像特征、病原学结果、临床诊断及治疗转归等资料。

结果 根据侵袭性曲霉菌病的诊断标准，综合高危因素、临床表现、影像特征及治疗转归等因素，167 例外周血 mNGS 检测到曲霉菌序列的患者中包括确诊 2 例、临床诊断 31 例、拟诊 67 例、假阳性 67 例。98 例临床诊断及拟诊病例均具有符合曲霉感染的高危因素、临床表现、影像特征及治疗转归，其中 9 例临床诊断病例在间隔 16（10，61）天采集的 2-4 次外周血 mNGS 中发现同一种曲霉菌。另外 67 例患者外周血 mNGS 检测出曲霉菌，但无曲霉菌感染的高危因素或临床特征，且缺乏其他病原学依据，判定为假阳性。本研究入组的病例中，外周血 mNGS 诊断侵袭性曲霉菌感染的阳性预测价值 59.9%。

结论 外周血 mNGS 检测对于诊断侵袭性曲霉菌感染具有重要参考价值，但仍需结合高危因素、临床特征及其他病原检测结果综合判断。

Negative associations between folate and bacterial vaginosis in the NHANES 2001 to 2004

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Abstract Content Bacterial vaginosis (BV) is one of the most common infections among women of reproductive age and accounts for 15–50% of infections globally. The role played by folate in the pathogenesis and progression of BV is poorly understood. The aim of this study was to investigate the association between serum folate, red blood cell (RBC) folate, and BV in American women.

Methods 1,954 participants from the 2001-2004 National Health and Nutrition Examination Survey (NHANES) program were included in this study. Multiple logistic regression was used to analyze the association between serum folate, RBC folate, and BV, and covariates including race, age, education level, and body mass index were used to construct adjusted models. Stratifed analysis was used to explore the stability of the above associations in diferent populations.

Results In the present cross-sectional study, we found that serum folate and RBC folate were inversely associated with the risk of BV. In the fully adjusted model, the risk of BV was reduced by 35% (OR=0.65, 95% CI: 0.51~0.83, p=0.0007) in the highest serum folate group and 32% (OR=0.68, 95% CI: 0.53~0.87, p=0.0023) in the highest RBC folate group compared to the lowest group.

Conclusion The results of this study indicated that serum folate and RBC folate were inversely associated with the risk of BV folate supplementation may play an important role in the prevention and management of BV.

1 例紫色尿袋综合征患者的治疗体会

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目的 为发生紫色尿袋综合征（PUBS）的患者提供临床处置经验。

方法 通过查阅相关文献资料并进行分析，参与 1 例 PUBS 患者的治疗过程。

结果 对本例患者的综合分析，符合发生 PUBS 的各项危险因素（老龄、女性、卧床、留置导尿、营养支持、碱性尿液及高尿细菌载量、使用 PVC 尿袋及导尿管），正确识别“尿路感染”临床表现，并结合及时的尿培养 + 药敏，针对目标细菌 – 奇异变形杆菌行抗感染治疗后，患者“尿路感染“治愈，PUBS 消失。

结论 PUBS 临床较少发生，通过合理的分析，可能是“尿路感染”的一种提示信号，及时的识别及做好相应处置，对患者具有较高的临床价值。

同型半胱氨酸与细菌性阴道病之间的关联：来自 2001–2004 年 NHANES 数据

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目的 虽然没有研究直接表明细菌性阴道病 (BV) 和同型半胱氨酸 (HCY) 之间的关系，但我们通过大量文献和数据分析发现这两者之间存在一些关联。BV 评分采用 Nugent 方法计算，小于等于 6 为阴性，大于等于 7 为阳性。本文描述了我们从 NHANES 提取的关于 BV 和 HCY 的数据中挖掘出的多个协变量下的相互关系。

方法 我们在研究中使用了 NHANES 2001–2002 和 2003–2004 的两个周期。我们的研究中有 2398 名完成访谈和 MEC 测试的参与者。通过研究多变量条件下 BV 和 HCY 之间的关系，进行多元线性回归分析。这些因素可能会影响结果，例如种族、年龄、教育水平、体重指数等。我们的研究选择血清维生素 B12、铁蛋白、分叶中心粒百分比和分叶中心粒数量作为潜在协变量。

结果 我们观察到，粗略模型和两个调整后的模型都显示出 HCY 和 BV 之间存在较高的相关性，并且相关性是阳性的。在粗略模型中，OR=1.26，95% 置信区间（CI）1.10、1.44，P= 0.0018；HCY 与 BV 呈正相关（OR=1.19，95% 置信区间（CI）1.05、1.34，P=0.0121）。使用多元线性回归分析来研究多变量设置下 BV 和 HCY 之间的联系。

结论 本研究结果表明，HCY 与 BV 患病率呈正相关，可能在 BV 的预防和治疗中发挥重要作用。

降糖药物的服用与脓毒症的不良预后：基于药物靶点遗传代理的孟德尔随机化研究

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目的 临床研究表明，糖尿病患者入院时的高血糖与住院期间因脓毒症的死亡率增加相关。拟探究对不同类型抗糖尿病药物对脓毒症发生易感性的影响。

方法 采用两样本孟德尔随机化设计，从编码抗糖尿病药物靶蛋白的基因中选择独立的遗传变异作为遗传工具。所研究的降糖药物包括胰岛素及其类似物、噻唑烷二酮类、SGLT-2i、二甲双胍等。从 FinnGen 和 UK biobank 中提取降糖药物靶点的遗传工具与 2 型糖尿病和脓毒症易感性的相关性。分别采用 Wald 比值检验、逆方差加权法等方法估计效应量的大小。

结果 SGLT-2i 诱导的血糖降低与脓毒症 28 天死亡率 (OR 8.48，95% CI 1.05 to 68.43) 的升高显著相关。二甲双胍的服用与较低的脓毒症易感性 (OR 0.97, 95% CI 0.96 to 0.98) 和脓毒症 28 天死亡率 (OR 0.94, 95% CI 0.90 to 0.98) 有关。

结论 为预防脓毒症发生，建议糖尿病患者服用二甲双胍。不推荐糖尿病患者在治疗中使用 SGLT-2i 作为一线药物，以减少其脓毒症 28 天死亡率。

隐球菌病的临床病例分析

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目的 隐球菌病（cryptococcosis）是一种遍及全球的侵袭性真菌病，发病率逐年升高。隐球菌病多见于免疫缺陷患者，尤其是 CD4+T 淋巴细胞缺陷的宿主，且因其流行病学特征、临床表现及影像学均缺乏特异性，早期诊断难度较大，常被误诊或漏诊，从而发展为严重感染。本研究收集了我院 2011 年 5 月至 2023 年 10 月期间隐球菌病患者的临床资料，分析隐球菌病的临床特点、危险因素，为隐球菌病的早期诊断提供依据。

方法 收集中国医科大学附属第一医院 2011 年 9 月至 2023 年 9 月临床诊断为“隐球菌病”患者的临床资料，包括基本资料、临床症状、影像学表现、实验室检查等。

结果 89 例隐球菌病患者中，孤立性肺隐球菌病（pulmonary cryptococcosis，PC）28 例（31.5%），均为非人类免疫缺陷病毒（human immunodeficiency virus，HIV）感染者；隐球菌脑膜炎（cryptococcal meningitis，CM）共 37 例，其中 12 例为 HIV 感染者，25 例为非 HIV 感染者。多部位感染者共 17 例，15 例合并 CM，其中者 12 例为 HIV 感染者，3 例为非 HIV 感染者，差异有统计学意义（P <0.001）。38 例非 HIV 感染者中，CD4+ T 细胞计数 > 400 的患者共 25 例，其中 PC 19 例，CM 5 例，无多部位感染的患者；CD4+ T 淋巴细胞计数 < 400 的患者共 13 例，其中 PC 2 例 ，CM 5 例，多部位感染 5 例，3 例合并 CM，差异有统计学意义（P <0.001）。

结论 1. 孤立性 PC 多见于非 HIV 感染者，CM 及多部位感染多见于 HIV 感染者（P <0.01）。2. 非 HIV 感染患者中，CD4+ T 淋巴细胞计数 < 400 者更易出现 CM 及多部位感染（P <0.01）。

Ceftazidime/avibactam resistance characteristics emerged diversely in carbapenem-resistant Klebsiella pneumoniae and carbapenem-resistant Pseudomonas aeruginosa from an intensive care unit

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Abstract Content Carbapenem-resistant Pseudomonas aeruginosa (CRPA) and Carbapenem-resistant Klebsiella pneumoniae (CRKP) 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 CRPA and CRKP infections.

Methods In this study we isolated 32 CZA-resistant strains including 12 CRPA strains and 20 CRKP strains from an ICU in August 2020-February 2021. MICs of 32 strains for 10 antibiotics were determined by antimicrobial susceptibility testing using agar dilution and broth microdilution method. Cloning experiments and S1-PFGE were performed to investigate molecular characteristics of ceftazidime-avibactam resistance genes. Whole genome analyze was performed to compared the genetic context of CZA resistant genes and explore the phylogenetic relationship of strains.

Results 19 CRKP strains co-producing KPC-2 and NDM-5 belonged to ST11-KL47 and the other one producing NDM-1 belonged to ST29. Seven CRPA 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.

Conclusion The study highlighted diverse resistance mechanisms that emerged in CRKP and CRPA in response to CZA in the ICU and observed the cross-regional transfer of CZA-resistant CRPA with the referral of a patient.

Glucose oxidase@Ruthenium-copper Nano-enzyme Aerogels in the Treatment of Biofilm Infections

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Abstract Content Biofilm infections are a class of infectious diseases characterized by biofilm formation. According to statistics, there are about 13.7 million infection-related deaths globally each year, with bacterial-related deaths accounting for 13.6% of all deaths, and the results of related investigations show that more than 70% of bacterial infections are associated with biofilms. In this study, we focused on the mechanism of biofilm infections, developed a novel nanotechnology-based nanoenzymes, and explored their therapeutic ability for biofilm infections.

Methods Initially, RuCu hydrogel was synthesized via hydrothermal reaction, followed by obtaining RuCu aerogel through freeze-drying. The synthesized nanozyme was then surface-modified with methoxy polyethylene glycol (m-PEG) and polyethyleneimine (PEI) to enhance its stability in aqueous solutions and provide active sites for crosslinking with glucose oxidase (GOx). Subsequently, glutaraldehyde was used to crosslink mPEG/PEI@RuCu with GOx, forming the composite enzyme system GOx-mPEG/PEI@RuCu.

To thoroughly analyze the nanozyme's properties, transmission electron microscopy (TEM) and scanning electron microscopy (SEM) were employed to observe its morphology and size. The particle size and Zeta potential were determined using a particle size zeta potential meter. At the structural level, fourier-transform infrared spectroscopy (FTIR) was utilized to assess the crosslinking between GOx and the nanozyme. At the functional level, the peroxidase-like activity of the nanozyme was tested through TMB/H2O2 colorimetric assays, and the kinetic parameters of the enzyme-catalyzed reaction were calculated. The electronic pH meter were used for dynamic monitoring of pH value changes to test the activity of GOx enzyme.

In the in vitro antibacterial experiments, a bacterial biofilm model on silicone disc carriers was established. The dilution plating counting method was used to evaluate the antibacterial performance of the nanozyme. Crystal violet staining was used to quantitatively assess the anti-biofilm capability of the nanozyme. In the in vivo antibacterial experiments, a rat biofilm infection model was established to test the nanozyme's antibacterial performance in a complex body environment. The cytotoxicity of the nanozyme was determined using the CCK-8 method with human umbilical vein endothelial cells. The serum biochemical parameters of the experimental animals were measured, and pathological changes in tissue sections were observed to assess the potential toxicity of the nanozyme on organs.

Results A uniformly shaped, well-dispersed, and loosely porous GOx-mPEG/PEI@RuCu nanozyme aerogel was successfully synthesized. Characteristic chemical bonding signals of Schiff base bonds generated by glutaraldehyde cross-linking detected by Fourier infrared transform spectroscopy. TMB colorimetric assay and EPR/ESR experiments demonstrated the peroxidase-like activity of the nanozyme, with enzyme catalytic kinetics parameters (pH=4.0) for TMB (Km= 0.44 mM, Vmax= 10.0×10-8 M/s) and H2O2 (Km= 0.17 mM, Vmax= 2.32×10-7 M/s). The electronic pH meter recorded a change in the solution's pH from 7 to approximately 4 within 300 minutes. In vitro antibacterial experiments showed that in the presence of glucose and GOx-mPEG/PEI@RuCu exhibited excellent antibacterial performance, with a 99% reduction in MRSA bacterial survival ($P < 0.05$). Crystal violet staining quantitatively demonstrated a significant reduction in biofilm residue on the silicone discs treated with GOx-mPEG/PEI@RuCu ($P < 0.01$). In vivo antibacterial experiments showed that rats treated with GOx-mPEG/PEI@RuCu and glucose had significantly lower white blood cell counts on the third day post-administration compared to the control group ($P < 0.01$), with a significant reduction in bacterial load around the silicone film and infected tissue ($P < 0.05$). Biosafety tests showed good biocompatibility of the nanoenzymes and no significant toxic reactions were observed.

Conclusion GOx-mPEG/PEI@RuCu nanoenzymes exhibit excellent spontaneous cascade catalytic reaction activity under both in vitro conditions and in vivo physiological conditions in animal models, with considerable antimicrobial and anti-biofilm properties, and GOx-mPEG/PEI@RuCu nanoenzymes possess good biocompatibility.

Association Between Red Blood Cell Folate and Trichomonas vaginalis Infection among Women

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Abstract Content Abstract

Background Increased folic acid has been found to be latently protective against gynecological infection, including several kinds of vaginosis. In this study, we laid emphasis on whether RBC (Red Blood Cell) folate status was associated with the infectious ratio of Trichomonas vaginalis, a kind of anaerobic parasitic protozoan.

Methods We set RBC folate as the exposure variable and Trichomonas vaginalis as the outcome variable. Other subsidiary variables were regarded as confounding variables that may work as potential modifiers. The cross-sectional study was conducted with two merged waves of the National Health and Nutrition Examination Survey (NHANES) from 2001 to 2004, and a sample of 1274 eligible women (1212 negative and 62 positive in Trichomonas vaginalis infection) was integrated for the exploration of the association between RBC folate and Trichomonas vaginalis infection. Multivariate regression analyses, subgroup analyses, and subsequent smooth curve fittings were conducted to estimate the relationship between RBC folate and Trichomonas vaginalis in women.

Results In the multivariable logistic regression analyses, a negative association was observed between stratified RBC folate status and Trichomonas vaginalis infection with all confounders adjusted. Referencing the lowest RBC folate concentration quartile, the higher concentration quartiles reported a relatively lower infection ratio, while there was a weak correlation between total RBC folate concentration and T.vaginalis (Trichomonas vaginalis) infection. In subgroup analyses stratified by BMI and age, this association was only found significant in high age and BMI groups.

Conclusions The cross-sectional study indicated a negative association between RBC folic acid and Trichomonas vaginalis infection, and latent effects of BMI and age on the association were found.

杭州市 2021-2023 年诺如病毒流行病例状况分析

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目的 了解感染 2021-2023 年度杭州诺如病毒流行病学特征，为完善杭州市医院定点检测系统提供依据，制定战略防止诺如病毒爆发及其流行，实现全面管理，为疫情提供真实有效数据。

方法 收集了 2021-2023 三年度杭州不同级别医院送往杭州迪安医学检验中心的样本，共 10383 份粪便样本，利用 PCR 荧光定量方法检测，赛默飞 ABI7500 扩增。从年龄、性别、季节方面对报告 CT 值小于 36 的粪便阳性标本进行分析阳性率。

结果 在送检病例中诺如病毒检出率在 26.14%，其中男性患者粪便标本阳性检出率为 15.61%、女性患者粪便标本阳性检出率为 10.23%，男阳性患者略高于女阳性患者，两者用卡方检验统计学得出，男性阳性率与女性阳性率 P=0.093 > 0.05，X2=4.752 无统计学意义。因此阳性率与性别无关。利用 EXCEL 表格图表纵坐轴阳性率横坐标为年份或者月份，由此可发现在年龄方面病人在婴幼儿中多为罕见，在季节方面分析发现诺如病毒有明显的季节性，且在冬春季节流行较多。

结论 冬春季节是诺如病毒的发病高峰期，加强对婴幼儿的保护，同时加强托儿所的管理，从而保护婴幼儿减少阳性率。持续开展及加强该项监测为杭州地区诺如病毒爆发防控提供科学依据。

布鲁菌性脊柱炎危险因素及预后分析

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目的 布鲁菌病（简称“布病”）患病人数逐年增多，是我国重要的公共卫生问题之一。脊柱炎是布病的严重并发症，易误诊、漏诊，且致残率高、预后差，对病人的身体和心理均造成严重影响。本研究旨在探讨布鲁菌性脊柱炎（Brucellar Spondylitis，BS）的危险因素及预后影响因素，为其早期预防、治疗以及改善患者预后提供科学依据。

方法 本研究采用回顾性病例对照研究，研究对象选取河北医科大学第三医院 2020 年 6 月至 2022 年 6 月诊确为布病的住院患者，根据是否并发脊柱炎分为单纯布病组和 BS 组，对 BS 组随访 1 年，根据临床结局将 BS 组分为预后良好组和预后不佳组。收集两组患者的人口学和临床资料建立数据集。使用 SPSS 26.0 软件分析数据：将两组患者的临床特征进行比较，采用 logistic 回归分析筛选 BS 的危险因素，使用 Cox 生存分析确定 BS 患者治疗结局的影响因素。

结果 1. 本研究共纳入布鲁菌病患者 300 例，其中单纯布病组 113 例，BS 组 187 例，多因素分析显示年龄、发病至确诊时间、腰背痛、血沉是 BS 的独立危险因素（$P<0.05$）。2.154 例 BS 组中预后良好组 121 例，预后不佳组 33 例。使用 Kaplan-Meier 生存分析对两组患者的临床资料进行 Log-Rank 检验， COX 回归分析显示发病至确诊时间、合并糖尿病、局部脓肿形成、合并神经功能损害为 BS 患者预后不佳的独立危险因素（$P < 0.05$）。

结论 1. 高龄、发病至确诊时间延长、腰背痛、血沉增快是布病患者发生脊柱炎的独立危险因素。2. 发病至确诊时间延长、合并糖尿病、局部脓肿形成以及神经功能损害为 BS 患者预后不佳的独立危险因素。

慢性阻塞性肺疾病急性加重期及慢性阻塞性肺疾病下呼吸道感染患者的病原菌分布及耐药性研究进展

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目的 由于国内对慢性阻塞性肺疾病急性加重期 (AECOPD) 及慢性阻塞性肺疾病 (chronic obstructive pulmonary disease，COPD) 患者下呼吸道感染病原菌病原菌研究和治疗方法存在地区上的差异和时间上的不断更新，病原菌的分布不同、对药物的敏感性也有所不同，充分了解 AECOPD 及 COPD 患者下呼吸道感染病原菌的种类及其药敏结果，有助于在临床上准确地对菌下药，进一步阻止疾病的发生发展，降低耐药率和死亡率。

方法 综合国内近几年不同地区 AECOPD 及 COPD 患者下呼吸道感染病原菌分布及耐药性相关文献，分析 AECOPD 及 COPD 患者下呼吸道感染病原菌分布及耐药性并掌握其变化趋势。

结果 本文通过综合分析国内不同地区的 AECOPD 及 COPD 患者下呼吸道感染病原菌分布与耐药性，发现各个地区以革兰阴性杆菌为主要的病原菌，其中铜绿假单胞菌、大肠埃希菌、肺炎克雷伯菌为较常见的病原菌，鲍曼不动杆菌也是较常见的病原菌。当抗感染治疗效果不佳时，应考虑其可能产生耐药并与耐药菌变异、混合感染、抗生素的长期不合理使用有关。可避免使用青霉素类、头孢类等耐药性高的抗菌药，各地区革兰阴性菌对于氨苄西林、环丙沙星、左氧氟沙星等耐药性也较高，而对阿米卡星、美罗培南、亚胺培南等敏感性高。其次，革兰阳性菌对青霉素类耐药率也很高，对替考拉宁、利奈唑胺、万古霉素等新型抗生素的耐药率较低。也有地区真菌分布多于革兰阳性菌分布。

结论 AECOPD 及 COPD 患者下呼吸道感染病原菌对抗生素的耐药性日渐增加，随着病原菌基因检测技术和抗生素佐剂的应用研究等的不断发展，将有利于快速、准确定位病原菌，结合不同的地区，根据患者病情、个体差异，确定病原菌种类，以提高抗菌药物的药效，降低死亡率。

通过生物信息学分析和机器学习来识别结核病和 SARS-CoV-2 感染之间的相互作用

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目的 严重急性呼吸系统综合征冠状病毒 2 引起的 COVID-19 患者数量仍在增加。就 COVID-19 和结核病（TB）而言，一种疾病的存在会影响到另一种疾病的感染状况。同时，合并感染可能导致并发症，使治疗更加隐匿。然而，TB 支持结核病和 COVID-19 相互作用的分子机制尚不清楚。因此，我们使用转录组分析来检测结核病和 COVID-19 中的共享通路和分子生物标志物，使我们能够确定 COVID-19 与 TB 之间的复杂关系。

方法 利用基因表达综合系统的两个 RNA-seq 数据集（GSE114192 和 GSE163151）研究 TB 和 COVID-19 之间的不同表达基因（DEGs），以确定共同的致病机制。检测共同的差异基因，并用于识别共享通路和药物靶点。采用几种进取的生物信息学工具进行路径分析、富集分析和网络分析。采用蛋白 - 蛋白相互作用分析和机器学习来鉴定枢纽基因并采用数据集 GSE171110、GSE54992 和 GSE79362 进行验证。

结果 共检测到结核和新冠感染共同的差异基因 124 个，并用于识别共享通路和药物靶点。共享通路包括细菌来源分子的反应、对脂多糖的反应和对炎症反应的调节，色氨酸代谢，补体和凝血级联，cGMP-PKG 信号通路等。我们筛选出前 10 个 TFs 作为枢纽，并筛选出 10 个枢纽 mirna。依那西普、利妥昔单抗、贝伐单抗、AV411、波生坦、西他森坦、安布生坦、马西坦、乙酰半胱氨酸和 NADH 的药物机制可能在 COVID-19 联合结核病治疗中具有重要的参考价值。

结论 本研究寻找了结核和新冠感染潜在的生物标志物和治疗靶点，促进诊断和治疗的发展。

血浆 mcfDNA 宏基因组二代测序揭示血液病与造血干细胞移植患者感染病原谱特征

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目的 应用 mNGS 技术检测血浆 mcfDNA 揭示血液病与造血干细胞移植 (HSCT) 患者感染病原谱特征。

方法 回顾性分析 2021-2023 年期间本院 497 例血液病患者与 2447 例造血干细胞移植患者非连续送检的 5248 例外周血样本 mNGS 检测结果。

结果 病毒是血液病 (52.29%) 与 HSCT(58.45%) 患者高发的感染病原体，排在前三位的分别为巨细胞病毒 (CMV)、细环病毒 (TTV) 和人疱疹病毒 4 型 (EBV)。mNGS 检出病原菌阳性率显著高于血培养 (41.68% VS 8.76%, P=0.000)。两组 G- 菌检出高于 G+ 菌。血液病患者 G- 菌检出频率最高为铜绿假单胞菌 (26.06%, 49/188)。HSCT 患者 G- 菌检出频率最高为大肠埃希菌 (22.36%, 297/1328)。在 HSCT 患者中，大肠埃希菌检出率明显高于血液病患者 (OR=0.594, 95%CI:0.400-0.883, P=0.009)，秋冬季高发。两组中 G+ 球菌检出均以屎肠球菌为主，春季高发。曲霉菌是血液病 (35.52%) 与 HSCT 患者 (42.03%) 主要的致病真菌，以烟曲霉和黄曲霉多见。血液病与 HSCT 患者真菌感染谱不同，在肺孢子菌、毛霉菌及念珠菌检出上均存在差异。血液病患者耶氏肺孢子菌感染率较 HSCT 高 (10.93% VS 3.59%, P < 0.001)。在 118 例疑似肺孢子菌肺炎的患者中，血浆 mNGS 诊断肺孢子菌肺炎的阳性预测价值为 78.12%(25/32)，阴性预测价值为 96.51%(83/86)，Youden 指数为 81.5%，具有临床诊断价值。除此之外，mNGS 检出分枝杆菌、立克次体与寄生虫等特殊病原。

结论 血液病与 HSCT 患者病毒感染率高，细菌和真菌感染谱不同，细菌感染存在季节性差异。应用 mNGS 检测血浆 mcfDNA，对于肺孢子菌肺炎的诊断具有较好的诊断效能。mNGS 在临床少见、特殊病原感染诊断方面具有显著优势。

感染

A five-year retrospective cohort study of patients with acinetobacter baumannii bloodstream infection: clinical characteristics, treatment, prognosis and their consequences

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Abstract Content Background The objective of this investigation was to evaluate the clinical features of patients with acinetobacter baumannii bloodstream infection (AB-BSI).

Methods Totally 200 inpatients with AB-BSI were included, clinical features of AB-BSI inpatients between 90-day survival and 90-day mortality groups, between patients infected with multidrug-resistant (MDR) and sensitive acinetobacter baumannii were analyzed, the prognostic factors of 90-day mortality in AB-BSI inpatients were also assessed.

Results The 90-day mortality patients had significantly higher carbapenem-resistant bacterial infection and critical care unit (ICU) admission. The 90-day mortality group showed higher proportion of patients without active antibiotic use and lower proportion of patients using active antibiotic within 48 hours than that in 90-day survival group. We also found that critical surgery, ICU admission and antibiotic treatment >48h indicated a poor outcome. We also analyzed the clinical characteristics of patients in the MDR group and sensitive group, the Kaplan-Meier curve indicated that patients in the MDR group had a significantly worse overall survival than the sensitive group.

Conclusion Active antibiotic within 48 hours may affect the outcome of AB-BSI. Critical surgery, ICU admission and antibiotic treatment >48h were independently prognostic risk predictors of 90-day mortality in AB-BSI patients. MDR group had a worse overall survival than the sensitive group.

脓毒症和脓毒性休克 1h 集束化治疗实施现状调查

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目的 调查 ICU 医护对脓毒症和脓毒性休克 1h 集束化治疗的 认知情况及实施现状，为制定相关培训内容及临床 持续的质量控制管理提供理论依据。

方法 采用自行设计的问卷，通过问卷星，在全国范围内 调查 ICU 医护对脓毒症和脓毒性休克 1h 集束化治疗的 认知情况及实施现状。

结果 32 个省市自治区，680 家医院，1339 名 ICU 医护参与 调查，有效问卷 1325 份，其中 92.5% 的 ICU 医护认为 掌握了脓毒症和脓毒性休克 1h 集束化治疗诊断指标 和治疗措施，但仅有 25.2% 的 ICU 医护能够正确回答 所有脓毒症和脓毒性休克 1h 集束化治疗相关问题。 有 69.9% 的 ICU 医护认为所在科室 1h 集束化治疗完成 率在 80% 以上，在具体措施中，有 77.2% 的 ICU 医护 认为所在科室液体复苏达标率在 80% 以上；80% 以上 的 ICU 医护认为所在科室一小时内使用抗生素达标 率、抗生素前留取血培养达标率、血乳酸测定达标 率均在 80% 以上；有 64.3% 的 ICU 医护所在科室有对 应质控小组并进行专项质控反馈。

结论 ICU 医护群体认为脓毒症和脓毒性休克 1h 集束化治疗 知识掌握程度高，但实际并不理想，仍需进一步加 强相关知识培训。ICU 医护自认脓毒症和脓毒性休克 1h 集束化治疗完成率高，同时对更具效率效果的脓 毒症相关知识培训以及建立健全的脓毒症集束化治 疗质控体系需求迫切。

感染

Metagenomic Sequencing Reveals Differences in Lung Microenvironment among Patients with Nontuberculous Mycobacterial Pulmonary Disease under Different Immune States

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Abstract Content Nontuberculous mycobacterial pulmonary disease (NTM-PD) is an increasingly recognized public health concern, characterized by a diverse spectrum of clinical manifestations and outcomes. The heterogeneity in the clinical presentation and progression of NTM-PD is influenced by a myriad of factors, including the host's immune status. Despite the growing incidence, the interplay between the pulmonary microenvironment and the immune state in NTM-PD remains inadequately understood. This study aims to investigate the differences in the pulmonary microenvironment of NTM-PD patients with different immune states using metagenomic sequencing. By correlating the microbial profiles with clinical characteristics, we seek to elucidate the potential mechanisms underlying the disease's pathogenesis and progression. Understanding these interactions is crucial for developing targeted therapeutic strategies and improving clinical outcomes for patients afflicted with NTM-PD.

Methods A total of 147 patients diagnosed with NTM-PD were selected from Zhongshan Hospital Fudan University between January 2019 and July 2023. Based on the host immune status, the patients were divided into two groups: the immunocompromised group and the control group. A total of 318 samples, including sputum, bronchoalveolar lavage fluid(BALF), and lung tissue, were collected from these patients. Metagenomic sequencing was performed on these samples to assess the microbial composition and diversity. Alpha diversity and beta diversity were calculated for each group to evaluate within-sample and between-sample diversity, respectively. LEfSe (Linear Discriminant Analysis Effect Size) analysis was conducted to identify differentially abundant taxa between the groups. Additionally, microbial co-occurrence networks were compared to understand the interaction patterns within the microbiota. Spearman correlation analysis was applied to clinical data from the different groups to explore potential correlations between microbiota alterations and clinical laboratory parameters.

Results Compared to the control group, the immunocompromised group exhibited significantly lower alpha diversity in sputum, BALF, and lung tissue samples ($P < 0.05$). Principal Coordinates Analysis (PCoA) of beta diversity for sputum and BALF samples revealed significant differences between the groups ($P < 0.05$). LEfSe analysis identified differential species between the two groups across various

sample types, with similar evolutionary branch distances. Co-occurrence network analysis indicated that the immunocompromised group had reduced network node count, node density, and average network distance compared to the control group. However, interactions between NTM species and other populations were markedly increased in the immunocompromised group. Integrating the LEfSe and co-occurrence network results, potential differential driver species were identified.Spearman correlation analysis confirmed that the abundance of these species was associated with clinical indicators such as the ratio of T cells and NK cells in patients.

Conclusion The pulmonary microbiota of immunocompromised patients exhibited reduced abundance and diversity compared to the control group, with distinct regulatory patterns of microbial communities between the two groups. The differences may be correlated with the number of immune cells.

微滴式数字聚合酶链反应在病原体检测中的研究进展

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目的 聚合酶链反应是一种分子生物学技术，用于使某些脱氧核糖核酸（DNA）片段扩增，它是一种常见且不可或缺的技术，已应用于许多领域，特别是在临床实验室中。第三代聚合酶链反应，微滴式数字聚合酶链反应（ddPCR）是常规聚合酶链反应方法的生物技术改进，可用于直接定量和克隆扩增 DNA, 现在广泛用于低丰度核酸检测，可用于感染性疾病的诊断。目前大众对它在病原体检测应用方面了解有所欠缺，因此我们致力于帮助大家了解 ddPCR 检测手段的发展及原理，总结了其在病毒性疾病、细菌性疾病和真菌性疾病临床诊断中的潜在优势，更好的为临床服务。

方法 通过在文献数据库中浏览近十年文章，总结及归纳 ddPCR 检测手段的发展及原理，总结了其在病毒性疾病、细菌性疾病和真菌性疾病临床诊断中的潜在优势。

结果 ddPCR 的优势有以下几点：更高的精密度和灵敏度、更高的重复性及通用性、更高的抗干扰能力和稳定性。ddPCR 应用于病原体检测的范围主要有：病毒学检测、细菌学检测、真菌学检测。

结论 ddPCR 对低丰度病原体的检测更灵敏、准 确、可重复，可能在未来临床应用中是比定量聚合酶链反应更好的选择。

创伤弧菌感染引起双足坏死继发脓毒血症一例

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目的 报告一例因创伤弧菌感染引起双足坏死继发脓毒血症的案例，对临床凶险病原菌进行报道，以引起临床医生和检验医生的重视。

方法 将从病例回顾分析、细菌鉴定过程及结果展示、讨论以下几个方面进行阐述，对临床凶险病原菌进行报道，并结合病例对于创伤弧菌进行文献复习。

结果 患者老年男性，糖尿病、肝病病史多年，从事水产行业，1 周前因双足伤口被海产品刺伤出现双下肢水肿、疼痛入院。患者查体示：低血压休克 、下肢皮肤发黑、破溃。入院后完善相关检查示 : 酸中毒、感染指标升高，伤口分泌物送培养后明确诊断为：创伤弧菌感染导致的脓毒性休克，予头孢西丁抗感染、补液等处理。入院后患者病情迅速发展出现感染性休克并存在多器官功能衰竭，三系降低、凝血功能异常、转氨酶及血肌酐居高不下、右下肢肌肉坏死并逐渐蔓延等情况，经多学科会诊后行右下肢截肢术，予输注成分血、降血氨、抗心衰、血液透析、补液纠酸、营养支持、下肢皮肤换药等对症治疗。治疗期间患者多次出现血氧降低、心衰等抢救情况，后家属决定转院治疗。

结论 创伤弧菌感染病情发展迅速、很快出现感染部位肌肉坏死、脓毒性休克、全身多器官功能衰竭等危重症情况，推荐使用三代头孢菌素联合四环素抗感染，早期清创及必要的截肢对改善预后有重要作用。对于诊断，建议尽早送伤口分泌物培养或者 NGS 测序以尽早明确诊断。

双歧杆菌四联活菌片及联合凝结芽孢杆菌活菌片对移植后患者粘膜炎的影响

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目的 探究单用双歧杆菌四联活菌片（四联益生菌）及联合凝结芽孢杆菌活菌片（五联益生菌）对移植后患者粘膜炎发生的影响。

方法 收集 2022 年在本院行造血干细胞移植的患者，依照益生菌补充类型将患者分为四联组及五联组，依照 WHO 粘膜炎分级标准对粘膜炎评级，并对临床患者特征进行描述性统计。

结果 共纳入 111 例患者，四联组 54 例，五联组 57 例，中位年龄分别为 32 岁（范围 13-58 岁）及 41.5 岁（范围 15-66 岁，P=0.471）。32 例行自体造血干细胞移植，四联组中行自体及异基因移植的患者数分别为 14 例和 40 例，五联组为 18 例和 39 例（P=0.511）。四联组中使用 MAC 和 RIC 预处理方案的患者数分别为 19 例和 35 例，五联组为 11 例和 46 例（P=0.060）。四联和五联组中性粒细胞植入率为 96.3% 和 98.2%（P=0.293），植入时间分别为 12 天（范围 9-23 天）和 11.5（范围 9-18 天，P=0.308）。血小板植入率为 92.6% 和 94.7%（P=0.642），植入时间分别为 12.5（范围 9-24 天）和 11 天（范围 9-18 天，P=0.042）。四联组患者粘膜炎 0 级，I-II 级，III-IV 级的发生率为 37%；50% 及 13%。五联组患者粘膜炎 0 级，I-II 级，III-IV 级的发生率为 52.6%；47.4% 及 0%（P=0.012）。使用有序多元 logistics 回归探究益生菌补充对粘膜炎发生的影响，单因素分析结果显示，相对于四联组，五联组粘膜炎显著减低（OR=0.43，95%CI[0.2-0.9],P=0.027），多因素分析显示五联益生菌补充是移植后粘膜炎的保护因素（OR=0.35，95%CI[0.16-0.77],P=0.010）。

结论 双歧杆菌四联活菌片联合凝结芽孢杆菌活菌片有助于降低移植后患者粘膜炎发生率及严重程度，结果需进一步采用大样本验证。

碳青霉烯类抗生素耐药铜绿假单胞菌菌血症不同抗菌治疗方案疗效分析

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目的 回顾性分析碳青霉烯类抗生素耐药铜绿假单胞菌菌血症发生和死亡高危因素及 CRPA 菌血症不同抗菌治疗方案的疗效。

方法 在 2021 年 1 月至 2022 年 6 月期间，对铜绿假单胞菌菌血症患者进行了一项单中心、回顾性比较分析。

结果 该研究入组了铜绿假单胞菌菌血症患者 152 例，其中 CRPA 为 65 例。合并血液系统恶性肿瘤、PITT 评分、菌血症发作前 2 周皮质类醇使用、低蛋白血症是铜绿假单胞菌菌血症患者死亡的危险因素。CRPA 菌血症组的存活率均显著低于非 CRPA 菌血症组。暴露于碳青霉烯类抗生素是 CRPA 的危险因素。对于 CRPA 菌血症的治疗，包含头孢他啶阿维巴坦的治疗组 7 天和 14 天病死率低于其他治疗组。

结论 碳青霉烯类抗生素暴露是 CRPA 菌血症的危险因素，CRPA 菌血症患者的死亡风险更高。含 CAZ/AVI 的治疗相对于其他药物治疗有更高的 7 天、14 天存活率。

脓毒症引起的肌萎缩与白介素 -6 相关研究的综述

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目的 在脓毒症中，炎症因子，如白细胞介素 -6 (IL-6)、IL-1β 、肿瘤坏死因子 (TNF) 和急性时相蛋白，血清淀粉样蛋白 A1 (SAA1) 在患者和小鼠的血清和骨骼肌中升高。然而，IL-6 信号在脓毒症诱导的肌肉萎缩中的作用尚不清楚。本文旨在总结关于脓毒症引起的肌萎缩及白介素 6 相关的最新基础研究。

方法 搜索最新的关于脓毒症引起的肌萎缩及白介素 6 相关的基础研究。

结果 IL-6 通过 gp130/JAK2/ stat3 通路介导脓毒症肌肉损伤萎缩并可能导致 ICUAW。白细胞介素 1β （IL-1β ）10 和急性期血清淀粉样蛋白 A1 （SAA1 ）促进脓毒症中的肌肉萎缩，并且它们的抑制减弱了脓毒症诱导的小鼠肌肉萎缩。IL-1β 和 SAA1 信号转导都接近转录因子 NF-kB 和白细胞介素 6 （IL-6 ） 的表达。促炎细胞因子（如 TNF、IL-1β 和 IL-6 ）增加了 C2C12 肌管中 TGF-β 受体 II (TβRII) 抑制剂 SPRY 结构域和 SOCS-box 蛋白 1 (SPSB1) 的表达。SPSB1 表达增加，与 TβRII 强烈相互作用，导致 TβRII 泛素化和不稳定化。SPSB1 损害了 TβRII-Akt-Myogenin 信号传导，并减少了肌细胞中的蛋白质合成，过表达降低了早期和晚期分化标记物的表达，并损害了肌母细胞融合和肌源性分化。局部应用胰岛素样生长因子（insulin-like growth factor-I， IGF-I ）抑制了脓毒症引起的肌肉 IL-6 mRNA 的升高。因此，肌肉导向的 IGF-I 通过增加肌肉蛋白质合成和潜在地减少蛋白质水解来明显地减轻脓毒症诱导的萎缩反应。脓毒症也可以通过影响肌肉中的线粒体超微结构起作用。IL-6 缺乏通过上调 PGC-1α 表达抑制线粒体 ROS 产生，从而减轻脓毒症小鼠的骨骼肌萎缩。

结论 IL-6 在脓毒症诱导的肌肉萎缩中的作用通过各种机制起作用。

发热伴血小板减少综合征患者合并侵袭性肺曲霉病的危险因素：一项多中心研究

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目的 袭性肺曲霉病（IPA）是发热伴血小板减少综合征（SFTS）的一种危及生命的并发症，本研究旨在确定 SFTS 相关 IPA（SAPA）的危险因素。方法：2013 年 5 月至 2022 年 9 月于湖北省和安徽省进行了一项多中心的回顾性队列研究。应用 LASSO 回归筛选变量并进行多变量 logistic 回归分析以确定 SAPA 的独立预测因素，COX 回归分析确定死亡相关的危险因素。

方法 2013 年 5 月至 2022 年 9 月于湖北省和安徽省进行了一项多中心的回顾性队列研究。应用 LASSO 回归筛选变量并进行多变量 logistic 回归分析以确定 SAPA 的独立预测因素，COX 回归分析确定死亡相关的危险因素。

结果 在 1775 名 SFTS 患者中，有 1650 名纳入研究，其中 169 人临床诊断为 IPA， 42 天死亡率为 26.6%。多变量 logistic 回归分析发现，高龄、瘀点、咯血、震颤、低白蛋白水平、活化部分凝血活酶时间（APTT）延长、入住重症监护室（ICU）、使用糖皮质激素、静脉注射免疫球蛋白（IVIG）和住院时间延长是 SAPA 发生的预测因素。Cox 回归确定了 42 天死亡率的危险因素，包括静脉穿刺部位瘀斑、凝血酶原时间（PT）延长、未入住 ICU、未使用抗真菌药、使用血管加压药和糖皮质激素。基于这些预测变量，构建了 SAPA 发生和 42 天死亡的列线图预测模型，一致性指数分别为 0.855（95%CI 0.826-0.884）和 0.778（95%CI 0.702-0.854）。Kaplan-Meier 生存曲线显示，接受糖皮质激素治疗的 SAPA 患者存活率较低（P<0.001），而抗真菌治疗可提高 14 天存活率（P=0.036）

结论 在 SFTS 流行地区，利用有效的预测工具协助加强 IPA 管理至关重要。

Temporal trends in global, regional, and national tuberculosis mortality, 1990-2019: An age-period-cohort analysis for the GBD 2019 study

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Abstract Content Tuberculosis is the third leading cause of death from infectious diseases worldwide and understanding trends in TB mortality is important to track disease progression and develop effective control measures. We report the trends in TB mortality and the association with age, period, and birth cohort for 204 countries and territories worldwide over the period 1990-2019.

Methods We used data from the Global Burden of Disease 2019 study (GBD 2019) to assess the global burden of death from tuberculosis. We used age-period-cohort models to estimate net drift (overall annual percentage change), local drift (age-specific annual percentage change), age effects (longitudinal age curves), and period and cohort effects (relative risk for period and birth cohort) in mortality over the period 1990-2019.

Results In 2019, the global TB age-standardized mortality rate was 14.64 (13.39, 16.03) per 100,000 people, and with the decrease in the sociodemographic index (SDI), the mortality rate of tuberculosis gradually increased. Over the last 30 years, the net drift of deaths was -3.47 (95% CI-3.53 to -3.42). The pediatric group (0-15 years) portrayed a more prominent mortality decline than the adults worldwide, especially in high SDI regions. Although high SDI regions performed well in terms of the period and cohort effects, limited improvement in TB mortality burden was observed in the elderly population. Mortality

declines were generally more pronounced in high SDI regions than in low SDI regions. Significant sex differences were found in TB mortality, and mortality rates were generally higher in males than in females.

Conclusion Over the past 30 years, there has been a significant decline in TB mortality worldwide, and the burden of TB varies significantly by region. The TB status of children and older adults needs more attention.

Global Publication Trends in Monkeypox Research: An Analysis through Bibliometrics

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Abstract Content Monkeypox (MPX) is a zoonotic disease caused by the monkeypox virus (MPV). Before 2022, human cases of MPX mainly occurred in the tropical rainforests of Central and West Africa, with few outbreaks outside Africa and limited local transmission. In May 2022, a sudden outbreak of MPX occurred, rapidly spreading to Europe, the Americas, and all six regions of the WHO. Approximately 87,000 cases were reported in 110 countries, resulting in 112 deaths. Currently, there are no approved drugs or vaccines for treating human MPV infections, necessitating vigilance against outbreaks of both new and existing viruses. Therefore, there is a need for a global perspective on MPX through bibliometric analysis. This study aims to describe the knowledge framework of the field from a holistic and systematic perspective using bibliometric analysis, to aid researchers and decision-makers in understanding the history and current status of MPX research and predicting future demands.

Methods In response to the sudden outbreak of MPX in 2022, we searched and selected relevant literature on MPX from the Web of Science Core Collection (WOSCC) database. The top 100 articles with the highest citation rates from all research journals and the top 100 articles from 129 specialized infectious disease journals were selected for bibliometric analysis. Citespace software was used to analyze the annual output, collaboration relationships, hotspots, research status, and development trends in the field. This was done to provide reference for future research, enabling MPV researchers to quickly and intuitively identify research focuses and scopes.

Results It is evident from the co-occurrence network that research on MPX mainly focused on 2022, as outbreaks were concentrated in countries such as the UK, Italy, and Spain, which have higher levels of public healthcare and were able to promptly respond to the outbreaks based on advanced research. Collaboration network maps of countries and institutions show that the US and the UK are leading in the volume of publications in the field of MPX research. In the country collaboration network map of all journals, countries where MPX is endemic such as South Africa and Nigeria, as well as countries affected by MPX outbreaks like Italy, France, and Switzerland, are also prominent. It is noteworthy that South Africa has a high centrality in all journals and infectious disease journals categories, indicating its high research value in the field of MPX. Africa is a hotspot for MPX, and thus, South Africa's attention to the MPV far exceeds that of other countries. Compared to other MPX endemic regions in Africa, South Africa has the strongest capacity to provide basic services, resulting in stronger research capabilities in MPX. However, the number of articles cited from South Africa is still lower than that of other European countries and the US. This indicates that while the quantity of articles from South Africa is relatively low, their research value is relatively high.

Conclusion In conclusion, these findings provide a data-driven and objective overview of MPX research, offering valuable reference for readers to guide future research endeavors.

浙江地区普通人群戊型肝炎病毒感染情况调查分析及研究

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目的 为了研究分析浙江地区普通人群戊型肝炎病毒感染情况，充分掌握浙江地区戊型肝炎病毒感染的检出率、发病率等基本流行病学规律，了解普通人群戊型肝炎病毒感染状况、基本流行病学特征以及现状分布，熟悉戊型肝炎病毒抗体 IgM 检测的过程，通过对戊型肝炎抗体 IgM[HEV-IgM] 检测，使感染患者尽早发现并积极针对性治疗，为戊型肝炎防控提供参考。

方法 采用随机整群抽样法选取 2023 年 1 ~ 6 月份来自公司 HEV-IgM 样本数据，检测戊型肝炎抗体 IgM[HEV-IgM] 的 432606 例浙江地区不同年龄段人群，采用 ELISA 方法学对检测者血清样本进行抗体检测。

结果 通过对 432606 例浙江地区不同年龄段人群检测，年龄区间范围在 1 ~ 90 周岁，男女比例相当，检测结果显示阳性有 855 例，阳性率为 0.20%。其中男性阳性例数 470 例，阳性率为 0.11%；女性阳性例数 385 例，阳性率为 0.09%。年龄区间范围在 10 周岁以下的人群中，戊型肝炎病毒感染比率为 0.23%，占比相对较小；年龄区间范围在 51 周岁以上的人群比率为 42.22%，占比相对较大，差异均有统计学意义（$P < 0.05$）。

结论 不同年龄段人群检测者中，男性戊型肝炎病毒的检出率普遍高于女性，且感染率随年龄增长而上升，重叠感染的比例也越高，尤其是中老年人的检出率更高，因中老年人的肝功能损害比年轻人严重，更容易感染戊型肝炎病毒。检测血清中戊型肝炎抗体 IgM 速度较快，且有较高的特异性和敏感性，可以有效地帮助临床寻找感染病因，有利于了解感染者的状况，协助戊型肝炎的诊断，为临床诊断和治疗提供重要依据。

Efficacy and safety of combination of colistimethate sodium aerosol and injection in the treatment of pulmonary infection caused by carbapenem-resistant organism: a real-world evaluation study

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Abstract Content Polymyxins are considered the last-line antibacterials for treating resistant Gram-negative bacteria. Colistimethate sodium (CMS) is commonly used as aerosol (AER-CMS) and for intravenous injection (IV-CMS) in treating pulmonary infection caused by carbapenem-resistant organism (CRO). However, the polycationic/hydrophilic structure of IV-CMS limits its penetration into the lung parenchyma, may leading to insufficient blood concentration in lung tissue. While AER-CMS has high alveolar penetration and minimal systemic diffusion, which can promote the therapeutic effect and systemically minimize adverse effects. Currently, the post marketing surveillance about the efficacy and safety of IV plus AER CMS from real world is limited. This study aims to evaluate the efficacy and safety of IV plus AER CMS (Tianyun®; Chiatai Tianqing Pharma, Jiangsu, China) in the treatment of pulmonary infection caused by CRO based on real-world data.

Methods This is a multi-center observational retrospective study. Patients with CRO-induced pulmonary infection who received CMS therapy between Dec 2021 and Dec 2023 were enrolled. Patients with IV plus AER-CMS regimen and IV-CMS alone regimen were grouped. Propensity score matching (PSM) was used to eliminate the confounding bias of observational study data. The primary endpoint was clinical effective rate, and the secondary endpoints included clinical cure rate, inpatient days, mortality and incidence of adverse effects (ADEs). Statistical analysis was performed with Wilcoxon rank sum test, students t-test, chi-square test, and Fisher's exact test as appropriate.

Results The IV plus AER CMS regimen group included 101 patients and the IV-CMS regimen group included 108 patients. After PSM at a ratio of 1:1, 70 patients remained in each regimen group. The results showed that the clinical effective rate of the IV + AER-CMS group was significantly higher than IV-CMS group (78.57% vs 60.00%, p=0.017). Other efficacy indicators, such as clinical cure rate, inpatient days, total mortality and 28-day all-cause mortality, presented no significant differences between the two regimen groups. For ADEs, there were no statistically significant differences in the incidences of nephrotoxicity (22 .86% vs 24.29%, p=0.842) and bronchospasm (5.71% vs 0.00%, p=0.128) between the two regimen groups.

Conclusion This is the first study investigating efficacy and safety of IV plus AER CMS (Tianyun®) vs IV-CMS and complementing real-world evidence.It proves IV plus AER-CMS had a remarkably greater clinical effective rate and well tolerance, provides guidance for treating pulmonary infection caused by CRO in clinical.

Incidence, Risk Factors, Microbiology and Outcomes of Bloodstream Infection During Conditioning before Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract Content Bloodstream infection (BSI) represents a substantial and recurrent complication that often arises during allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite its considerable occurrence, there has been a conspicuous absence of focused research delving into BSI specifically during the conditioning phase before HSCT.

Methods A single-center cohort study, comprising 2395 consecutive patients who underwent allo-HSCT from 2013 to 2023 was conducted. We examined the characteristics of BSI during the conditioning phase, risk factors and its prognosis on patients.

Results The cumulative incidence of BSI during conditioning was 4.7%, with a median onset on day 8 post-agitation of the conditioning regimen. The most frequently isolated pathogens included Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and coagulase-negative staphylococci. A multivariate analysis identified several variables associated with BSI during conditioning, including neutropenia lasting $\geqslant$ 7 days before conditioning, a hematopoietic cell transplantation-comorbidity index (HCT-CI) $\geqslant$ 1, and "in vivo" T-cell depletion using antithymocyte globulin (ATG). Furthermore, the analysis indicated that BSI caused by carbapenem-resistant Enterobacteriaceae (CRE) significantly increased the risk of all-cause mortality within 90 days following BSI (hazard ratio = 7.492; 95% confidence interval: 1.389, 40.429; P = .019).

Conclusion Reducing the incidence of BSI during conditioning phase can significantly improve early transplantation outcomes in haematological patients. Strategies to achieve this include increasing patients' pre-conditioning neutrophil levels, minimizing comorbidities, and optimizing conditioning regimens.

Efficacy of Short Course Antibiotic Therapy for Uncomplicated Staphylococcus aureus bacteremia in Neutropenic Patients with Hematological Diseases: A Retrospective Comparative Study

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Abstract Content Data regarding duration of antibiotic therapy for Staphylococcus aureus bacteremia (SAB) in neutropenic patients with hematological diseases were limited. The objective of this study was to explore the impact of neutropenia on the clinical outcomes of SAB in patients with hematological diseases and evaluate the effect of antibiotic treatment duration for hematological patients with SAB.

Methods We performed a retrospective single-center cohort study including hematological adult patients (≥ 14) with SAB. Clinical characteristics and treatment outcomes were compared between neutropenic and non-neutropenic hematologic patients. In addition, logistic regression models fitted with inverse probability of treatment weighting were used in a subgroup of patients with uncomplicated SAB to assess the association between the clinical outcomes and treatment duration.

Results Between January 2013 and December 2023, a total of 242 hematological patients infected with SAB were included, of whom 181 (74.8%) were neutropenic and 61 (25.2%) were non-neutropenic patients. Mortality or relapse within 90 days of the onset of SAB occurred in 22 (12.2%) neutropenic patients and in 15 (24.6%) non-neutropenic patients (P =0.020). Recurrent fever within 7 days of completing therapy occurred in 14 (7.7%) neutropenic patients and in 11 (18.0%) non-neutropenic patients (P =0.022). Multivariate analysis indicated that, relapse or refractory hematological malignancies (aOR=6.384, p=0.001), MRSA infection (aOR=3.504, p=0.020), polymicrobial bacteremia (aOR=3.182, p=0.045) were significant risk factors associated with 90-day mortality or relapse, while chemotherapy or immunosuppressive therapy within 1 month prior to SAB (aOR=0.283, p=0.040) and neutropenia (aOR=0.248, p=0.012) were protective factors. Acute lymphocyte leukemia, compared with acute myeloid leukemia, was a risk factor of 7-day fever recurrence (aOR=3.673, p=0.025). A total of 210 patients met the eligibility criteria of uncomplicated SAB, of whom 95 (45.2%) received short-course antibiotic therapy (median, 8.0 days; IQR, 7.0-9.0) and 115 (54.8%) received long-course therapy (median, 15.0 days; IQR, 12.0-20.0). In the weighted cohort, the univariate and multivariate analysis indicated that short course

of antibiotic treatment showed no significant relation with 90-day mortality or relapse (p= .766), 30-day mortality or relapse (p= .231), or 7-day recurrent fever (p= .060).

Conclusion For hematological patients infected with SAB, neutropenia neither increased the incidence of 90-day mortality or relapse nor the incidence of recurrent fever. And short-course antibiotic therapy for treatment of uncomplicated SAB seemed to yield similar clinical outcomes as long-course one.

Analysis of the Burden of Disease and Attributable Risk Factors for Myocarditis in the Western Pacific Region, 1990-2019

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Abstract Content Background Myocarditis is a cardiac disease that poses a threat to health and has increasingly garnered attention. This article aims to study the changing trends in disease burden and risk factors of myocarditis in the Western Pacific region over the past 30 years, further exploring the epidemiological situation of the disease to provide reference for its prevention and control.

Methods This study is based on Global Burden of Disease (GBD) data from 1990 and 2019. It employs metrics such as prevalence, mortality, Disability-Adjusted Life Years (DALYs), age-standardized incidence rates, mortality rates, DALYs rates, etc., to assess the epidemiological patterns and disease burden trends of myocarditis in Western Pacific countries and regions, as well as their relationship with sociodemographic factors.

Results In 2019, the age-standardized incidence and mortality rates of myocarditis in the Western Pacific region were 16.97/100,000 and 0.67/100,000, respectively, representing a decrease of 0.29% and 0.49%, respectively, compared to 1990. DALYs also decreased from 504,841.15 years in 1990 to 393,632.86 years in 2019. In 2019, the disease burden of myocarditis among males in the Western Pacific

region was higher than that among females. Similarly, the burden of myocarditis among children under 5 years of age was more significant compared to other age groups. Deaths and age-standardized mortality rates attributable to myocarditis and cardiomyopathy can be attributed to metabolic, environmental/ occupational, and behavioral risks, with metabolic risks having the greatest impact.

Conclusion Overall, although the age-standardized incidence, mortality rates, and DALYs rates of myocarditis in the Western Pacific region have decreased since 1990, the disease burden of myocarditis remains significant. Promoting the development of healthcare in the Western Pacific region and formulating prevention policies based on attributed risk factors may reduce the disease burden. Furthermore, due to heterogeneity in disease burden among different countries, healthcare resource allocation should tilt towards countries with a heavier burden of myocarditis to maximize improvements in disease burden in the Western Pacific region.

基于生物信息学筛选并验证识别脓毒症相关凝血功能障碍新型生物标志物研究

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目的 脓毒症相关凝血病（sepsis-induced coagulopathy，SIC）是脓毒症常见的并发症之一，合并 SIC 的患者发生器官功能障碍以及死亡风险均显著增加。但目前缺乏精准识别 SIC 的生物标志物，不能实现 SIC 的早期识别和干预。本研究通过生物信息学分析筛选并验证诊断 SIC 的潜在生物学标志物，实现 SIC 的早期诊断。

方法 纳入东南大学附属中大医院重症医学科脓毒症生物样本库患者参考国际血栓与止血学会 ISTH-SIC 评分标准，根据患者入住 ICU 第一天的凝血功能指标将患者分为 SIC 和非 SIC 两组，对两组患者进行外周血转录组检测，通过差异表达基因分析，筛选在 SIC 和非 SIC 组中表达具有显著差异的基因。进一步在公共数据集中验证差异基因的变化趋势，共同筛选与 SIC 相关的潜在差异基因。对 DEGs 进行基因本体论和京都基因与基因组百科全书富集，探究其可能的功能。纳入前瞻性验证队列通过 Q-PCR 方法对筛选基因进行验证，同时收集活化部分凝血活酶时间，纤维蛋白降解产物及 D- 二聚体等凝血功能指标，通过绘制受试者特征曲线评估筛选基因诊断 SIC 的效能。

结果 共纳入生物样本库脓毒症患者 16 例，其中 SIC 组 7 例，非 SIC 组 9 例，通过 DEGs 并结合公共数据库差异基因集中变化趋势，共筛选到 155 个变化趋势一致的差异基因，富集分析发现差异表达基因主要集中于免疫信号调节和免疫细胞分化等相关通路。前瞻性验证队列共纳入 60 例脓毒症患者，其中 SIC 患者 29 例，非 SIC 患者 31 例， Q-PCR 验证结果发现仅有 LGALS2 的表达在 SIC 和非 -SIC 患者中存在显著差异，SIC 患者外周血 LGALS2 的表达量相比非 SIC 患者降低更为显著。LGALS2 诊断 SIC 的效能优于 APTT,FDP 和 D-dimer。

结论 脓毒症相关凝血病患者基因表达存在差异，LGALS2 可能是预测和治疗 SIC 的潜在生物标志物和新的作用靶点。

中国临床金黄色葡萄球菌对磷霉素耐药性分析及耐药机制研究

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目的 磷霉素在近年来越来越多地被单独或联合用于临床金黄色葡萄球菌感染的治疗。在本研究中，我们旨在评估中国临床金黄色葡萄球菌分离株对磷霉素的耐药情况，并揭示其主要的耐药机制。

方法 我们对来自全国 22 家医院的 1900 株金黄色葡萄球菌通过琼脂稀释法测定磷霉素的最小抑菌浓度 (MIC)，同时通过生物信息学分析明确其中 471 株进行了全基因组测序的甲氧西林耐药金黄色葡萄球菌 (MRSA) 的磷霉素 MIC 值在不同克隆复合体中的分布情况。通过 ResFinder 和 Snippy 检测已测序 MRSA 菌株中的磷霉素修饰酶基因的携带情况及其他关键磷霉素耐药基因的突变情况。

结果 1900 株金黄色葡萄球菌的磷霉素敏感率为 83.74%，其 MIC 范围为≤ 0.125 mg/L 至≥ 256 mg/L。其中 763 株 MRSA 的磷霉素耐药率为 38.27%，而 1137 株甲氧西林敏感金黄色葡萄球菌（MSSA）的耐药率仅为 1.5%。根据 471 株测序 MRSA 的 MLST 分型显示不同谱系间的磷霉素敏感性存在差异。属于 CC59 克隆复合体（中国主要社区获得性克隆）的所有 MRSA 对磷霉素均敏感，而来自医院获得性克隆 CC5 和 CC239 的 MRSA 对磷霉素表现出耐药性，耐药率分别为 75% 和 51.72%。91.67% 的磷霉素耐药 CC5 MRSA 的 MIC 值≥ 256 mg/L，而 86.67% 的磷霉素耐药 CC239 MRSA 的 MIC 值在 64 mg/L 至 128 mg/L 之间。几乎所有磷霉素耐药的 CC5 MRSA 均在参与编码磷霉素转运系统的基因 glpT 和 hptRSA/uhpT 中存在突变，而大多数耐磷霉素的 CC239 仅在 hptR 基因中存在突变。所有 ST764 分离株均携带 fosD 基因，仅一株 ST88 分离株携带 fosB4 基因。

结论 磷霉素对临床金黄色葡萄球菌仍表现出有效性，特别是对 MSSA 和社区获得性 MRSA 显示出很好的抗菌活性。MRSA 的主要磷霉素耐药机制涉及转运蛋白的突变。

MRSA ST764 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（MRSA）是一种机会性、多功能致病菌。MRSA ST764 克隆在中国、日本和其他亚洲地区的流行增加。然而，目前我国 MRSA ST764 的基因特征和毒力特征的了解仍然有限。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 ST764 菌株的分子克隆特征，并重点关注涉及患者和 ICU 环境的传播事件（transmission events，TEs）。

方法 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 ST764 菌株之间的亲缘关系，研究其传播情况。此外，通过与其他来源 ST764 菌株比较，进一步分析本研究中获得的 MRSA ST764 分离株的毒力特征。

结果 本研究共收集 16 株 MRSA ST764 菌株，cgMLST 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（图 1a），MRSA 在 ICU 中的时间上和空间上的传播模式见图 1b。本研究中 ST764 菌株表现为多重耐药性，且 93.8% 菌株携带消毒剂耐药基因 qacB，表明其高度适应了大量使用抗生素和消毒剂的医院环境（图 2a）。此外，本研究中 ST764 菌株的 agrB 基因被转座子 IS1181 打断，agr 功能缺陷，表型上表现为溶血能力下降、α－毒素表达下降、RNA Ⅲ转录水平下降，而生物膜形成能力上升（图 2b）。

结论 本研究中，agr 突变的 ST764 是 ICU 院内 MRSA 定植的优势克隆株，WGS 也确定了 ICU 环境内和环境与患者甚至医护人员之间可能存在的 MRSA ST764 传播事件。综上所述，积极监测 MRSA 定植情况以及 agr 突变情况，结合去定植和及时隔离治疗，有助于预防 MRSA 定植、感染和传播。

多黏菌素 B 治疗感染 CRO 肾移植患者相关性急性肾损伤的影响因素分析

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目的 对感染碳青霉烯类耐药革兰氏阴性杆菌（CRO）的肾移植患者在使用多黏菌素 B（PMB）治疗中出现的急性肾损伤（AKI）进行影响因素分析，为其合理用药提供临床依据。

方法 采用病例对照研究设计方案。收集 2020 年 1 月至 2023 年 10 月在中南大学湘雅二医院肾移植后接受 PMB 治疗 3 天以上感染碳青霉烯类耐药革兰氏阴性杆菌（CRO）患者的临床资料。依据患者在临床治疗过程中是否发生急性肾损伤（AKI）分为 AKI 组和非 AKI 组，对比分析两组患者的临床资料。将单因素分析中有统计学差异的变量以及有重要临床意义的变量纳入 Logistic 回归分析模型进行 PMB 治疗相关性 AKI 的多因素分析。

结果 研究共纳入 96 例感染碳青霉烯类耐药革兰氏阴性杆菌（CRO）肾移植患者，其中 AKI 组患者 48 例，非 AKI 组患者 48 例。AKI 组 48 例患者平均年龄为 48.08 ± 12.03 岁，平均体重为 59.29 ± 11.44 Kg，男女比为 41/7；非 AKI 组平均年龄为 46.27 ± 11.19 岁，平均体重 58.54 ± 11.47 Kg，男女比 31/17。单因素分析结果显示：住院天数、男女性别比、入住 ICU、连续性肾脏替代治疗（CRRT）、用药前的肌酐清除率（Ccr）、PMB 每日剂量、PMB 总剂量、PMB 疗程以及同时使用糖肽类、噁唑烷二酮、呋塞米 > 20 mg/day、托拉塞米 > 10 mg/day、他克莫司、地塞米松药物等因素在两组间的差异均有统计学意义（P<0.05）。多因素 Logistic 回归分析结果显示：与非 AKI 组相比，AKI 组中用药前的肌酐清除率 Ccr（OR=0.961,P=0.026）及联合使用呋塞米 > 20 mg/day（OR=4.122,P=0.014）与 PMB 相关性肾毒性的关联均具有统计学意义（P<0.05）。

结论 用药前的肌酐清除率（Ccr）和联合使用呋塞米 > 20 mg/day 是肾移植患者使用 PMB 治疗相关性 AKI 的影响因素。

基于单细胞转录组测序技术的肺曲霉菌感染的免疫机制研究

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目的 肺曲霉病是指曲霉孢子侵入肺部，引起严重免疫反应和组织损伤的肺部真菌感染性疾病，死亡率高，发病机制尚未完全阐明。本研究运用单细胞转录组测序（Single-Cell RNA Sequencing，scRNA-seq）技术探索肺曲霉病的免疫炎症机制。

方法 于宁波大学附属第一医院招募符合入组标准的肺曲霉病患者和健康对照者的肺泡灌洗液，每组各 3 人，制备成单细胞悬浮液，进行 scRNA-seq，对测序数据进行分析。之后建立曲霉感染细胞模型，使用 PCR 验证测序数据的准确性及可靠性。

结果 研究结果显示在中性粒细胞亚群的分析中，发现了两种新的中性粒细胞亚群（Neutrophils_FABP4 和 Neutrophils_GBP4），它们在抗曲霉菌感染过程中发挥着不同的作用。在巨噬细胞亚群分析中，发现曲霉感染组富集 Macrophages_CXCL10 亚群，既表达 M2 巨噬细胞 marker 基因，又存在促炎表型，上调炎症反应，但吞噬功能减弱。在 T 和 NK 细胞亚群分析中，发现曲霉感染组 T 和 NK 细胞亚群呈现免疫抑制状态，TIGIT 或许是 T 和 NK 细胞抗真菌感染的新型免疫治疗靶点。在肺上皮细胞亚群分析中，发现曲霉菌感染引起肺上皮细胞代谢和生物功能受损，特别是抗原提呈功能。

结论 曲霉感染组和健康对照组在免疫细胞数量、免疫细胞亚群细胞比例、功能分析、基因表达和分化轨迹等多个方面存在显著差异。

动态血脂谱对新冠肺炎患者死亡率的预测价值

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目的 基于动态数据评估血脂异常对新冠肺炎死亡率的预测能力。

方法 采用回顾性观察性研究设计方案，共纳入 2020 年 1 月 1 日至 3 月 26 日期间入院的 135 名新冠肺炎患者。

结果 研究发现，感染新冠肺炎并死亡的患者在住院初期表现出持续的血脂异常，包括总胆固醇（TC）、高密度脂蛋白（HDL）和低密度脂蛋白（LDL）水平降低，而甘油三酯水平升高。值得注意的是，无论是 TC、HDL 和 LDL 的绝对值还是其变化值均与死亡率密切相关，这三个指标及其变化值在所有时间点的曲线下面积（AUC）均大于 0.7。尤其在第 3 周，TC、HDL 和 LDL 的 AUC 分别为 0.891、0.895 和 0.879，而它们第 1 周至第 3 周变化值的 AUC 分别为 0.975、0.950 和 0.925。Spearman 相关性分析显示，TC、HDL 和 LDL 与 C 反应蛋白、D- 二聚体、尿素氮、肌酸激酶和 B 型钠尿肽在各个时间点上显著相关。

结论 第三周的血脂水平及从第 1 周至第 3 周血脂水平的变化值对于预测新冠肺炎死亡率尤为重要。医疗卫生工作者应密切关注新冠肺炎患者的血脂动态变化。

In vitro activity of cefiderocol against carbapenem-resistant Escherichia coli (CREC): A multicenter study in China

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Abstract Content CREC is a significant concern globally due to its resistance to carbapenem antibiotics, with Escherichia coli being a major contributor to infections. Cefiderocol, a novel cephalosporin antibiotic, has shown promise in treating multidrug-resistant Gram-negative bacteria, including CRE. This study aims to investigate the antimicrobial susceptibility of CREC isolates in China to cefiderocol and other agents, along with identifying primary resistance mechanisms in cefiderocol-resistant isolates.

Methods A total of 638 non-duplicate clinical CREC isolates were collected from 27 hospitals across 24 provinces and municipalities in China between January 1st, 2019, and October 31st, 2022. Minimum inhibitory concentrations (MICs) of antimicrobial agents were determined by using agar dilution and broth microdilution methods. Whole-genome sequencing was employed for resistance mechanism studies.

Results In vitro testing of 16 antimicrobial agents against all CREC isolates revealed that tigecycline exhibited the highest antibacterial activity (100%), followed by colistin (95.65%) and cefiderocol (82.76%). The MIC50 and MIC90 of cefiderocol were determined to be 2 mg/L and 128 mg/L, respectively. Among 99 cefiderocol-resistant Escherichia coli isolates, sequence type 167 (ST167) accounted for the highest proportion at 58.16%.Among the cefiderocol-resistant strains, 96 strains exhibited mutations or deletions in the cirA gene, leading to truncated translation, and all of these strains exhibit NDM production.

Conclusion Cefiderocol demonstrates potent antibacterial activity against carbapenem-resistant Escherichia coli in China. The primary resistance mechanisms to cefiderocol in CREC involves the synergistic effects of CirA inactivation and NDM production.

The downregulation of Tapasin in dendritic cell regulates CD8+ T cell autophagy to hamper hepatitis B viral clearance in the induced pluripotent stem cell-derived hepatocyte organoid

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Abstract Content Tapasin, a crucial molecular chaperone involved viral antigen processing and presentation, plays an important role in antivirus immunity. However, its impact on T cell differentiation in the context of virus clearance remains unclear.

Methods In this study, we employed induced pluripotent stem cells to differentiate into hepatocyte-like cell, which were subsequently inserted to the inverted colloidal crystal scaffolds, thus establishing a hepatocyte organoid (HO). By inoculating hepatitis B virus (HBV) particles in the system, we successfully engineered a robust in vitro HBV infection model for at least 3 weeks. Furthermore, we aimed to explore the effects of lentivirus-mediated short hairpin RNA (shRNA) targeting human Tapasin on the differentiation and antiviral function of CD8+ T cells. Specifically, we transfected dendritic cells (DCs) with Tapasin-shRNA and cocultured with T cells.

Results The results demonstrated that Tapasin-shRNA transfected DCs effectively suppressed T cell proliferation and impeded HBV-specific cytotoxic T lymphocyte responses. Our investigation also revealed the role of mTOR pathway activation in reducing autophagy activity within CD8+ T cells. Expressions of autophagy-related proteins, beclin-1, LC3II/ LC3I were decreased and PI3K/AKT/mTOR activity was increased in Tapasin-shRNA group.

Conclusion Collectively, our findings elucidate that shRNA targeting the Tapasin gene within DCs inhibits T cell differentiation by reducing autophagy activity to hamper viral clearance in the HBV-infected HO.

低频超声通过抑制 TNFR1-NF-κB 途径减轻肺炎克雷伯菌诱导的小鼠肺部炎症

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目的 低频超声（LFU）已被报道可以协同抗菌药增强体内外抗菌活性。本实验探究了 LFU 对肺炎克雷伯菌（Kp）诱导的小鼠肺部炎症的抗炎和免疫调节作用。

方法 小鼠肺部接种菌液于不同感染时间点接受 270 mW/cm2、29.36 kHz 的 LFU 作用 10 min。转录组测序发掘与 LFU 作用有关的基因及免疫调节途径；RT-qPCR 检测小鼠肺组织炎症因子 mRNA 含量；ELISA 检测支气管肺泡灌洗液（BALF）和血浆中炎症因子蛋白表达水平；Western-blot 和免疫荧光检测 TNFR1、p65、p-p65、IκBα 和 p-IκBα 蛋白及 p65 荧光强度。流式细胞术检测外周血细胞和 BAL 细胞中 M1/M2、Th1/Th2、Th17/Treg 免疫细胞分型及占比。

结果 Kp 感染 48 h（感染恢复期）接受 LFU 作用，具有促炎效应的炎症因子基因下调，这种潜在的抗炎作用可能与 LFU 抑制 TNFR1-NF-κB 途径有关。在 Kp 感染恢复期，TNFR1-NF-κB 途径被激活，小鼠 BALF 和血浆中炎症因子升高；LFU 作用后在基因和蛋白水平上降低了小鼠肺组织和 BALF 中的 TNF-α、IL-17 和 GM-CSF 的含量。LFU 主要减少了胞质 p-p65 和胞核 p65 的蛋白水平及 p65 向细胞核的位移。270 mW/cm2、29.36 kHz、10 min 的 LFU 的抗炎效应与腹腔注射单剂 20 mg/kg NF-κB 抑制剂的抗炎效果相当，均能在基因和蛋白水平减少感染恢复期小鼠炎症因子含量，抑制 p65 向细胞核的位移；但在给予 NF-κB 抑制剂后再给予 LFU 作用，双重抑制效果不佳。接受 LFU 作用的小鼠 BAL 细胞中抗炎表型免疫细胞，如 M2 型巨噬细胞、Th2 和 Treg 淋巴细胞，占比有所增加。

结论 LFU 可以通过抑制 TNFR1-NF-κB 途径以减轻 Kp 诱导的小鼠肺部炎症的严重程度，是一种潜在的免疫调节疗法。因此，结合前期研究基础，LFU 可以同时兼具协同抗菌和炎症调节。

mNGS 技术在危重症患者病原学诊断中的应用价值

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目的 探讨宏基因组二代测序（mNGS）在 ICU 住院危重症患者病原学诊断中的应用价值。

方法 选取 2021 年 6 月至 2022 年 2 月 在 ICU 住院的危重症患者 57 例，即临床拟诊脓毒血症患者 41 例和颅内感染患者 16 例，分别采集血液和脑脊液应用 mNGS 技术和常规培养法进行检测，分别记录病原体检出率及病原体分布情况，以常规培养法为金标准，评价 mNGS 技术对病原体检测的灵敏度。

结果 57 例送检标本中 mNGS 技术共检测出病原体 21 例（36.84%），其中血液标本检出病原体 19 例；脑脊液标本检出病原体 2 例，常规培养法共检出病原体 7 例（12.28%），其中血液标本检出病原体 5 例而脑脊液标本检出病原体 2 例，两种检测方法比较，病原体的阳性检出率差异有统计学意义（P<0.01）。在脑脊液标本中，两种方法的检测效能是一致的；常规培养法检测的 7 例阳性患者，用 mNGS 技术检测出相同的病原体，但是， mNGS 技术比常规培养法多检测出 14 例阳性，mNGS 技术和常规培养法在诊断危重症患者病原体的灵敏度、特异度比较，差异有统计学意义（P<0.01）。

结论 对 ICU 住院危重症患者，采用 mNGS 技术检出的病原体株数多于常规培养法，可作为常规培养法的有效补充。mNGS 技术具有快速、高效的特点，其结果结合临床综合分析能为临床早期合理用药提供指导。

医院获得性肺炎患者多粘菌素 B 的药代动力学及其影响因素分析

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目的 本研究旨在探索 HAP 患者中多粘菌素 B 的药代动力学及其影响因素。

方法 本研究回顾性纳入 2020 年 1 月至 2023 年 7 月，入住东南大学附属中大医院 ICU 接受多粘菌素 B（PMB）治疗的 HAP 患者。排除经单独雾化或其他非静脉途径使用 PMB、未监测 PMB 稳态血药浓度以及用药时间小于 72 小时的患者。入组后记录患者一般人口学特征、基线血常规、肝功能、肾功能等化验指标、器官支持情况、患者致病菌种类及药敏结果、PMB 用药时间及剂量、PMB 稳态剂量（第 6 剂）用药前血药浓度 / 谷浓度（Cmin）、用药后 1 小时血药浓度 / 峰浓度（Cmax）、用药后 6 小时血药浓度（C6h）、以及 24 小时内药物浓度 – 时间曲线下面积（AUC）等药代动力学（PK）指标。

结果 1. 入组患者 PMB 药代动力学参数特征

本研究共纳入了 125 名患者，PMB 的 AUC 为 81.7(55.8, 110.0)mg · h/L，Cmax 为 6.7(5.1, 9.9)mg/L，Cmin 为 1.5(0.8, 2.4)mg/L，C6h 为 2.7(1.5, 4.2)mg/L。

2. PMB 药代动力学参数的影响因素分析

2.1 患者基础肾功能影响 PMB 药代动力学参数

将入组患者根据有无肾功能不全（GFR<90 ml/min）分组，肾功能不全组患者 PMB 的 Cmax[P=0.002] 及 Cmin[P=0.030] 显著高于肾功能正常组患者。两组之间 PMB 的 C6h 以及 AUC 无统计学差异。

2.2 同时接受 CRRT 治疗影响 PMB 药代动力学参数

将入组患者分为 CRRT 组与非 CRRT 组，CRRT 组患者 PMB 的 C6h[P=0.001] 及 Cmin[P=0.002] 显著低于非 CRRT 组患者。两组之间 PMB 的 Cmax 以及 AUC 无统计学差异。

结论 HAP 患者在应用 PMB 治疗时，基础肾功能下降以及在用药期间接受 CRRT 治疗显著影响 PMB 的药代动力学参数。

不同益生菌补充治疗对于干细胞移植患者感染的影响

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目的 评估接受造血干细胞移植期间患者服用联合双歧杆菌四联活菌片及凝结芽孢杆菌活菌片（五联）相对于单独服用双歧杆菌四联活菌片（四联）的临床特征，为预防移植患者感染提供初步研究依据。

方法 回顾性分析 2023 年 4 月至 2023 年 8 月在华中科技大学同济医学院附属协和医院接受造血干细胞移植治疗的同时服用了四联或五联益生菌患者的临床资料。根据他们服用的益生菌方案分为四联组（20）和五联组（32）。对于连续变量和等级资料比较采用 Mann-Whitney U 检验，对于无序分类变量比较采用卡方检验或 Fisher 精确概率法。采用二元 logistic 回归进行单因素及多因素分析，以验证预测 NGS 阳性的变量。

结果 相对于五联组，四联组患者 NGS 阳性率显著增加（60% vs. 3.1%，$p < 0.001$），发热性中性粒细胞减少率增加（65% vs. 28.1%，$p = 0.009$），发热≥ 38℃的中位时间更长（1.50 天 vs. 0，$p = 0.009$），且中性粒细胞植入的中位时间延长（10 天 vs. 11.5 天，$p = 0.037$）。多因素分析显示，五联益生菌的使用（OR = 0.017，95% CI 0.001-0.185，$p < 0.001$）是发生 NGS 阳性的保护因素， 口腔粘膜炎（OR = 10.794，95% CI 1.503-77.502，$p < 0.018$）与发生 NGS 阳性的风险增加独立相关。

结论 五联益生菌方案可能有助于预防接受造血干细胞移植的患者发生感染，并且不影响患者造血重建及移植结局。

多粘菌素 B 药代动力学参数与 HAP 患者临床预后的相关性研究

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目的 本研究旨在探讨多粘菌素 B（PMB）药代动力学参数与 HAP 患者临床预后之间的相关性。

方法 本研究为回顾性纳入 2020 年 1 月至 2023 年 7 月，入住东南大学附属中大医院 ICU 接受 PMB 静脉使用治疗 HAP 的患者。排除经单独雾化或其他非静脉途径使用 PMB、未监测 PMB 稳态血药浓度、用药时间小于 72 小时以及接受 CRRT 治疗的患者。入组后记录患者一般人口学特征、基线化验指标、患者病原学类型及药敏结果、PMB 用药时间及剂量、PMB 稳态剂量（第 6 剂）用药前血药浓度 / 谷浓度（Cmin）、用药后 1 小时血药浓度 / 峰浓度（Cmax）、用药后 6 小时血药浓度（C6h）、以及 24 小时内药物浓度 – 时间曲线下面积（AUC）等药代动力学指标。本研究中，细菌清除定义为在应用 PMB 治疗期间，连续两次痰 / 肺泡灌洗液中原致病菌培养阴性。药物相关性肾损害定义为在应用 PMB 治疗期间发生 AKI（根据 KDIGO 指南诊断及分级标准）。

结果 1. 入组患者一般人口学情况及基线特征

本研究共纳入 76 名 HAP 患者，患者的 APACHE Ⅱ评分为 22(17, 28) 分，SOFA 评分为 8(5, 10) 分，44(57.9%) 名患者基础合并感染性休克。

2.PMB 的 AUC ≥ 83.12mg · h/L 与细菌清除率升高相关

对 PMB 药代动力学参数进行受试者工作特征曲线（ROC）分析，AUC 预测患者细菌清除的 ROC 曲线下面积为 0.661，最佳预测阈值为 83.12mg · h/L，P=0.045。

3. PMB 的 AUC ≥ 106.69mg · h/L 与 AKI 发生率升高相关

对 PMB 药代动力学参数进行 ROC 曲线分析，AUC 预测患者发生 AKI 的 ROC 曲线下面积为 0.637，最佳预测阈值为 106.69mg · h/L，P=0.045。

结论 在 HAP 患者中，PMB 的 AUC ≥ 83.12mg · h/L 与患者细菌清除率的升高相关，AUC ≥ 106.69mg · h/L 与患者发生 AKI 的风险增加相关。

VAP 患者静脉联合雾化应用多粘菌素 B 的 PK/PD 临床研究

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目的 本研究旨在探究在多重耐药菌（MDR）引起呼吸机相关性肺炎（VAP）的患者中多粘菌素 B（PMB）静脉联合雾化途径是否能够提高肺组织药物浓度，以及是否能改善患者的临床预后。

方法 本研究为单中心、前瞻性、观察性队列研究。筛选入住东南大学附属中大医院中重症医学科住院接受 PMB 治疗的 VAP 患者。按照临床医师医疗决策，患者在接受 PMB 治疗的 24 小时内被纳入研究，根据其临床实际用药情况，分别纳入单独静脉注射（IV）PMB 组与静脉联合雾化（IV+IH）用 PMB 组，记录所有患者用药前、用药时以及用药后一般资料。分别于两组患者稳态（第 6 剂）用药后 1、6、12 小时收集外周血标本及支气管肺泡灌洗液（BALF）标本，标本经 1500g 离心 10 分钟处理后，取上层血浆液及 BALF 清液放置于 -80℃冰箱保存，用于检测 PMB 药物浓度及尿素氮浓度。使用高效液相色谱法测量 PMB 和尿素氮在血浆和 BALF 液中的浓度，通过尿素扩散法计算肺泡上皮衬液（ELF）中 PMB 的浓度。使用 DAS2.0 数据分析软件计算药代动力学参数。观察患者至开始用药后第 28 天。主要观察指标为两组患者血浆及 ELF 的 PMB 药物浓度。

结果 1. 入组患者一般人口学情况及基线特征

本研究共纳入 17 名患者。两组患者在一般人口学特征、基线病情严重程度、基线实验室检查指标、PMB 治疗剂量等情况间均无明显差异（$P > 0.05$）。

3. IV+IH 和 IV PMB 在 MDR VAP 患者外周血和 ELF 中的 PK/PD 差异

IV+IH 组与 IV 组患者血浆 PMB Cmax、C6h、Cmin 均无显著差异（$P>0.05$）。IV+IH 组患者的 PMB ELF Cmax、C6h、Cmin 显著高于 IV 组（$P<0.05$）。IV 组患者 ELF 药物浓度低于仪器检测下限。

结论 在 MDR 致 VAP 患者中，PMB 静脉联合雾化治疗能显著提高患者肺组织药物浓度。

营养支持时机对不同病原菌所致脓毒症患者预后的影响：一项单中心、回顾性、队列研究

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目的 脓毒症患者营养支持时机仍存在争议。基础研究证据显示在细菌和病毒感染所致脓毒症模型中，积极的营养支持策略对两个模型的预后有相反的影响。本研究旨在评估营养支持时机对细菌和病毒感染所致脓毒症患者预后的影响。

方法 本研究采用单中心、回顾性、队列研究方法，纳入 2016 年 6 月 1 日至 2023 年 6 月 30 日入住东南大学附属中大医院重症医学科（ICU）并诊断为脓毒症的成人患者。收集患者的临床资料进行分析。早期营养支持定义为诊断脓毒症 48 小时内开始实施肠内或肠外营养，根据患者是细菌感染或病毒感染所致脓毒症进行分层分析。使用包括倾向匹配 – 逆概率加权和多元逻辑回归的双重稳健的方法分析评估营养支持时机对脓毒症患者住院病死率的影响。

结果 研究纳入 2278 例脓毒症患者，其中细菌感染 2159 例，病毒感染 119 例。在细菌感染患者中，早期营养支持组比延迟营养支持组患者的年龄更大、BMI 和 SOFA 评分更低、男性患者更多。

经矫正混杂因素后，在病毒感染所致脓毒症患者中，与延迟营养支持相比，早期营养支持对细菌感染组患者住院病死率无显著影响 (aOR, 0.97; 95%CI, [0.94, 1.01]; p=0.156)，但显著增加细菌感染组患者住院时间 (aMD, 3.20 ; 95%CI, (0.76, 5,65); p=0.010)。在病毒感染所致脓毒症患者中，早期营养支持患者的住院病死率 (aOR, 0.78; 95%CI, [0.62, 0.98]; p=0.044) 和 ICU 病死率 (aOR, 0.78; 95%CI, (0.62, 0.98, p=0.044) 显著低于延迟营养支持患者。在针对总体患者的亚组分析发现，男性、年龄≥ 70 岁、营养风险高的患者更能够从早期营养支持中获益。

结论 早期营养支持降低病毒感染所致脓毒症患者的住院病死率；对细菌感染所致脓毒症患者的住院病死率无显著影响，但增加细菌感染患者的住院时间和机械通气时间。

支气管扩张患者合并活动性肺结核风险因素分析及列线图预测模型的建立

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目的 探讨支气管扩张患者发生活动性肺结核的风险因素，并建立列线图预测模型。

方法 选择近 5 年广东医科大学附属医院及附属第二医院住院治疗的支气管扩张合并活动性肺结核患者 390 例为病例组，同期支气管扩张合并其他感染的患者 818 例为对照组。首先，使用单因素与 LASSO 回归分析筛选潜在的风险因素，随后使用 LASSO 回归分析的结果进行多因素 Logistic 回归分析，并建立列线图预测模型。校准曲线、C 指数、ROC 曲线用于评估模型的有效性，Bootstrap 方法用于内部验证。

结果 Lasso 回归分析筛选出 28 个潜在的风险因素。多因素分析结果提示：年龄、性别、TC、ALB、FIB、LYM、MCV、PDW、咯血和高血压是独立的风险因素。每个指标都有相应的分数，总分为各指标得分的总和，分数的高低与支气管扩张患者发生活动性肺结核的概率成正比。C 指数为 0.762（95%CI：0.733-0.791），Bootstrap 法内部验证的 C 指数为 0.753，AUC 为 0.762，暗示了模型的良好辨别力和预测意义。临床决策分析提示，当患者和医生的阈值概率分别为 4% 和 90% 时，列线图模型对肺结核感染风险的预测能够带来更多的收益。

结论 利用血清学等特征构建的列线图模型对评估支气管扩张患者合并活动性肺结核有重要的临床价值。

多黏菌素 B 治疗碳青霉烯耐药革兰阴性杆菌所致血流感染的疗效与安全性分析

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目的 评估多黏菌素 B 治疗碳青霉烯耐药革兰阴性杆菌（CR-GNB）所致血流感染的疗效与安全性

方法 回顾性分析南昌大学第一附属医院 2019 年 1 月 -2021 年 1 月接受多黏菌素 B 治疗的 CR-GNB 所致血流感染患者住院资料。

结果 共纳入 28 例患者，男女比 2.5，平均年龄 47.9 ± 15.7 岁。临床疗效：对 CR-GNB 所致血流感染，多黏菌素 B 临床治愈率达 64.3%；致病菌清除 3 例，假设清除 13 例，总清除率 57.1%；安全性：共 8 例发生（28.6%）不良反应，其中肾毒性 6 例（21.4%）；单因素分析显示多黏菌素 B 使用疗程是治疗失败的危险因素（$P < 0.05$）。

结论 对碳青霉烯耐药革兰阴性杆菌所致血流感染，以多黏菌素 B 为基础的足疗程抗感染方案可有效地缓解其症状及体征，具有更高的细菌清除率。

重症 COVID-19 患者继发细菌、真菌感染的危险因素与临床特征

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目的 确定重症 COVID-19 患者继发细菌、真菌感染的危险因素、发生率与临床特征，为临床减少或早期发现继发感染，及时精准治疗提供理论依据。

方法 分析 2022 年 12 月 -2023 年 12 月入住郑州大学附属郑州中心医院 ICU 的 151 例重症 COVID-19 患者，重症包括重型与危重型。根据入 ICU48 小时后病原学检出情况，分为继发感染组 (SI 组) 与未继发感染组 (NSI 组)，组间比较基线信息、治疗措施、转归等；确定影响继发感染的相关因素，分析 SI 组病原菌分布情况。

结果 纳入研究的 151 例重症 COVID-19 患者中，SI 组 91 例 (60.26%)，NSI 组 60 例 (39.74%)，多因素 logistic 回归分析显示查尔森合并症指数，入 ICU 时急性生理学与慢性健康状况评分、氧合指数、淋巴细胞计数和行有创机械通气 (IMV) 是重症 COVID-19 患者继发感染的相关危险因素（$P < 0.05$）。SI 组共收集病原菌 328 株，以革兰氏阴性菌为主（65.4%），其次是真菌（20%）和革兰氏阳性菌（14.6%）。继发呼吸道感染最常见，主要致病菌为鲍曼不动杆菌（25.21%）、肺炎克雷伯菌（17.65%）、曲霉菌（11.76%）、洋葱伯克霍尔德（7.98%）和铜绿假单胞菌（6.30%）。其中，耐碳青霉烯类的鲍曼不动杆菌（CRAB）与肺炎克雷伯杆菌（CRKP）检出率高，分别占两者的 96.67% 和 92.86%。继发血流感染次之，常见鲍曼不动杆菌（22.73%）和凝固酶阴性葡萄球菌（15.91%），CRAB 检出率为 90%。与 NSI 组相比，SI 组的 ICU 住院时间、总住院时间和 28 天死亡率均显著增加（$P < 0.05$）。

结论 重症 COVID-19 患者易继发细菌、真菌感染，增加治疗难度。在高风险患者中，需高度重视并尽早明确、及时干预，提高生存率。继发感染以耐碳青霉烯类革兰阴性菌为主。呼吸道中洋葱伯克霍尔德菌与血流中凝固酶阴性葡萄球菌的检出较既往研究增多。

RT-LAMP 诊断寨卡病毒感染的系统评价和 Meta 分析

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目的 寨卡病毒是黄病毒科的一个成员。这种病毒通常通过受感染的蚊子传播，并可导致各种疾病，如格林 - 巴利综合征。ZIKV 的快速可靠诊断对其早期诊断、治疗和预后至关重要。近年来，一种名为环介导等温扩增（LAMP）的新技术已成功应用于 ZIKV 相关疾病的快速检测。因此，在本研究中，我们进行了一项荟萃分析，以评估 LAMP 检测 ZIKV 的诊断效率。

方法 我们在 PubMed、Embase、Cochrane Library 和 Web of Science 数据库中搜索了 LAMP 用于检测 ZIKV 的原始研究。然后，我们使用 QUADAS-2 工具独立提取数据并评估研究质量。我们对 I2 统计数据进行了分析，以评估异质性的存在，并利用 Deek 漏斗图来评估潜在的发表偏倚。我们使用 Meta disc1.4 软件构建显示集灵敏度（SEN）、特异性（SPE）等的森林图。我们计算了曲线下面积（AUC）和诊断优势比（DOR），以评估通过灯检测 LAMP 的总体效率。

结果 最终共有五项研究和九个样本被纳入本次评估。ZIKV 检测的综合敏感性和特异性分别为 70%（95%CI:0.64-0.76）和 82%（95%CI:0.77-0.87）。正似然比（PLR）、负似然比（NLR）和 DOR 分别为 3.86（95%CI:1.61-9.26）、0.40（95%CI:0.24-0.65）和 14.01（95%CI:3.67-53.52）。此外，AUC 为 0.8642，Deek 图表明这些研究中没有发表偏倚。

结论 我们的研究结果表明 LAMP 在检测 ZIKV 方面具有高灵敏度和特异性。与聚合酶链式反应（PCR）相比，LAMP 是一种更便宜、更容易诊断 ZIKV 的方法。然而，额外的证据对于确认 LAMP 是否可以用作识别 ZIKV 的临床诊断标准至关重要。

A single center retrospective clinical epidemiological study on infections in renal transplant recipients

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Abstract Content Objective To study the epidemiological and clinical characteristics of infection in renal transplant recipients in this region and the risk factors affecting the outcome of the disease.

Methods A total of 196 cases of renal transplant recipients with infection were collected from January 2012 to December 2021 in The First Hospital of China Medical University. The time of renal transplant recipients with infection, immunosuppression regimen, infection site, pathogen, clinical symptoms and signs, laboratory indicators, treatment and disease outcome were retrospectively analyzed.

Results In 196 cases of renal transplant recipients with infection, male (53.06%) was slightly more than female (46.94%), the average age was 47.91±13.26 years old, and hypertension (60.71%) was the most common underlying disease. The most common sites of infection in renal transplant recipients in our hospital were: pneumonia (43.88%), urinary tract infection (20.41%) and multi-site infection (11.22%). Among the cases with identified pathogens, the most common pathogen of pneumonia was Pneumocystis jirovecii (18 cases); the most common pathogen of urinary tract infection was Escherichia coli (6 cases); and the most common pathogen of multi-site infection was Escherichia coli (10 cases). According to the infection pattern after solid organ transplantation, 137 cases of infection occurred more than 12 months after surgery (69.90%). Among the 4 cases of perioperative - 1 month after surgery, 2 cases of cases with identified pathogens were multi-site infection, and mixed infection, both isolated ESBLs-producing gram-negative bacilli; 1 month - 6 months and 6 months - 12 months after surgery, opportunistic pathogens were the most common, such as Pneumocystis jirovecii and CMV, but the proportion of bacterial infections increased from 6 months to 12 months after surgery; more than 12 months after surgery, bacterial infections were mainly seen, among which Escherichia coli was the most common (12 cases). Of the 196 cases of renal transplantation infection, 184 (93.88%) cases improved, 11 (5.61%) cases of graft failure, and 1 (0.51%) case died.

Conclusion The most common infections among kidney transplant recipients in this region are pneumonia and urinary tract infections. According to the infection pattern after solid organ transplantation, bacterial infection was the main infection during perioperative period to one month after surgery in this

region, and ESBLS-positive gram-negative bacilli should be vigilant. Opportunistic pathogens were the most common infections at 1 to 6 months and 6 to 12 months after surgery. Pneumocystis yersii and CMV were the pathogens that needed attention, but the proportion of bacterial infections at 6 to 12 months after surgery increased compared with the previous period. Most infections in kidney transplant recipients occur more than 12 months after surgery and are mainly bacterial infections. Days in hospital and creatinine value at admission are risk factors for poor prognosis of infection in renal transplant recipients. BMI and other surgical history are risk factors for recurrent infection in kidney transplant recipients, and length of hospital stay is protective factor for recurrent infection.

肾脏血流动力学联合生物标志物对脓毒症相关急性肾损伤患者肾脏预后的预测价值

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目的 联合肾脏血流动力学参数与生物标志物预测 SA-AKI 患者的肾脏预后。

方法 本研究为单中心、前瞻性、观察性研究，纳入东南大学附属中大医院重症医学科 SA-AKI 患者。患者入组第 1 天进行肾脏超声检查，测量肾血流半定量评分（SQP）、肾动脉阻力指数（RRI）、超声造影参数，包括到达时间（AT）、达峰时间（Ttop）、峰值强度（PI）、半峰全宽时间（TWH）、曲线下面积（AUC）。同时留取患者的血液、尿液，测量血 NGAL、Cys-c、PENK、尿 CCL14 浓度。根据入组后第 7 天血清肌酐有无下降到 1.5 倍基础值以下，分为肾功能恢复组和未恢复组，采集患者临床资料，比较两组患者 SQP、RRI、超声造影参数、生物标志物浓度差异，采用受试者工作特征曲线下面积（AUROC）评价各指标对 SA-AKI 患者肾功能恢复的预测价值。

结果 研究共纳入 37 名 SA-AKI 患者，24 名（64.9%）患者肾功能未恢复，两组患者的性别、年龄、基线时的 SOFA 评分无统计学差异，肾功能未恢复组患者基线 APACHE II 评分较高。与恢复组患者相比，未恢复组患者 SQP、TWH、AUC 较低，RRI 较高。ROC 曲线分析显示，AUC 可以早期预测 SA-AKI 患者肾脏转归，AUROC 为 0.788。与肾功能恢复患者相比，未恢复组患者 NGAL、Cys-c 及 CCL14 明显升高。ROC 曲线分析显示，NGAL、CCL14 可以早期预测 SA-AKI 患者第 7 天肾功能恢复，AUROC 分别为 0.849、0.784。联合肾脏血流动力学指标与生物标志物，结果显示 AUC 联合 NGAL、AUC 联合 CCL14 对 SA-AKI 患者第 7 天肾脏转归具有较高的预测价值，AUROC 分别为 0.946、0.883。

结论 肾脏血流动力学联合生物标志物能够早期预测 SA-AKI 患者肾脏转归，AUC 联合 NGAL、AUC 联合 CCL14 对 SA-AKI 患者第 7 天肾脏转归具有较高的预测价值。

Pathogen spectrum and clinical characteristics in Lung cancer patients: a 10 years retrospective study

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Abstract Content Infection is the most common non-cancerous cause of death in lung cancer (LC) patients, yet there is a lack of original research reports with large sample sizes on the epidemiology, pathogen spectrum, immune status changes, and prognostic analysis among these patients.

Methods A retrospective study among LC patients with concurrent infections was performed at Guangxi Medical University Cancer Hospital from 2014 to 2023.

Results A total of 699 LC patients with concurrent infections were included. The data showed that the infectious incidence rate increased from 4.61% in 2014 to 9.77% in 2023 among LC patients. Of these, 90.56% (633 cases) of patients were diagnosed with proven infection, while 9.44% (66 cases) of patients were diagnosed with clinical probable infection. A total of 109 types of pathogens were detected. The most prevalent pathogenic organisms in each category were bacteria (Klebsiella pneumoniae [118, 17.03%] and Escherichia coli [77, 11.11%]), fungi (Candida spp. [25, 43.18%] and Aspergillus spp. [33, 37.50%]), viruses (COVID-19 [36, 40.45%] and EBV [28, 31.46%]), and special pathogens (Mycobacterium tuberculosis [59, 95.16%] and Mycoplasma pneumoniae [2, 3.23%]). The lung was the most commonly infected site. The pathogen spectrum differed among different subgroups. Specific pathogens were more common in stages IIIA-IIIC, while viruses were more likely to be found in stage IV. Mycobacterium tuberculosis and Klebsiella pneumoniae were the most common pathogens associated with community-acquired and hospital-acquired infections, respectively. Bacteria accounted for 92.91% and 71.02% of severe and non-severe infections, respectively. The incidence rates of severe infections varied significantly among different anti-tumor treatment regimens, with chemotherapy exhibiting the lowest rate (14.74%), and other treatment regimens (including radiotherapy, immunotherapy, and multi-line treatment, etc.) showing the highest rate (31.40%). Upon diagnosis of infection, total T lymphocytes, helper T cells, Th/Ts ratios, and B lymphocytes decreased, while natural killer cells and suppressor T cells increased. Other treatment regimens resulted in the largest changes in immune status before and after infection ($P < 0.001$). Mixed infections, hospital-acquired infections, and severe infections were all associated with higher mortality rates ($P = 0.037$, HR = 1.549; $P = 0.037$, HR = 1.277; $P < 0.001$, HR = 2.380). In contrast, targeted therapy and chemotherapy plus immunotherapy reduced the risk of death ($P = 0.001$, HR = 0.607; $P = 0.026$, HR =

0.662). COX analysis showed that other pathological types of tumors (poorly differentiated/undifferentiated carcinoma), bone metastases, brain metastases, and severe infections were poor prognostic factors, while targeted therapy, chemotherapy plus immunotherapy, and high IgM level were protective factors. ECOG performance status, neuroendocrine carcinoma, and hospital-acquired infections were risk factors for severe infections.

Conclusion This study reveals that the incidence rate of LC complicated with infections has been increasing annually. Infection is a crucial risk factor affecting the prognosis and mortality of LC. The susceptibility of LC to infection may be related to immunodeficiency resulting from anti-tumor treatment and disease progression.

内皮细胞外囊泡重编程单核细胞在脓毒症相关ARDS中的作用和机制研究

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目的 探明内皮细胞外囊泡（EC-EVs）在脓毒症相关 ARDS 中的作用及机制，为临床救治提供新的靶点和策略。

方法 经尾静脉向健康小鼠体内注入 LPS 刺激内皮细胞产生的 EC-EVs（L-EC-EVs），对照组小鼠注入生理条件下内皮细胞释放的 EVs（N-EC-EVs），通过肺组织病理评分、肺组织炎症因子水平检测评估 L-EC-EVs 的致病效应。将荧光标记的 L-EC-EVs 经尾静脉注入小鼠体内，明确单核细胞是 L-EC-EVs 的靶细胞。应用酶联免疫吸附实验、实时荧光定量核酸扩增技术和流式细胞术系统地探究 L-EC-EVs 对单核细胞表型和功能的影响。此外，通过对 N-EC-EVs 和 L-EC-EVs 进行蛋白质谱测序，并对这两种 EVs 分别处理的单核细胞进行转录组测序，以探明 L-EC-EVs 作用于单核细胞的分子机制。最后，回到临床验证脓毒症相关 ARDS 患者血浆中这部分 EC-EVs 的数量变化。

结果 L-EC-EVs 处理的小鼠肺组织炎症因子表达显著上调，且病理切片结果显示 L-EC-EVs 介导 ALI 的发生。注入小鼠体内的 L-EC-EVs 优先被肺部单核细胞摄取，耗竭外周单核细胞后，L-EC-EVs 介导的 ALI 减轻。体内外研究表明 L-EC-EVs 可以驱动单核细胞向促炎 M1 型巨噬细胞分化，而对组织驻留巨噬细胞表型没有显著影响。机制研究表明，L-EC-EVs 上过表达的 VCAM1 通过与单核细胞表面的 ITGA4 相互作用激活 NF-κB 通路，从而对单核细胞进行重编程，降低 EC-EVs 上的 VCAM1 水平或阻断单核细胞上的 ITGA4 可减弱这种作用。脓毒症相关 ARDS 患者血浆中 VCAM1+ EC-EVs 数量显著增加。

结论 脓毒症诱导的 ALI 期间循环 EC-EVs 靶向并重编程单核细胞向 M1 型巨噬细胞分化，进而介导 ALI 发生。L-EC-EVs 上高表达的 VCAM1 通过与单核细胞表面的 ITGA4 相互作用激活 NF-κB 通路进而重编程单核细胞。（已发表）

基于真实世界不同厂家美罗培南治疗肺部感染的有效性与安全性评价

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目的 基于真实世界数据评价不同厂家注射用美罗培南治疗肺部感染患者的有效性和安全性

方法 纳入 2023 年 1 月 -2023 年 6 月使用美罗培南治疗的肺部感染住院患者，按照注射用美罗培南的厂家将患者分为 A 组（江苏省集采中选品种）和 B 组（非江苏省中选品种）。比较两组的临床疗效、病原菌清除率、住院时间及不良反应

结果 研究共纳入 100 例患者，治疗后，A 组病原清除率为 76.5%，B 组病原清除率为 81.6%，两组患者病原清除率无显著差异；A 组患者白细胞减少 21.3%，B 组为 18.4%，A 组中性粒细胞比率减少为 15.5%，B 组为 11.4%，A 组超敏 C 反应蛋白减少为 159.3%，B 组为 113.9%，两组患者在白细胞计数和中性粒细胞比率减少上无显著性差异，超敏 C 反应蛋白减少率上 A 组优于 B 组（$P < 0.05$）；A 组患者平均住院时间 16.98 天，B 组患者平均住院时间 24.54 天，A 组患者平均住院时间短于 B 组（$P < 0.05$）；A 组患者总有效率为 78.4%，B 组患者总有效率为 67.3%，A 组患者经治疗后总有效率表现优于 B 组（$P < 0.05$）。不良反应方面，A 组发生 2 例胃肠道相关不良反应，不良反应发生率为 3.9%，B 组未发现不良反应，两组间不良反应发生率无显著性差异

结论 集采注射用美罗培南与非集采注射用美罗培南有效性和安全性均相似

喀什地区细菌性脑膜炎的临床特征及结局的回顾性研究

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目的 了解喀什地区细菌性脑膜炎的特征，为临床医生早期识别此病并制定合理的经验性治疗方案提供参考。

方法 检索喀什地区第一人民医院 2013 年 -2021 年 诊断为细菌性脑膜炎、化脓性脑膜炎、颅内感染的患者，根据入排标准，分为社区获得性细菌性脑膜炎、医院获得性细菌性脑膜炎，分析社区获得性细菌性脑膜炎、医院获得性细菌性脑膜炎的临床特点、病原体组成、药敏情况。

结果 共 355 例病例，社区获得性细菌性脑膜炎有 225 例（63.4%），医院获得性细菌性脑膜炎有 130 例 (36.6%)。社区获得性细菌性脑膜炎中，发热（99.1%）、头痛（97.7%）、意识障碍（66.4%）、颈强直（62.8%）、抽搐（51.0%）为最常见的临床表现。共分离出肺炎链球菌 37 株，其次是流感嗜血杆菌，共计 12 例，然后是金黄色葡萄球菌及脑膜炎奈瑟菌，各有 7 例、6 例。分离出来的肺炎链球菌有 6 例对青霉素耐药，耐药率为 18.18%（6/33）。医院获得性细菌性脑膜炎中，发热（86.1%）、头痛（97.7%）、颈强直（70.7%）、意识障碍（52.5%）是最常见的临床表现。最常分离出的病原体是鲍曼不动杆菌，共有 15 例，其次是凝固酶阴性葡萄球菌，共有 13 例。分离出来的鲍曼不动杆菌均为耐碳青霉烯类菌株。相比于社区获得性细菌性脑膜炎，医院获得性细菌性脑膜炎不良结局发生率更高（40.5% VS 23.4%，P=0.001）。

结论 1. 喀什地区社区获得性细菌性脑膜炎常见病原体为肺炎链球菌、流感嗜血杆菌、金黄色葡萄球菌、脑膜炎奈瑟菌；分离出的肺炎链球菌对青霉素、头孢三代抗生素等敏感性较好。

2. 医院获得性细菌性脑膜炎常见病原体为鲍曼不动杆菌、凝固酶阴性的葡萄球菌；分离出来的鲍曼不动杆菌均为耐碳青霉烯类菌株。

3. 医院获得性细菌性脑膜炎结局较社区获得性细菌性脑膜炎差。

恶性血液病患者发生铜绿假单胞菌感染的临床特征及预后分析

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2. 福建医科大学附属南平第一医院血液科

3. 福建医科大学附属第一医院滨海校区国家区域医学中心血液科

4. 福建医科大学附属协和医院血液科

5. 福建医科大学附属第一医院血液科

6. 福建医科大学精准医学研究所

目的 探讨恶性血液病患者发生铜绿假单胞菌（Pseudomonas aeruginosa，PA）感染的临床特征及预后分析

方法 回顾性分析 2019 年 01 月 01 日至 2021 年 12 月 31 日期间在福建医科大学附属协和医院血液科 197 例合并铜绿假单胞菌感染的恶性血液病患者的临床资料。根据对碳青霉烯类药物的敏感性将患者分为 CSPA 感染组和 CRPA 感染组，应用 SPSS25.0 进行分析，比较两组患者临床特征的差异，分析容易发生 CRPA 感染的危险因素及预后情况。

结果 福建医科大学附属协和医院血液科 2019 年 01 月 01 日至 2021 年 12 月 31 日经病原学检查确诊为恶性血液病伴铜绿假单胞菌感染 197 例，共 205 株标本，标本类型主要为血液（23.4%）、痰（32.3%）、口咽拭子（22%）。单因素分析显示：CRPA 组感染前使用激素、1 年内行造血干细胞移植、住院天数 >50 天、抗生素暴露史、感染前化疗次数 >2 次的比例均高于 CSPA 组（P<0.05）。Logistic 多因素回归分析进一步显示住院天数 >50 天、抗生素暴露史、感染前化疗次数 >2 次为发生 CRPA 的独立危险因素（P<0.05）。57 例恶性血液病伴 CRPA 感染患者进行死亡风险因素分析，结果显示血流感染 (Bloodstream infections，BSI)、白蛋白 <30g/L、血小板计数≤ 10×109/L、中性粒细胞计数与患者的预后不良相关（P<0.05）；Logistic 多因素回归分析进一步显示血流感染是恶性血液病伴 CRPA 感染死亡的独立危险因素（P<0.05）。

结论 住院天数 >50 天、抗生素暴露史、感染前化疗次数 >2 次为发生 CRPA 感染的独立风险因素（P<0.05）。恶性血液病伴 CRPA 感染的死亡率高，如合并血流感染、白蛋白 <30g/L、血小板计数≤ 10×109/L、中性粒细胞减少，提示患者 30 天死亡高风险，其中血流感染为恶性血液病伴 CRPA 感染死亡的独立危险因素。

识别肺炎克雷伯菌肝脓肿患者发生菌血症的生物标志物探索

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目的 肺炎克雷伯菌肝脓肿（KPLA）继发菌血症的发生率较高，这类患者往往病情更重，治疗棘手。我们期望通过与 KPLA 未继发菌血症患者、非肺炎克雷伯菌肝脓肿（NKPLA）继发菌血症患者对比，分析 KPLA 患者的临床指标，探索 KPLA 患者继发菌血症的生物标志物。

方法 纳入北京大学第三医院 2016 年 1 月至 2020 年 12 月收治的 98 例 BLA 患者，将患者分为：①KPLA：继发菌血症组（42 人）、未继发菌血症组（30 人），②菌血症：KPLA（42 人）、NKPLA（11 人），收集并比较各组患者的实验室指标。

结果 KPLA 继发菌血症组患者的血小板水平（PLT）显著低于 KPLA 未继发菌血症组（P=0.034），当 PLT 截断值为 194×10*9/L 时，PLT 预测 KPLA 继发菌血症的 ROC 曲线下面积（AUC）为 0.654，约登指数为 0.243。相比于 NKPLA 继发菌血症患者，KPLA 继发菌血症患者的天门冬氨酸氨基转移酶（AST，P=0.041）水平显著降低而葡萄糖（GLU，P=0.001）水平显著升高，且 KPLA 合并菌血症患者中糖尿病占比 52.38%，NKPLA 合并菌血症患者中糖尿病占比 18.18%。

结论 引起 BLA 的主要病原体是肺炎克雷伯菌，占比 73.47%，KPLA 继发菌血症组患者的 PLT 水平相比于 KPLA 未继发菌血症组显著降低，而 AST 相对于 NKPLA 继发菌血症患者显著降低，血糖相对于 NKPLA 继发菌血症患者显著升高。

耶尔森菌素在经典肺炎克雷伯菌肺部感染中发挥关键毒力作用

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目的 肺炎克雷伯菌 KP 存在多种毒力因子，但其对于机体致病力的研究尚不明确。本研究旨在分析不同毒力基因对于血液细胞的毒理作用。

方法 本研究收集了本院 2017 年 1 月至 2023 年 4 月 KP 肺部感染患者 627 例。收集患者的 KP 菌株序列、血常规及第 14 天、28 天和 90 天死亡率。包含沙门菌素、气杆菌素、rmpA、rmpA2 和 peg344 等任一毒力基因即定义该菌株为高毒力肺炎克雷伯菌 hvKP，以此为依据分为 hvKP 组和 cKP 组。

结果 本研究共纳入 KP 肺部感染患者 627 例，其中女性 180 例，男性 447 例，平均年龄 72.95 ± 15.71 岁。hvKP 组 362 例，cKP 组 265 例，匹配年龄及性别后，cKP 组患者红细胞和血红蛋白水平更低以及单核细胞绝对值水平更高。考虑此结果和既往研究报道存在矛盾，我们进一步分析发现耶尔森菌素 ybt 的存在可能影响了这一结果。分别在 hvKP 和 cKP 组中以是否携带 ybt 进行亚组分析。在 cKP 组患者中，携带 ybt 患者血常规红细胞、血红蛋白及血小板下降更显著。而并未在 hvKP 亚组分析中发现类似结果。

结论 在经典肺炎克雷伯菌肺部感染患者中，耶尔森菌素可能发挥了关键毒力作用。

基于 MIMICIV 数据库中 ICU 患者动态体温特征构建辅助识别脓毒症的模型

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目的 脓毒症是 ICU 常见疾病，早期诊断困难。在临床实践中体温与感染密切相关，本研究基于 MIMICIV 数据库中 ICU 患者动态体温数据开发辅助识别脓毒症的模型

方法 本研究纳入标准：① ICU 患者②年龄≥ 18 岁③体温记录跨度≥ 24h。排除标准：①体温记录出现极端值≥ 50℃②体温记录缺失率＞ 30% ③患有转移性实体肿瘤、恶性肿瘤、艾滋病④使用 CRRT 或 ECMO。变量提取：①确诊 sepsis 患者，提取体温等变量时间段为 sepsis 初次诊断至出 ICU。②非 sepsis 患者，提取时间段为入 ICU 至出 ICU。提取预后指标住院病死率用以评估模型识别效果

结果 纳入 18966 名确诊和 19262 名非 sepsis 的 ICU 患者。确诊 sepsis 患者住院病死率 12.62%，非 sepsis 患者住院病死率 4.48%。非 sepsis 患者中最大 sofa<2(n=4131) 亚组住院病死率 0.97%，最大 sofa ≥ 2(n=15131) 亚组住院病死率 5.43%。确诊 sepsis 患者住院病死率显著高于非 sepsis 且最大 sofa<2 亚组，将该亚组排除脓毒症识别分析。统计分析得出时间段内最高体温 (Tmax,℃) 和最大升温速率 (ΔTmax,℃ /h)(即提取变量时间段内体温曲线斜率最大值) 在确诊 sepsis 与非 sepsis 患者中统计学差异最大。对于非 sepsis 且最大 sofa ≥ 2 亚组，联合 Tmax 与 ΔTmax 指标分析得出体温具备① Tmax>38.3,ΔTmax>0.1 或 ② Tmax ≤ 36.8,ΔTmax>0.3 条件的患者（n=1449，占比 9.58%）住院病死率 13.66%，与确诊 sepsis 患者接近，提示可能为漏诊患者。在确诊 sepsis 患者中具备 Tmax>36.8,ΔTmax ≤ 0.1 条件的患者（n=1906，占比 10.04%）住院病死率 6.40%，提示可能为 sepsis 低危或过度诊断人群

结论 联合最高体温和最大升温速度可辅助识别脓毒症并进行风险评估

成人肺炎支原体感染对大环内酯类抗生素耐药的研究

谢盼盼、张越、方云、牛文凯、苑鑫
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目的 肺炎支原体 (MP) 是成人社区获得性肺炎的首位致病菌。MP 感染常用抗生素有三类：大环内酯 (ML)、氟喹诺酮和四环素类。ML 因抗菌效果较好及不良反应少常作为 MP 感染的首选，特别是儿童患者。近 10 余年我国儿童患者 MP 对 ML 耐药率高达 90% 以上，且耐药多为靶点突变所致，而成人患者 MP 对 ML 的耐药性研究较少。本研究旨在评估成人 MP 对 ML 的耐药性并分析耐药机制。

方法 收集 2010 年 1 月至 2017 年 12 月就诊于我院门诊、高度怀疑 MP 感染的成人患者咽拭子标本。经聚合酶链反应 (PCR) 法和液 – 固 – 液交替培养鉴定并纯化 MP 菌株后，采用肉汤微量稀释法测定 MP 对 3 种 ML（红霉素，阿奇霉素，麦迪霉素）的最低抑菌浓度 (MIC)。通过对 MP 分离株 23S rRNA 基因测序，PCR 扩增靶位修饰基因 ermA/B/C、ML 药基因 mphC 和外排泵基因 mefA、msrA/B，以及观察外排泵抑制剂（利血平）对 MIC 的影响，进行耐药机制分析。

结果 共获得 72 株 MP 临床分离株，MIC 结果显示 MP 对 ML 耐药率为 41.7%（30/72，红霉素 MIC ≥ 32 μg/ml）。在三种 ML 中，MP 对 14 元环红霉素耐药率最高 (41.7%)，其次是 15 元环阿奇霉素 (38.9%,28/72)，而 16 元环麦迪霉素耐药率最低 (1.4%,1/72)。30 株耐药 MP 中 29 株存在 A2063G 突变；1 株为 A2063R 杂合子突变。一株耐药 MP 中存在外排泵 msrA/B 基因，该基因与屎肠球菌中编码 ABC 转运蛋白的 msrC 基因高度相似。外排泵抑制剂利血平使 25 株耐药 MP 的阿奇霉素 MIC 降至原来的 1/4~1/2。未发现靶位修饰基因和灭活酶 mphC 基因。

结论 我国成人 MP 对 ML 耐药率呈较高态势；16 元环麦迪霉素对 MP 耐药率较低，具有较好的体外抗菌活性；首次在成人 MP 临床分离株中发现外排泵 msrA/B 基因；外排泵抑制剂利血平能降低耐药 MP 的阿奇霉素 MIC 值。

感染

造血干细胞移植过程中肠道微菌群与血清 / 尿液代谢物的动态变化及其临床意义

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6. 成都中医药大学智能医学学院
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9. 福建医科大学附属协和医院血液科

目的 分析异基因造血干细胞移植（Allogeneic hematopoietic stem cell transplantation, Allo-HSCT）患者肠道菌群、血清及尿液代谢物在纵向时间上的动态变化，并解析其与临床特征的相关性和预测价值。

方法 本研究纳入 2022 年 10 月至 2023 年 4 月本中心 21 例确诊血液病并接受 Allo-HSCT 治疗的患者，运用 16s rDNA 测序及广靶代谢组学技术检测肠道菌群及血清 / 尿液代谢物，分析 Allo-HSCT 肠道菌群及代谢物的动态变化特点，探讨患者粒细胞减少伴发热时菌群及代谢物的特征及预测价值。

结果 在 Allo-HSCT 患者中，肠道菌群的检出丰度最高的菌科依次为肠杆菌科、拟杆菌科和毛螺菌科。从移植前至移植后 30 天，患者肠道微生物群的多样性呈现先下降后逐渐恢复的动态变化，其中韦荣氏球菌科表现最为显著。粒细胞减少伴发热（Febrile neutropenia，FN）组与非粒细胞减少发热组的差异菌科为坦内雷拉菌科、肽链球菌科和支原体科。通过筛选相关临床检测指标，发现坦内雷拉菌科与血小板计数联合预测 FN 的曲线下面积（Area under the receiver operating characteristic curve, AUC）为 0.752。同时对 FN 组血清和尿液代谢物进行差异及 KEGG 分析主要富集在发热通路。通过联合分析坦内雷拉菌科、血小板计数、血清肉碱 5:0 及尿液肉碱 8:1，预测 FN 的 AUC 为 0.880。

结论 Allo-HSCT 患者的肠道菌群及血清 / 尿液代谢物在造血干细胞移植过程中呈现出动态

变化。研究发现，坦内雷拉菌科、血小板计数、血清肉碱 5:0 及尿液肉碱 8:1 的组合预测模型对 FN 具有良好的预测能力。这些发现提示，微生物组学和代谢组学分析能够作为筛选和预测 Allo-HSCT 并发 FN 的新型工具。

搭建用于病原高通量测序的感染性病理样本核酸提取流程

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目的 本研究靶向感染性 FFPE 样本，搭建样本前处理及核酸提取流程，使得可以从中获取高质量的病原微生物核酸。

方法 病理医生筛选明确感染或强烈怀疑感染的的 FFPE 样本，宏组学实验室对样本进行脱蜡、PK 酶消化、56℃孵育过夜（≥ 8h）、珠磨后提取 DNA，提取到的核酸进行文库构建、探针宏捕获（Metagenomics Capture, MetaCAP），测序并分析结果，进一步分析和病理结果的符合度。

结果 共筛选到 32 份样本（包括实验重复）进行验证，经评估，切片厚度全部为设置为 3μm，面积在 1~10mm3，切片数量 1~10 张。其中消化道组织 14 份，淋巴结 6 份，鼻和鼻窦 5 份，女性生殖系统 4 份，皮肤软组织 2 份，浆膜组织 1 份，均有明确诊断结果。经病理分析诊断，明确幽门螺杆菌感染的 10 份，结核或疑似结核 8 份，真菌（包括共感染）7 份，HPV（包括共感染）4 份，特殊病原 1 份，非感染性样本 4 份。经严格的 5 重前处理后，核酸提取效果均满足继续构库的要求；文库质控、测序数据也均达到质控要求，但总体积较小的样本，可明显发现非预期病原的检出序列增高，可能是 FFPE 制作过程带入的污染或背景菌。其中 30 份样本中检出了病理预期的病原，2 个疑似结核的样本，未检出结核，总体符合度为 93.75%。

结论 本研究建立了稳定的 FFPE 样本核酸提前流程，使其在病原 NGS 检测中能提供有保障的分子基础。

固有免疫反应在 HAdV 感染疾病进程中的关系探讨

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目的 基于人腺病毒感染的免疫反应过程探讨固有免疫反应在 HAdV 感染疾病进程中的关系

方法 通过 PubMed、Web of Science、Sci Finder、Citeline Pharma Intelligence-Pharmaprojects 和 BMJ Best Practices 数据库检索文献并进行分析

结果 固有免疫主要由病毒体成分驱动，控制宿主对病毒感染的即时反应，对多种病原体进行快速检测和消除。宿主对固有免疫系统的抗病毒作用有许多途径，包括 I 型干扰素应答，抗体 - 补体作用和细胞因子释放导致的细胞炎性反应等作用。

Ⅰ型 IFN 对 HAdV 的诱导有两种机制：（a）TLR 依赖性，在非离体分离的 pDC 中由 DNA 的胞浆识别和 MyD88 独立触发；（b）TLR 非依赖性，在树突状细胞和巨噬细胞中通过胞质 DNA 刺激 IRF-3，从而触发 IFN-α 反应和促炎反应。Ⅰ型 IFN 作用通过抑制病毒体结构的合成抑制病毒复制从而导致直接抗病毒状态的产生。补体系统可共同检测和标记病原体行使多种效应功能。补体级联反应随经典途径、凝集素途径和旁路途径进行。主要感知 HAdV 对细胞的作用，HAdV 诱导细胞损伤和死亡产生的内源性危险信号是激活补体的重要媒介。HAdV 感染宿主并从细胞中释放后，与靶细胞表面受体作用启动下游信号传导，刺激促炎细胞因子和趋化因子基因的表达，机体免疫系统释放大量炎症介质，导致正常细胞损伤和组织机体炎症反应，从而诱发严重的肺部感染。严重的 HAdV 感染与炎症细胞和细胞因子反应的显著失衡有关，包括 TNF-α、IL-1、IL-6、IL-8 和 IFN 等。

结论 本研究通过对固有免疫反应三种防御机制的叙述，探讨了其在 HAdV 感染疾病进程中的关系

伏立康唑成功治愈奥默柯达血流感染 1 例

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目的 提高关于免疫功能低下患者关联奥默柯达酵母（Kodamaea ohmeri）菌血流感染的诊治水平。

方法 结合 1 例胃肠外科术后患者继发奥默柯达血流感染的临床资料，对奥默柯达感染导致真菌血症的临床表现、诊断和治疗进行总结。

结果 奥默柯达作为一种罕见真菌，早期诊断困难，多发生在免疫抑制人群，容易误诊和漏诊。奥默柯达感染的临床表现和影像学特征不太典型，初步诊断需要依赖病原菌培养结果。奥默柯达对唑类（除氟康唑外）、棘白菌素类药物和两性霉素 B 敏感。本例患者在培养结果明确后，给予静脉应用伏立康唑抗真菌治疗取得较好效果。

结论 应用广谱抗生素治疗无效的免疫低下患者，需要警惕罕见奥默柯达血流感染的可能，在设计治疗策略时需要进行准确的物种鉴定和及时的体外药敏试验。

重症患者体内多黏菌素 B 药物浓度监测及评价指标

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目的 建立超高效液相色谱联合质谱法监测重症感染患者多黏菌素 B 的血药浓度，并比较其 AUC0-24h 与谷浓度的达标率。

方法 采用高效液相色谱联合质谱法监测重症感染患者多黏菌素 B 的血药浓度式下采集 2016 年 1 月至 2023 年 12 月本院 239 例重症感染患者静脉输注多黏菌素 B 50-100 万单位，每日 2 次，输注时间为 1 h，稳态后分别于给药前、给药后 1 和 6 h 收集患者血液样本，并利用 Phoenix WinNonlin 6.4 软件计算药动学参数，再根多黏菌素药物浓度监测共识指南，用 SPSS 22.0 软件比较多黏菌素 B 的 AUC0-24h 与谷浓度的达标率。

结果 血浆中线性范围为 0.2~20 mg/L（r2=0.993），定量下限为 0.2 mg/L，多黏菌素 B 提取回收率为 86.5%，精密度相对标准偏差（RSD）均小于 15%。239 例重症感染患者中有 186 例男性（77.82%），53 例女性（22.18%），平均年龄为 61.54 ± 16.31 岁，平均谷浓度和 AUC0-24h 分别为 1.89 ± 1.53mg/L 和 91.20 ± 58.22mg/L*h。平均谷浓度和 AUC0-24h 达标例数（达标率）分别为 68 例（28.45%）和 105 例（43.93）。

结论 本研究建立的测定方法专属性强、准确度高，操作简便，灵敏度高，可用于临床多黏菌素 B 血药浓度的测定。临床中多黏菌素 B 药物监测达标率比较低，并且该药平均谷浓度和 AUC0-24h 的达标率存在明显差异，具有统计学意义，单独的多黏菌素 B 谷浓度无法取代 AUC0-24h，临床中仍需要 AUC0-24h 进行优化重症患者的给药方案和个体化治疗。

Identifying mortality-related risk factors of bloodstream infections due to Escherichia coli and Klebsiella pneumoniae in hematological patients

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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Abstract Content Identifying mortality-related risk factors of bloodstream infections due to Escherichia coli and Klebsiella pneumoniae in hematological patients

Abstract

Background After chemotherapy and hematopoietic stem cell transplantation, the chance of infection greatly increased in patients with hematological diseases. Especially gram-negative bacteria (GNB) bloodstream infections (BSI) infection, which is the main complication and important cause of death. In GNB BSI, the most common pathogens are Escherichia coli (EC) and Klebsiella pneumoniae (KP). The article aims to explore the general characteristics and clinical outcomes of patients with hematological diseases with ECKP (EC and KP) BSI .

Methods We retrospectively analyzed the general characteristics of ECKP BSI patients in our hospital between January 2017 and December 2022. The Kaplan-Meier curve described the survival of overall population and different subgroups. Multivariate regression analysis was employed to identify important risk factors affecting the prognosis.

Results A total of 1709 patients with ECKP BSI were included, and 127 patients was carbapenems resistant (CR) (7.43%), the proportion of extended-spectrum β-lactamase (ESBL)-producing ECKP BSI was approximately 43.42%, and 804 patients was fluoroquinolones (FQ) resistant. The total 30-day mortality was 7.67%, among which the CR patients had the highest mortality rate of 26.0%. On

multivariate analysis, pulmonary source of infection (OR 14.629 95%CI 7.08-30.228, P<0.001), shock (OR 10.037 95%CI 5.445-18.502, P<0.001), pneumonia (OR 5.524 95%CI 2.808-10.868, P<0.001), CR (OR 3.323 95%CI 1.47-7.509, P=0.004), previous FQ (OR 2.442, 95%CI 1.284-4.643, P=0.006) were risk factors for 30-day mortality.

Conclusions: For hematological diseases patients with ECKP BSI, CR, prior antibiotic exposure, especially FQ, greatly increased the risk of death. In addition, appropriate antimicrobials should be given as early as possible in Pulmonary source of infection patients and salvage patients to improve survival.

Risk factors for hospitalization and pneumonia development of pediatric patients with seasonal influenza during February-April 2023

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Abstract Content Objectives In China influenza has remained a low activity for continuous three years due to COVID-19 controls. We here sought to study the clinical characteristics and risk factors of influenza infection among children after the mandatory COVID-19 restrictions were lifted.

Methods We included 1006 pediatric patients with influenza A virus (IAV) infection, enrolled in one tertiary hospital in Zhenjiang, Jiangsu Province, China, from February to April 2023. Patients were divided into the outpatient (n=798) and inpatient (n=208) groups, and their baseline characteristics were compared between the two groups to conclude the risk factors for pediatric hospitalization. Separately, pediatric inpatients (n=208) were further divided into the pneumonia and non-pneumonia groups with a comparison of their clinical characteristics, including their laboratory test results and representative radiological features, to derive the key determinants for pneumonia development after hospitalization.

Results Compared to outpatients, IAV-infected pediatric inpatients exhibited younger age, higher female: male ratio, more co-infection of influenza B virus (IBV) and hematological abnormality. Multivariate regression analysis determined the independent risk factors of hospitalization to be the clinical symptom of abdominal pain (OR=2.63, [95% CI, 1.05-6.57], p=0.039), coinfection of IBV (OR=44.33, [95% CI,], p=0.001), elevated levels of lymphocytes (OR=2.24, [95% CI,1.65-3.05], p=0.001) and c-reactive proteins (CRPs) (OR=1.06, [95% CI, 1.03-1.08], p=0.001) upon hospital admission. Furthermore, the cough symptom (OR=17.39, [95% CI, 3.51-86.13], p=0.001) and hospitalization length (OR=1.36, [95% CI, 1.12-1.67], p=0.002) were determined to be risk factors of pneumonia acquirement for pediatric inpatients.

Conclusion While the abdominal pain, viral co-infection and some hematological abnormality mainly contribute to hospitalization of pediatric patients with IAV infection, the length of hospital stay and clinical sign of coughing upon hospital admission constitute the key determinants for nosocomial pneumonia development.

Analysis of Pulmonary Bacterial Infection and Antimicrobial Agent Use in Elderly Patients

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Abstract Content Background: Elderly patients often experience multi-morbidity and are prescribed multiple drugs due to physical decline. The inflammatory response triggered by bacterial infection can worsen the patient's condition. Pulmonary bacterial infection is a common issue in elderly patients. This study aimed to identify the main types of pulmonary bacterial infections, drug resistance, and the commonly used antimicrobial agents in elderly patients.

Methods The study was conducted retrospectively from March 2023 to September 2023. Patients meeting the inclusion criteria were included: (a) patients over sixty; (b) positive sputum culture for bacteria and bacterial susceptibility results; (c) use of antimicrobial agents for over 24 hours. Patients with the primary infection not being pulmonary infection were excluded.

Results A total of 442 bacterial strains were identified from 228 patients. Gram-negative bacteria constituted 91.9% of the isolates, with Acinetobacter baumannii (AB) being the most prevalent at 24.2%, followed by Klebsiella pneumoniae (KP) at 22.2%, Pseudomonas aeruginosa at 11.5%, and Stenotrophomonas maltophilia at 9%. Gram-positive bacteria comprised 8.1% of the isolates, with Staphylococcus aureus being the most common at 3.8%. Among them, 83.2% of AB, 69.4% of KP, 37.3% of P. aeruginosa, and 76.5% of S. aureus showed multi-drug resistance (MDR). 57.1% mortality in patients infected with two or more strains, one of which is MDRAB or MDRKP, and the mortality increased to 65.1% in the group aged over 80. Most AB and KP were resistant to penicillin / β-lactamase inhibitors, carbapenems, cephalosporins, and quinolones. Carbapenems were the main antimicrobial agents used for anti-infection, followed by cephalosporins / β-lactamase inhibitors, glycopeptides, quinolones, tetracyclines, cephalosporins, penicillin / β-lactamase inhibitors, oxazolidinones.

Conclusion MDR Gram-negative bacteria are the primary pathogens responsible for pulmonary bacterial infections in elderly patients and are associated with high mortality rates. Carbapenems and cephalosporins / β-lactamase inhibitors remain commonly used antibacterial agents. Given the high incidence of multidrug-resistant bacterial infections in elderly patients, there is an urgent need to develop new therapeutic strategies.

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 以中国知网辅以万方、维普网等数据库作为计量文献分析的数据来源，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 3693 篇文献，经过数据清洗去除重复文献后，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整体呈现波浪式增加趋势，其中以 2018-2020 年期间发文量最多。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、中国抗生素杂志等。根据普莱斯定律，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，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。其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。

不同益生菌补充治疗方案对于干细胞移植患者感染的影响

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目的 评估接受造血干细胞移植期间服用联合双歧杆菌四联活菌片及凝结芽孢杆菌活菌片（五联）相对于单独服用双歧杆菌四联活菌片（四联）的患者的临床特征，为预防移植患者感染提供初步研究依据。

方法 回顾性分析 2023 年 4 月至 2023 年 8 月在华中科技大学同济医学院附属协和医院接受造血干细胞移植治疗的同时服用了四联或五联益生菌患者的临床资料。根据他们服用的益生菌方案分为四联组（20）和五联组（32）。对于连续变量和等级资料比较采用 Mann-Whitney U 检验，对于无序分类变量比较采用卡方检验或 Fisher 精确概率法。采用二元 logistic 回归进行单因素及多因素分析，以验证预测 NGS 阳性的变量。

结果 相对于五联组，四联组患者 NGS 阳性率显著增加（60% vs. 3.1%，$p < 0.001$），发热性中性粒细胞减少率增加（65% vs. 28.1%，$p = 0.009$），发热≥ 38℃的中位时间更长（1.50 天 vs. 0 天，$p = 0.009$），且中性粒细胞植入的中位时间延长（10 天 vs. 11.5 天，$p = 0.037$）。多因素分析显示，五联益生菌的使用（OR = 0.017，95% CI 0.001-0.185，$p < 0.001$）是发生 NGS 阳性的保护因素， 口腔粘膜炎（OR = 10.794，95% CI 1.503-77.502，$p < 0.018$）与发生 NGS 阳性的风险增加独立相关。

结论 五联益生菌方案可能有助于预防接受造血干细胞移植的患者发生感染，并且不影响患者造血重建及移植结局。

Antithrombotic strategies in adult COVID-19 patients: a systematic review and Bayesian network meta-analysis

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Abstract Content Multiple randomized controlled trials (RCTs) have extensively discussed various treatment methods for COVID-19-related coagulopathy. However, the optimal antithrombotic strategy has not yet been determined. We conducted a network meta-analysis to systematicly compare various antithrombotic strategies for benefits and risks in adult COVID-19 patients.

Methods We conducted a network meta-analysis (NMA) using a Bayesian framework to compare different antithrombotic strategies in adult COVID-19 patients. We only included RCTs that compare different antithrombotic strategies published in English without regional restrictions. Any antithrombotic strategy would be included, mainly including anticoagulants, antiplatelet agents, fibrinolytic agents, and their different combinations. Eligible trials should involve at least one active arm of antithrombotic therapy, and controls can be other types of antithrombotic strategies or standard of care (SoC). The primary outcome was the all-cause mortality at 28 days. Secondary outcomes included major thrombotic events and major bleeding. The risk of bias was assessed using the Cochrane Collaboration's tool. Publication bias was evaluated through funnel plots and Egger's test, while the confidence in network meta-analysis (CINeMA) framework was utilized to assess the quality of evidence.

Results 35 randomized controlled trials that randomly assigned 39949 participants were included in the main analysis. Evidence of moderate certainty suggested that compared to SoC, both prophylactic-dose anticoagulation (PA) (RR 0.71, 95% CrI 0.44 to 0.99) and therapeutic-dose anticoagulation (TA) (0.65, 0.38 to 0.94) can reduce the 28-day all-cause mortality. TA (0.19, 0.09 to 0.31), TA+ antiplatelet (AP) (0.27, 0.05 to 0.95), PA (0.33, 0.18 to 0.53), and AP+PA (0.52, 0.25 to 0.94) were effective in reducing major thrombotic events. AP was associated with an increased risk of major bleeding events (2.27, 1.01 to 5.07). For nonhospitalized patients, PA can significantly reduce the 28-day mortality compared with SoC (0.52, 0.26 to 0.90), but all antithrombotic strategies did not show significant differences for hospitalized patients. Subgroup analysis based on severity of hospitalized patients indicated that TA was more favorable than

PA in decreasing the 28-day mortality (fixed-effect model: RR 0.75,95% CI 0.61 to 0.91; random-effect model: RR 0.71, 95% CI 0.48 to 1.05), but for critically ill patients, all antithrombotic strategies showed no significant difference.

Conclusion Our NMA indicates that both prophylactic-dose anticoagulation and therapeutic-dose anticoagulation can reduce the 28-day all-cause mortality of adult COVID-19 patients, while achieving a good balance between reducing thrombotic events and bleeding risks.

Omicron caused stronger macrophage pyroptosis than wild-type strains

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Abstract Content Although the severity of patients infected with the Omicron variant has decreased compared to earlier strains, the high transmissibility and large number of infections have resulted in a significantly higher number of excess deaths. Analyzing the differences in immune responses between severe patients infected with Omicron and those infected with earlier strains will help in finding effective methods for preventing and treating severe cases caused by viral infections.

Methods To explore the unique immune characteristics of severe patients infected with the Omicron variant, single-cell RNA sequencing (scRNA-seq) was performed on bronchoalveolar lavage fluid (BALF) from severe Omicron patients and healthy volunteers. The sequencing data were combined with publicly available scRNA-seq data from severe patients infected with the wild-type strain to analyze specific differences between severe Omicron patients and severe wild-type strain-infected patients. After identifying significant differences in the fate of alveolar macrophages between Omicron and wild-type strain-infected patients, peripheral blood mononuclear cell (PBMC)-derived macrophages and PMA-induced THP1 cell lines were infected with different titers of the wild-type strain and Omicron variant in a BSL-3 laboratory. RT-PCR, RNA-Scope, and immunofluorescence were conducted to assess the differential infection capabilities of the strains on macrophages. Electron microscopy, Western blot, immunofluorescence, and ELISA were used to detect differences in macrophage pyroptosis levels following infection with different strains. Additionally, stable cell systems expressing different coding proteins from the wild-type strain and Omicron variant were constructed to elucidate the specific mechanisms underlying the differences in pyroptosis levels.

Results Integrated scRNA-seq data indicated that the number of macrophages in the BALF of severe Omicron patients was significantly reduced compared to the wild-type strain. Both the Omicron and wild-type strains were capable of infecting macrophages, with the wild-type strain demonstrating a stronger infection capability at the same viral titer, as evidenced by the presence of more viral particles within the cells. However, after Omicron infection, the secretion levels of IL-18 and IL-1β in macrophages were higher than those infected with the wild-type strain, with noticeable cell membrane perforation and more pronounced pyroptosis. Further research revealed that Omicron-induced macrophage pyroptosis was mainly

mediated by the NLRP3 inflammasome pathway. Through constructing stable cell systems expressing different coding proteins from the wild-type and Omicron variants, we found that various coding proteins of Omicron played distinct roles in mediating macrophage pyroptosis.

Conclusion Compared to the wild-type strain, the Omicron variant has a reduced capability to infect macrophages but induces stronger cell pyroptosis. This may be an important factor contributing to the differing clinical manifestations between Omicron and earlier strains.

1 例支气管扩张并感染患者住院期间高热处理经验分享

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目的 分享 1 例支气管扩张并感染患者住院期间合并甲型流行性感冒病毒感染后高热的处理思路，为抗生素合理应用提供依据。

方法 对 1 例以 " 反复咳嗽、咳痰 7 年，加重半月 " 入院的 58 岁支气管扩张并感染女性患者住院期间突发高热的病例的临床症状、流行病学调查、实验室指标及治疗等进行回顾性分析。

结果 该患者入院前反复左氧氟沙星片治疗史，2023 年 11 月 27 日入院后完善血常规白细胞计数 5.88*109/L、中性粒细胞百分比 66.2%、肺 CT 提示左肺支气管扩张并感染，查痰培养提示粘液型铜绿假单胞菌阳性，根据药敏结果应用头孢他啶单药抗感染、化痰、止咳等治疗 6 天后症状明显好转，12 月 3 日突发高热，体温最高 39.2℃，伴畏寒、四肢酸痛、少许咽痛，咳嗽、咳痰略增多，予布洛芬退热治疗后体温可下降至正常，12 月 4 日查 WBC 6.39*109/L、中性粒细胞 82.5%，CRP1.06mg/dL，PCT0.028ng/ml，IL-64 5.30 略高，考虑其隔壁床甲型流行性感冒病毒感染并发热 3 天，本患者感染甲型流行性感冒病毒感染可能性大，不调整头孢他啶抗生素治疗方案，加用口服磷酸奥司他韦累计 5 天并适当补液、退热、利咽及预防电解质紊乱，12 月 6 日测甲型流行性感冒病毒核酸阴性，但 12 月 7 日体温已恢复正常，符合甲型流行性感冒病毒感染自然病程，症状好转出院。

结论 支气管扩张并感染患者住院期间突发高热，需警惕同病房患者或家属是否感染流行病毒株，抗生素的调整需慎重，痰培养药敏结果可为抗生素选用提供依据。



呼吸

呼吸

新型冠状病毒肺炎病情严重程度与预后指标相关性的 Meta 分析

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目的 探索 COVID-19 病情严重程度和预后指标的相关性，从而确定预后指标对病 情严重程度的评估和预测价值，为临床 COVID-19 的病情转归及预后评估提供参考。

方法 计算机检索 The Cochrane Library、EMBase、PubMed、Web of Science、SinoMed、中国知网、万方数据知识服务平台、维普网，收集分为重症组和非重症组或死亡组和存活组的 COVID-19 随机对照试验，并且包含降钙素原（PCT）、C 反应蛋白（CRP）、淋巴细胞计数（LYM）、白介素 -6（IL-6）、D- 二聚体（D-dimer）预后相关指标。采用改良 Jaded 评分量表对文献进行质量评价，运用 Stata 12.0 软件进行 Meta 分析。

结果 Meta 分析结果显示，重症组患者的 PCT〔SMD=-2.28，95%CI（-3.60，-0.98），P<0.001〕、CRP〔SMD=-2.23，95%CI（-3.38，-1.07），P<0.001〕、IL-6〔SMD=-2.97，95%CI（-4.94，-1.00），P<0.001〕、D-dimer〔SMD=-1.22，95%CI（-2.66，0.21），P=0.008〕高于非重症组。（因字数限制，其余内容见全文）

结论 重型 COVID-19 患者的 PCT、CRP、IL-6、D-dimer 高于非重型 COVID-19 患者，LYM 低于非重型 COVID-19 患者；死亡组 COVID-19 患者的 PCT、 CRP、IL-6、D-dimer 高于存活组，LYM 低于存活组，提示 PCT、CRP、IL-6、D-dimer 可能与病情严重程度呈正相关，LYM 可能与病情严重程度呈负相关。

热毒宁注射液治疗老年急性肺炎的临床疗效

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目的 分析热毒宁注射液治疗老年急性肺炎患者的临床疗效。

方法 选取 2022 年 2 – 6 月桂林医学院附属医院收治的 60 例老年急性肺炎患者作为研究对象，采用随机数字表法分为对照组和试验组，每组 30 例。对照组采用常规西药抗感染治疗，试验组在对照组基础上加用热毒宁注射液强化治疗。比较两组治疗前后的 C 反应蛋白、降钙素原水平，比较两组的肺炎症状缓解时间、胸部 CT 改善时间及住院时长。

结果 治疗后，试验组 C 反应蛋白、降钙素原水平低于对照组，试验组的肺炎症状缓解时间、胸部 CT 改善时间、住院时长短于对照组，差异有统计学意义（$P < 0.05$）。

结论 热毒宁注射液可有效治疗老年急性肺炎患者。

烟曲霉胶霉毒素抑制巨噬细胞自噬及炎症的机制研究

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目的 烟曲霉感染引起的侵袭性肺曲霉病是全球性健康问题，胶霉毒素是烟曲霉分泌的主要毒素，本研究旨在探究胶霉毒素对巨噬细胞自噬及炎症反应的的影响及其作用机制，以期提供崭新临床治疗思路。

方法 使用蛋白印迹、激光共聚焦检测 THP1 衍生的巨噬细胞 LC3、ULK1、ATG5、Beclin1、Rubicon 等自噬标志蛋白的表达；利用 RT-qPCR 及 Elisa 技术探究细胞因子、趋化因子表达的变化；胶霉毒素、烟曲霉膨胀孢子（B5233、Glip △、GlipR）用于刺激 THP1 细胞；使用透射电镜观察巨噬细胞吞噬体的结构；最后，通过 RNA-Seq 筛选胶霉毒素干预后的差异表达基因并通过蛋白印迹及 RT-qPCR 进行验证。

结果 蛋白印迹及激光共聚焦结果显示胶霉毒素刺激的巨噬细胞自噬表达被抑制，包括经典自噬途径的 ULK1 及非经典自噬途径的 Rubicon；通过 RNA-Seq 预测 JNK3 基因参与胶霉毒素影响的细胞自噬；细胞因子、趋化因子的表达被胶霉毒素显著抑制；透射电镜观察到 GlipR 及 B5233 菌株干预的巨噬细胞相对 Glip △具有更明显的自噬体结构。

结论 烟曲霉胶霉毒素抑制巨噬细胞自噬及细胞因子、趋化因子的表达，且 JNK3 在其中发挥重要作用，可能为侵袭性肺曲霉病的治疗提供新思路。

布地格福吸入气雾剂在慢性阻塞性肺病中的临床研究进展

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目的 布地格福吸入气雾剂是一种由布地奈德、格隆溴铵、富马酸福莫特罗以固定剂量组合并利用创新性共悬浮技术制成的三联药物，能有效的改善 COPD 患者的肺功能、控制炎症状态、抑制氧化应激损伤、降低 NO 浓度和不良反应的发生率，同时安全性和耐受性良好，主要用于 COPD 的治疗。综述布地格福吸入气雾剂在 COPD 患者临床治疗的有效性和安全性。

方法 就布地格福的作用机制、临床应用、不良反应等方面回顾布地格福的最新研究，以期为布地格福在 COPD 患者人群的临床应用提供参考。

结果 总体来说，布地格福可有效改善 COPD 患者的肺功能、控制炎症状态、降低不良反应，但在 COPD 以外其他呼吸道疾病中的治疗效果还较少，且缺乏更多与其他固定剂量和开放三联联合治疗的 RCT 研究。

结论 布地格福吸入剂在 COPD 患者中的临床应用总体疗效和安全性均较好，期待未来出现更多诊疗方案，为临床用药提供更多新思路。

低密度中性粒细胞在结核病发病中的表达及功能影响

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目的 通过对活动性结核病患者肺泡灌洗液中低密度中性粒细胞表达的探索，为临床理解低密度中性粒细胞在结核病发病中的作用提供理论依据，为临床制定结核病的防治策略提供新视角。

方法 一、BALF 收集：临床医生在标准防护下，在肺结核影像显示病灶的叶段行支气管肺泡灌洗检查，灌洗液使用室温下（25℃左右）生理盐水。将支气管镜楔入肺段或亚段支气管，每次灌入生理盐水 10 ~ 20ml，总量 50 ~ 60ml，后经负压吸引入标本收集瓶，0.5h 内送至实验室，在 2 ~ 3h 内处理。

二、LDN 制取：肺泡灌洗液样本（10mL）收集到 EDTA 管中，通过密度梯度离心法分离出 PBMCs 和 LDNs 级分。

三、流式细胞仪分析：流式细胞仪进行计数及细胞因子、ROS 测定。

结果 低密度中性粒细胞在结核病发病初期表达明显增加，达 13.6%；通过流式细胞技术分析提示 IL-10 水平升高、TNF 水平下降、ROS 水平升高。

结论 低密度中性粒细胞在结核病发病中表达明显增加，且对相关细胞因子产生了功能性调节，靶向 LDN 是一种有应用前景的抗结核治疗策略。

基于多样化筛选的儿童重症腺病毒肺炎全因素分析及预测模型构建与评价

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目的 基于对腺病毒肺炎患儿重症临床特点的全因素对比探究，筛选分析危险因素，构建儿童重症腺病毒肺炎的预测模型，并评估其临床应用价值。

方法 变量统计：对 2017 年 1 月至 2024 年 3 月期间在南京市儿童医院住院治疗的 699 例 AVP 患儿进行回顾性研究。分为重症组（SAP 组，284 例）和轻症组（AVP 组，415 例）。统计两组患儿的医生诊断和实验室检验（包括血常规，凝血功能，生化功能和淋巴细胞百分比）数据。

变量分析：对差异化分析变量中 P<0.05 的变量使用 Ridge 回归进一步筛选，对 Ridge 回归 Coefficient>0 的变量执行多因素 logistic 回归分析，最终确定 SAP 的重症预测因素。最后对各重症预测因素的 β 值进行简化赋分，绘制 ROC 曲线，使用 Hosmer- Lemeshow 检验和曲线下面积 (AUC) 来评价模型的校准度和区分度

结果 重症感染患儿中有 189 例 (66.55%) 伴随混合感染，以支原体感染为主 (33.10%)。通过 Ridge 回归算法进行变量筛选，在最佳 lambda 值为 0.0275 时计算得到 Coefficient>0 的变量有 16 个。对回归结果执行多因素 logistic 回归分析后得到 T-spike、NEUT、d-dimer、FDP、B cell 和 LDH 是儿童发生 SAP 的独立危险因素（P < 0.05）。

构建模型并绘制受试者工作特征（ROC）曲线，其 AUC 为 0.980，95% CI 为 0.970 - 0.990，Hosmer- Lemeshow 检验 P 值为 0.7023 (P>0.05), 表明实际发生数与预测发生数的吻合程度较高，显示该模型的校准度较好，预测能力较强。

结论 本研究对 AVP 患儿的临床变量作分析和筛选，并基于 T-spike、NEUT、d-dimer、FDP、B cell 和 LDH 水平的潜在危险因素构建儿童 SAP 的发生预测模型，具有良好的区分度与准确度。

降糖药使用引起的细菌性肺炎发生风险和获益——基于遗传基因水平的孟德尔随机化研究

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目的 细菌性肺炎是全球发病率和死亡率的主要原因。既往认为糖尿病 DM 患者细菌性肺炎发生风险升高，然而，真实世界研究发现 DM 患者的细菌感染风险存在相互矛盾，死亡率并未显著上升。我们推断这可能与 DM 患者服用降糖药物改善或增加细菌性肺炎风险有关，为了明确降糖药物的使用对 DM 患者细菌性肺炎的发生可能带来的风险或获益，故此本研究使用孟德尔随机化研究 MR 分析不同降糖药物对 DM 患者细菌性肺炎易感风险的影响。

方法 从 UK biobank 数据库提取 DM 患者 GWAS、细菌性肺炎患者 GWAS 数据作为人群队列，以及降糖药物靶蛋白所对应的基因遗传变异 SNPs 作为遗传工具，采用两样本 MR 设计，估计降糖药物靶点 SNPs 对细菌性肺炎易感风险的影响。

结果 胰岛素及其类似物诱导的血糖降低与与细菌性肺炎风险的降低显著相关 (OR 0.01，95% CI 0.00 to 0.18)。二甲双胍作用靶点 AMPK γ2 (PRKAG2) 诱导的 HbA1c 降低与较低的细菌性肺炎风险 (β −0.42, 95% CI −0.72 to −0.11) 有关。然而，噻唑烷二酮类 (OR 48.77，95% CI 2.61 to 911.24)、磺酰脲类 (OR 7.97，95% CI 1.55 to 40.91) 降糖药作用的血糖降低与细菌性肺炎风险的升高显著相关。

结论 M 患者通过服用不同的降糖药物从而改变了细菌性肺炎的发生风险的升降。因此，肺炎高危易感的 DM 患者推荐其使用胰岛素 / 胰岛素类似物和二甲双胍作为 DM 治疗的主要药物，以减少其发生细菌性肺炎风险，从而改善预后。

服用降糖药物引发的病毒性肺炎发生：基于药物靶点遗传代理的孟德尔随机化研究

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目的 临床研究表明，高血糖会增加肺部感染机会。一些降糖药物可能通过影响患者的免疫反应，或通过降低血糖水平，对抵抗病毒性肺炎有影响。本研究拟探究对不同类型抗糖尿病药物对病毒性肺炎发生易感性的影响。

方法 采用两样本孟德尔随机化设计，选择了编码胰岛素及其类似物、噻唑烷二酮类、二甲双胍等抗糖尿病药物靶蛋白的基因中的独立遗传变异作为遗传工具。通过 FinnGen 和 UK Biobank 数据库，提取了仪器与 2 型糖尿病和病毒性肺炎易感性的相关性。进一步使用 Wald 比值检验或逆方差加权法，以估计药物靶点的遗传变异对病毒性肺炎易感性的潜在作用。

结果 噻唑烷二酮诱导的血糖降低与流感性肺炎风险 (OR 70.83, 95% CI 4.34 to 1155.86) 的升高显著相关，磺酰脲类诱导的血糖降低与 COVID-19 重症风险的降低显著相关 (OR 0.14，95% CI 0.02 to 0.92)，GPD1 诱导的 HbA1c 降低与较低的病毒性肺炎风险 (β −0.46, 95% CI −0.82 to −0.09) 有关（表 1）。

结论 为预防病毒性肺炎发生，建议糖尿病患者服用二甲双胍，有重症新冠风险患者建议使用磺酰脲类药物。不推荐糖尿病患者在治疗中使用 SGLT-2i 和噻唑烷二酮类药物作为一线药物，以减少其病毒性肺炎患病易感性。

临床药师参与一例多重耐药非结核分支杆菌肺病治疗的药学监护

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目的 探讨临床药师在多重耐药非结核分枝杆菌药物治疗的药学监护，为该类感染药学监护提供参考

方法 对临床药师参与 1 例非结核分枝杆菌患者的诊断和治疗过程进行分析。临床药师对药敏报告分析后，建议按照非结核分枝杆菌药敏试验标准再次行药敏试验，结合药物药代动力学特点，将治疗方案由头孢西丁 + 亚胺培南 / 西司他丁 + 乙胺丁醇 + 克拉霉素调整用药为头孢西丁 + 亚胺培南 / 西司他丁 + 阿米卡星雾化吸入 + 阿奇霉素 + 替加环素，治疗 20d 后患者病情有所好转。按照非结核分枝杆菌药敏试验结果提示，结合患者病情将抗感染治疗方案调整为头孢西丁 + 阿米卡星 + 阿奇霉素 + 替加环素 + 莫西沙星，治疗 20d 后患者病情进一步好转出院，转社区医院继续治疗。临床药师还参与了评估、预防治疗过程中的药物不良反应，并对患者出院后用药进行用药指导。

结果 医师采纳了临床药师的建议。经过两次调整治疗方案，患者治疗 3 个月后，病情得到了良好控制，未发生严重不良反应。

结论 临床药师参与了该患者的诊疗过程，为其制订了个体化的抗感染治疗方案并取得了良好的效果，体现了临床药师的专业能力和服务水平，为多重耐药非结核分枝杆菌临床诊疗提供了思路。

一例百日咳肺炎合并心力衰竭患儿的护理

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目的 本文报道了 1 例百日咳肺炎合并心力衰竭患儿的护理。

方法 该患儿住院期间经历了典型百日咳的三个临床阶段：卡他期、痉挛期和恢复期，治疗期间并发心力衰竭，根据不同阶段的临床表现及特点，在治疗的基础上加强呼吸道管理、心力衰竭的护理、感染防控、喂养护理以及家庭宣教等护理措施。

结果 经过精心的治疗与护理，患儿疾病得到有效治疗，体重逐步增加，治疗 40d 后痊愈出院。

结论 新生儿因胸廓尚未完全发育成熟，咳嗽无力，且呼吸道狭窄，细菌感染后产生大量毒素，并释放于全身，纤毛运动停止，无法及时将呼吸道分泌粘液有效排除，造成百日咳患儿病情迁延，治疗时间长。护理过程中应根据不同临床阶段及表现给予针对性呼吸道管理；重视患儿随日龄增长，情感需求愈发明显，呼吸道管理时辅以情感支持可有效提高护理质量。同时重视并发症的处理，以及感染的控制，关注喂养护理，防止呛奶发生。最后，在强化患儿住院期间护理的同时，亦要关注家长心理护理，获取家长理解与配合，保证治疗护理的有效进行。经过精心治疗和护理 40d 后患儿痊愈出院。

机化性肺炎的多组学免疫景观

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目的 机化性肺炎（OP）是间质性肺炎中最常见和致命的类型。脂代谢重编程是许多疾病（包括癌症、心血管疾病、以及纤维化相关疾病等）的新型机制，由鞘氨醇和脂肪酸组成的神经酰胺水平增加，参与了急性和慢性肺疾病的发病机制。然而，其在 OP 中的病理生理学意义尚不明确。因此，本研究的目的是探讨脂质代谢重编程在 OP 中的作用，重点关注炎症和纤维化。

方法 单细胞测序 / 空间转录组 / 蛋白质组学 / 代谢组学 / 免疫荧光 /qPCR/Western Blot 等。

结果 结果显示，OP 与脂质代谢重编程显著相关，几种与脂质代谢相关的基因（如 CD36、SCD1 和 CES1）在巨噬细胞中异常表达。肺泡巨噬细胞中的 CD36 缺失导致 C16/24 神经酰胺的表达增加，这些神经酰胺积累在线粒体中，导致线粒体自噬或线粒体功能障碍。OP 中肺泡巨噬细胞的数量显著减少，这可能是由于 CD36 介导的 GSH/SLC3A2/GPX4 铁死亡信号通路在 OP 中下调。此外，巨噬细胞分泌的 COLGALT、DPP4 和 FABP4/5 影响上皮细胞纤维化。

结论 CD36 通过调节脂质代谢在 OP 组织的肺泡巨噬细胞中抑制了 SLC3A2/GPX4 铁死亡信号通路，该过程部分由神经酰胺介导。



临床药理

基于一体化闭环药学服务的国家骨科医学中心抗菌药物合理应用实践

杨全军
上海交通大学医学院附属第六人民医院

目的 回顾国家骨科医学中心抗菌药物的一体化闭环药学服务建立及改进措施，分析其对于改善骨科合理用药的作用和价值。

方法 回顾性分析我院骨科事前事中事后一体化闭环药学服务措施，利用数据平台信息总结一体化药学服务对促进抗菌药物合理应用的价值。

结果 一体化闭环药学服务是抗菌药物合理应用的重要环节，特别是药学审方关联事前和事后的药学服务建设。2021年1月-2023年12月药师共审核医嘱109756条，审核打回医嘱24472条，减少抗菌药物使用4520次。骨科抗菌药物使用强度不断下降，从2020年为每百人每日33 .8 DDDs，2021年为每百人每日25.6 DDDs， 2022年为每百人每日27.3 DDDs，2023年为每百人每日32.0 DDDs。合理用药指标持续改善，尤其是Ⅰ类切口预防性使用抗菌药物比例， 2020为65.1%， 2021为39.7%， 2022年为26.5%, 2023年为22.4%。不合理用药结构得以改善，药学人才队伍建设和学科建设提升。

结论 我院一体化闭环药学服务促进骨科抗菌药物合理使用，加速了国家骨科医学中心的高质量发展和转型引领。

基于院科上下联动事前事中事后服务闭环的抗菌药物管理实践及规范

杨全军
上海交通大学医学院附属第六人民医院

目的 回顾院科上下联动的抗菌药物工作模式，分析事前事中事后服务闭环的抗菌药物合理应用管理实践。

方法 从医院管理和药学学科发展角度分析我院 2021 年 4 月至 2023 年 9 月抗菌药物合理应用的工作模式。

结果 我院 2020 年抗菌药物使用强度为每百人每日 57.8DDDs。2021 年加强院科上下联动事前事中事后闭环管理，促进抗菌药物使用强度下降，达到每百人每日 39.4DDDs。2022 年基于公立医院高质量发展需求，完善网格化合理用药服务体系，实现抗菌药物使用强度下降至每百人每日 32.1 DDDs。在改善抗菌药物使用强度过程中，合理用药指标也得以改善。

结论 院科上下联动事前事中事后服务闭环的抗菌药物工作模式促进了抗菌药物的规范化使用。

Antibacterial Therapy of Listeriosis: Experience and Perspective from a Tertiary First-class Teaching Hospital in China

Naiju Zhang
The First Affiliated Hospital of Bengbu Medical College

Abstract Content Objectives To investigate antibiotic selection and understand the listeriosis knowledge in healthcare providers.

Methods First, we performed a retrospective study in patients with listeriosis from January 2013 to March 2023. Patient characteristics and antibiotic selections were recorded. Effective and ineffective antibiotics were based on the Sanford Guide to Antimicrobial Therapy (50th edition). We then conducted a questionnaire survey of healthcare providers to investigate their listeriosis knowledge.

Results Fifteen listeriosis patients were identified, with a case fatality rate of 26.7% (4/15). Empirical treatments with effective antibiotics and ineffective antibiotics were given to 33.3% (5/15) and 73.3% (11/15) patients, respectively. After identifying Listeria monocytogenes, 40% (6/15) of patients had their antibiotics adjusted. Effective and ineffective antibiotics were given to 20% (3/15) and 13.3% (2/15) patients, respectively. The questionnaire survey of 77 participants showed that 32.9% (24/73) of clinicians were unaware of appropriate antibiotics for listeriosis. Most participants (83.1%, 64/77) would read the drug sensitivity report to select the antibiotics. There was a difference when selecting effective antibiotics between infection and other departments ($P < 0.001$). There was no difference when selecting effective antibiotics between other titles and junior titles ($P = 0.088$).

Conclusions Most patients with listeriosis did not receive appropriate antibiotics, which might account for the high fatality rate. This might be due to inadequate listeriosis knowledge. More education as well as correctly reporting drug sensitivity results, are urgently required.

Evaluations of prescribing practices of ceftazidime-avibactam at a tertiary first-class teaching hospital in China: A retrospective analysis for future improvement

Naiju Zhang
The First Affiliated Hospital of Bengbu Medical College

Abstract Content Background Drug Utilization Evaluation (DUE) criteria are used to assess drug usage appropriateness.

Aim To establish DUE criteria for intravenous ceftazidime-avibactam (CZA) and use the criteria to retrospectively evaluate the clinical use of CZA to help establish guidelines for the rational use of CZA.

Methods CZA drug instructions, relevant clinical guidelines, and expert consensus were involved in establishing CZA DUE standards. Forty-three patients receiving intravenous CZA from May 2020 to March 2023 were included. Their CZA usage, including indication, dosage, outcomes, and data management, was retrospectively evaluated based on the DUE standards, informing proposed clinical guidelines.

Results Compliance with CZA DUE standards was complete regarding route, solvent, incompatibility, and contraindications. However, the indication was only 41.9% (18/43) compliant. Dosage regimen, infusion time, combination therapy, drug interaction, and duration of treatment were 58.1% (25/43), 25.6% (11/43), 53.5% (23/43), 37.2% (16/43), and 30.2% (13/43), respectively. Bacteria culture testing pre-CZA use was 95.3% (41/43). Treatment course recording and prescription authorization were 95.3% (41/43) and 81.4% (35/43) compliant, respectively. No adverse reactions were reported.

Conclusions Established CZA DUE criteria facilitate a comprehensive evaluation of its use. Most clinicians had poor prescribing practices for CZA. More education training and administrative intervention are urgently required.

The enhancement effect of small molecule Lyb24 reveals AzoR as a novel target of polymyxin B

Wei Huang
Shenzhen People's Hospital

Abstract Content Given the important role of polymyxin B (PB) in the treatment of drug-resistant Gram-negative bacterial infections, the emergence of PB resistance poses a serious threat to public health. Adjuvant development is a supplementary strategy that can compensate for the lack of novel antibiotics by protecting PB. In this study, we found a small molecule named Lyb24 that showed weak antibacterial activity (minimum inhibitory concentration ≥ 10 μg/ml) but potentiated and revitalized the efficacy of PB against Gram-negative pathogens, including mcr-1- and mgrB-deletion-mediated PB-resistant strains. Our results showed that Lyb24 inhibits the translational levels of genes associated with the modification of lipid A. In addition, Lyb24 increases the permeability, disrupts the integrity and induces the depolarization of the membrane. We further found that both Lyb24 and PB could directly bind to AzoR and inhibit its activity. Structural analysis showed that Lyb24 binds to the isoalloxazine ring of flavin mononucleotide (FMN) through pi-pi stacking and loop η4 of AzoR. A pneumonia model was used to confirm that the activity against clinical PB-resistant Klebsiella pneumoniae was enhanced due to Lyb24 on PB. In conclusion, we provide a potential therapeutic regimen by combining Lyb24 and PB to treat Gram-negativeresistant bacterial infections. Our findings not only explain the synergistic effect of Lyb24, but also expand our knowledge on the mechanism of action of PB.

Methods Chequerboard assay
Time-kill assay
Growth curves of bacteria
Proteome analysis
Lipid A extraction and structural analysis
Membrane integrity assay
Transmission electron microscopy
Structure determination and refinement
Mouse infection model

Results Lyb24 enhances the activity of PB
Lyb24 affects membrane permeability and integrity

The interaction between Lyb24, PB and AzoR

Protein complex structure of AzoR-FMN-Lyb24

Lyb24 alters the loop η5 structure of AzoR

Lyb24 binds with FMN isoalloxazine ring through pi-pi stacking

Lyb24 enhances the antibacterial activity of PB in vivo

Conclusion In conclusion, we show that a small molecule revitalizes the antibacterial activity of PB in PB-resistant strains. The multiple effects on bacteria, including lipid A modification determine the usefulness of Lyb24 in a variety of PB resistance mechanisms. The discovery of AzoR as a new target of PB suggests a new mechanism of action of PB, and also provides a novel candidate for the development of PB adjuvants.

TBAJ-587 对临床相关非结核分枝杆菌的体外抗菌活性研究

樊峻晟、谭至立、李冰、褚海青
上海市肺科医院

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。

Therapeutic drug monitoring of ceftazidime-avibactam concentrations in carbapenem-resistant K. pneumoniae-infected patients with different kidney statuses

屈健
中南大学湘雅二医院

Abstract Content We investigated the use of TDM to assess the concentration of CAZ-AVI in CRKP-infected patients with different kidney statuses.

Methods CAZ-AVI concentrationswere determined using high-performance liquid chromatography.

Results 75 CRKP-infected patients were enrolled, including renal insufficiency (58.10%), normal renal function(31.08%), and augmented renal clearance(ARC) (10.81%). CAZ-AVI Cmin in ARC patients were significantly lower than in patients with normal renal function and renal insufficiency ($p<0.001$). CAZ-AVI Cmin showed a negative correlation with creatinine clearance ($r=-0.54$, $r=-0.51$, both $p<0.001$). Details please see the uploaded files.

Conclusion The concentrations of CAZ-AVI varied among patients with different kidney statuses. ARC may require higher daily doses than the standard dose.

慢性炎症的中医疗法

薛慧
三峡大学基础医学院

目的 慢性炎症极大地危害着人们的健康，寻找治疗慢性炎症的有效方法具有重要的意义。此文目的是了解中医在治疗慢性炎症中的方法及效果。

方法 CNKI 搜索输入主题：慢性炎症治疗，学科：中医学。

结果 共检索 36 篇文章，其中 6 篇针刺（针灸、电针）治疗肥胖、盆腔炎、咽喉炎等慢性炎症的经验分享。中药治疗的如藏茵陈、当归芍药液、直白八位口服液、五金石、鱼白消炎方等分别治疗肝脏、妇科、眼科、外科、男性生殖慢性炎症。中药用药采用了清热化瘀法、益气活血健脾补肾、益元扶正、甘温除热、温通和营清热解毒等方法。还有国医大师们治疗慢性炎症的经方分享。以上中医药方法在治疗各种慢性炎症时均取得了较好疗效。

结论 针刺及中药不失为治疗慢性炎症的有效方法，且中医的整体观使机体各个系统更好协调，也避开了抗生素的耐药及副作用，值得推广。

Vancomycin combined with piperacillin-tazobactam increases the risk of acute kidney injury compared with vancomycin plus other anti-pseudomonal beta-lactams: a systematic review and network meta-analysis

Kunming Pan, Ranyi Li, Zhangzhang Chen, Qianzhou Lv
ZhongShan Hospital Fudan University

Abstract Content Purpose We aimed to conduct this comprehensive network meta-analysis of all cohort studies to explore whether VAN+PTZ actually increases nephrotoxicity compared to other anti-pseudomonal beta-lactams (BLs).

Methods PubMed, Embase, Web of Science, Cochrane, CNKI, Wanfang and VIP were searched from inception to October 02, 2023. The primary outcome were acute kidney injury (AKI) and severe stage 2-3 AKI, and other outcomes including dialysis, and mortality. Subgroup analyses of studies that performed propensity score matching (PSM) and subgroup analysis of critically ill patients and children were conducted.

Results We included 70 studies (76,638 patients). Network meta-analysis indicated that VAN+PTZ was associated with significantly higher AKI risk than VAN+FEP (OR 2.55, 95%Cl. 2-3.28), VAN+MEN (OR 2.26, 95%Cl. 1.71-3.02), VAN+UC-BLs (OR 2.47, 95%Cl. 1.87-3.29), PTZ monotherapy (OR 2.2, 95%Cl. 1.43-3.39) and VAN monotherapy (OR 2.59, 95%Cl. 2-3.35) (70studies, 76,638 patients) . Also, VAN+PTZ was associated with significantly higher stage 2-3 AKI risk than VAN+FEP (OR 2.22, 95%Cl. 1.34-3.62), VAN+MEN (OR1.96, 95%Cl. 1.22-3.25), VAN+UC-BLs (OR 2.81, 95%Cl. 1.66-4.91), PTZ monotherapy (OR 3.44, 95%Cl. 1.25-9.9) and VAN monotherapy (OR 2.01, 95%Cl. 1.15-3.66) (35 studies, N=48,516). VAN+PTZ did not result in a significant difference in the incidence of receiving dialysis treatment, mortality, length of stay and time to AKI, compared to VAN plus other BLs. Subgroup analyses of studies conducting PSM demonstrated VAN+PTZ was associated with significantly higher AKI rates than VAN+FEP (OR 2.19, 95% Cl. 1.38-3.47) and VAN+MEN (OR 1.38, 95% Cl. 1.18-1.60) (8 studies, N=20479). Subgroup analysis of critically ill patients and children indicated that VAN+PTZ was associated with significantly higher AKI rates than VAN plus other BLs.

Conclusion VAN+PTZ significantly increased the risk of AKI and severe stage 2-3 AKI compared to VAN+FEP, VAN+MEN, VAN+UC-BLs, PTZ monotherapy and VAN monotherapy. Innovative analyses of studies conducted with PSM still showed that VAN+PTZ increased the risk of AKI compared to VAN plus

other BLs. For patients combined with multiple risk factors for kidney injury, VAN+FEP or VAN+MEN may be one of the alternatives to VAN+PTZ.

苦练内功强本领，真抓实干出实招—明光市人民医院多措并举推进抗菌药物管理取得实效

陈刚、房震、陈良、马开江
明光市人民医院

目的 结合多年抗菌药物使用和管理工作经验，探索一种行之有效的、适合基层医疗机构的抗菌药物管理方法。

方法 通过建立高效的管理体系、积极提升业务水平、严格的行政干预和动态科学指导等手段，努力探索适合基层医疗机构的抗菌药物管理方案，为基层医疗机构抗菌药物合理使用提供参考。

结果 通过一系列行之有效的举措，可以显著提升基层医疗机构抗菌药物管理水平。

结论 通过建立高效的管理体系、积极提升业务水平、严格的行政干预和动态科学指导相结合等综合举措，可以显著提升基层医疗机构抗菌药物管理水平。

TBAJ-587 对临床相关非结核分枝杆菌的体外抗菌活性的研究

樊峻晟、谭至立、李冰、褚海青
上海市肺科医院

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。

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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。

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The impact of polymyxin B pharmacokinetics on clinical outcomes in critically ill patients: A single-center retrospective study

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Abstract Content The aim of this study is to investigate the impact of polymyxin B pharmacokinetics and dose adjustments on the clinical outcomes of critically ill patients.

Methods This single-center, retrospective, observational study includes critically ill patients admitted to the Intensive Care Unit (ICU) of Zhongda Hospital, Southeast University, who received polymyxin B (PMB) treatment from January 2020 to July 2023. Data were extracted from electronic medical records, including demographic information, comorbidities, clinical and microbiological features of the infection, antimicrobial treatment regimens, laboratory test parameters on the day of polymyxin B initiation, SOFA score and APACHEII score. Additionally, therapeutic drug monitoring (TDM) data of polymyxin B including area under the concentration at steady state (AUCss,24h), trough concentration (Cmin), peak concentration (Cmax) and 6 hours concentration (C6h), and organ support therapies were obtained from medical records. The primary clinic outcome is the 28-day mortality. Secondary outcomes encompass favorable clinical response, microbiological eradication, length of hospital and ICU stay, adjustments in polymyxin B drug dosages, and the occurrence of acute kidney injury (AKI).

Results From January 2020 to June 2023, a total of 146 patients were included in the analysis at last, the 28-day mortality was 43.2% (63/146). The Cox regression analysis indicated that comorbidity diseases [Hazard Ratio (HR) 2.914, 95%CI 1.310-6.484, P=0.009], SOFA score at admission [HR 1.11, 95%CI 1.048-1.176, P<0.001], Polymyxin B treatment days[HR=0.896, 95%CI 0.849-0.946, P<0.001], polymyxin B combined with tigecycline therapy[HR 2.442, 95%CI 1.451-4.110, P=0.001],AUCss,24h [HR 0.993, 95%CI 0.988-0.999, P=0.019]were independent risk factors for 28-day mortality in patients with PMB treatment.

Based on the range of AUCss,24h the patients were categorized into three groups, high AUCss,24h group (>100 mg·h/L), moderate AUCss,24h group (50 to 100 mg·h/L), and the low AUCss,24h group (<50 mg·h/L). The 28-day mortality rates for patients in the high, moderate, and low AUCss,24h groups

were 27.7% (13/47), 45.6% (31/68), and 61.3% (19/31), respectively(P=0.012). Two multivariable Cox regression models were constructed based on different adjusted confounding factors, the results indicate that AUCss,24h, C6h, and Cmin were inversely correlated with the 28-day mortality in patients. Ordinal logistic regression analysis and multivariable logistic analysis both found that baseline albumin level was important risk factor associated with increased AUCss,24h.

80 patients with AUCss,24h values greater than 100 mg·h/L or less than 50 mg·h/L. Among them, 35 patients underwent dose adjustment, while 45 patients did not undergo dose adjustment, there was no significant difference in the 28d-mortality between the two groups (42.9% vs.40%, P=0.797). AKI was observed in 40.6% of patients (41/101). However, there was no difference in AUCss,24h value between the AKI group and non-AKI group (87.2 mg·h/L; IQR, 68.5-131.1 mg·h /L vs. 84.5 mg·h/L; IQR, 55.6-115.4 mg h/L, P=0.338). Similarly, there was no difference in the 28-day mortality rate between the two groups of patients (36.6% vs.33.3%, P=0.736). Multivariable logistic regression analysis indicated that baseline eGFR was associated with a reduced incidence of AKI (Adjusted OR 0.979,95%CI 0.963-0.994, P=0.007), while the duration of polymyxin B treatment was associated with an increased incidence of AKI (Adjusted OR 1.101,95%CI 1.007-1.204, P=0.034).

Conclusion AUCss,24h is an important determinant of 28-day mortality in polymyxin B therapy. High AUCss,24h levels may tend to improve clinical outcomes in critically ill patients. Serum albumin level is a significant risk factor influencing AUCss,24h. Adjustment of polymyxin B dosage increases the duration of polymyxin B therapy but does not significantly affect patient mortality.

Effect of Ceftazidime- Avibactam Combined with Different Antimicrobials against Carbapenem-Resistant Klebsiella pneumoniae

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Abstract Content This study aimed to assess the in vitro efficacy of ceftazidime-avibactam (CZA) in combination with various antimicrobial agents against carbapenem-resistant Klebsiella pneumoniae (CRKP).

Methods We selected 59 clinical CRKP isolates containing distinct drug resistance mechanisms. The minimum inhibitory concentrations (MIC) of meropenem (MEM), colistin (COL), eravacycline (ERA), amikacin (AK), fosfomycin (FOS) and aztreonam (ATM), both individually and in combination with CZA, were tested using the checkerboard method. The interactions of antimicrobial agent combinations were assessed by fractional inhibitory concentration index (FICI) and susceptible breakpoint index (SBPI). The time-kill curve assay was employed to dynamically evaluate the effects of these drugs alone and in combination format.

Results In the checkerboard assay, the combination of CZA+MEM showed the highest level of synergistic effect against both KPC-producing and carbapenemase-non-producing isolates, with synergy rates of 91.3% and 100%, respectively. Following closely was the combination of FOS+CZA . For metallo-beta-lactamases (MBL) producing strains, ATM+CZA displayed complete synergy, while the combination of MEM+CZA showed a synergy rate of only 57.14% for NDM-producing strains and 91.67% for IMP-producing strains. In the time-kill assay, MEM+CZA also demonstrated significant synergistic effects against the two KPC-2-producing isolates (Y070 and L70), the two carbapenemase-non-producing isolates (Y083 and L093) and the NDM-1-producing strain L13, with reductions in log10 CFU/mL exceeding 10 compared to the control. Against the IMP-producing strain Y047, ATM+CZA exhibited the highest synergistic effect, resulting in a log10 CFU/mL reduction of 10.43 compared to the control.

Conclusion our study confirmed the efficacy of the combination CZA+MEM against KPC-producing and non-carbapenemase-producing strains. For metalloenzyme-producing strains, CZA+ATM demonstrated the most significant synergy. Additionally, CZA exhibited a notable synergy effect when combined with FOS. These combination therapies present promising new options for the treatment of CRKP infection.

Comparative Pharmacokinetics of Polymyxin B in Critically Ill Elderly Patients with Extensively Drug-Resistant Gram-Negative Bacteria Infections

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Abstract Content Elderly patients are more prone to develop acute kidney injury during infections and polymyxin B (PMB)-associated nephrotoxicity than young patients. The differential response to PMB between the elderly and young critically ill patients is unknown. We aimed to assess PMB exposure in elderly patients compared with young critically ill patients, and to determine the covariates of PMB pharmacokinetics in critically ill patients.

Methods Seventeen elderly patients (age ≥ 65 years) and six young critically ill patients (age < 65 years) were enrolled. Six to eight blood samples were collected during the 12 h intervals after at least six doses of intravenous PMB in each patient. PMB plasma concentrations were quantified by high-performance liquid chromatographytandem mass spectrometry. The primary outcome was PMB exposure as assessed by the area under the concentration-time curve over 24 h at steady state (AUCss, 0–24 h).

Results The elderly group had lower total body weight (TBW) and higher Charlson comorbidity scores than young group. Neither AUCss, 0–24 h nor normalized AUCss, 0–24 h (adjusting AUC for the daily dose in mg/kg of TBW) was significantly different between the elderly group and young group. The half-life time was longer in the elderly patients than in young patients (11.21 vs 6.56 hrespectively, $p = 0.003$). Age and TBW were the covariates of half-life time ($r = 0.415$, $p = 0.049$ and $r = -0.489$, $p = 0.018$, respectively). TBW was the covariate of clearance ($r = 0.527$, $p = 0.010$) and AUCss, 0–24 h ($r = -0.414$, $p = 0.049$). Patients with AUCss, 0–24 h ≥ 100 mg·h/L had higher baseline serum creatinine levels and lower TBW than patients with AUCss, 0–24 h < 50 mg·h/L or patients withAUCss, 0–24 h 50–100 mg·h/L.

Conclusion The PMB exposures were comparable in elderly and young critically ill patients. High baseline serum creatinine levels and low TBW was associated with PMB overdose.

Trial registration ChiCTR2300073896 retrospectively registered on 25 July 2023.

替加环素致低纤维蛋白原血症的危险因素

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目的 替加环素作为一种新型四环素类抗菌药物，抗菌谱较广，对多种耐药菌有效，临床上应用广泛。本研究旨在探讨替加环素致重症感染患者发生低纤维蛋白原血症的相关危险因素。

方法 回顾性分析 2021 年 6 月至 2023 年 6 月在东南大学附属中大医院 ICU 接受替加环素治疗的 114 例重症感染患者。根据使用替加环素后患者是否发生低纤维蛋白原血症，将患者分为低纤维蛋白原血症组 (纤维蛋白原 < 2.0 g/L) 和正常组 (纤维蛋白原 ⩾ 2.0 g/L)，收集患者临床资料，采用 Logistic 回归分析替加环素致重症感染患者发生低纤维蛋白原血症的危险因素。

结果 共纳入 114 例患者，其中有 68 例患者在使用替加环素期间出现了低纤维蛋白原血症。多因素 Logistic 回归分析显示患者的基线纤维蛋白原、谷浓度 (Cmin)、峰浓度 (Cmax)、给药后 6h 浓度 (C6h) 和 24 小时浓度 - 时间曲线下面积 (AUC0-24) 是重症感染患者发生低纤维蛋白原血症的主要危险因素 ($P < 0.05$)。

结论 低纤维蛋白原血症的发生与替加环素的血药浓度和患者基线纤维蛋白原有关。临床在应用替加环素治疗重症感染时，有必要定期进行血药浓度和凝血功能的监测。

TDM 指导下美罗培南治疗耐药菌感染的重症成人糖尿病患者

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目的 血药浓度指导下美罗培南治疗耐药菌感染的重症成人糖尿病患者临床特征及 TDM 达标率

方法 回顾性分析 2022 年 1 月 1 日 -2022 年 12 月 31 日期间东南大学附属中大医院收治的耐药菌感染的重症成人糖尿病患者资料，包括基本信息、基础疾病、实验室检查、抗菌药物使用情况等，并分析患者临床特征及 TDM 达标率。

结果 共纳入 21 例患者，17 例合并高血压，10 例合并肾功能不全。感染的病原体中多药耐药鲍曼不动杆菌感染 10 例，多药耐药肺炎克雷伯菌菌感染 9 例，铜绿假单胞菌感染 7 例。同时感染革兰氏阴性菌和真菌的患者 10 例。感染部位在肺部的 17 例，血流感染 4 例，尿路感染 4 例。21 例患者静脉持续输注美罗培南 4 小时为基础的单药（11 例）或多药（10 例）治疗方案，给药方案为 1g q8h 的 11 例患者中，有 2 例未达标，其余患者中有 1 例未达标。13 例患者应用抗菌药物治疗后明显好转，白细胞、C- 反应蛋白、降钙素原指标下降。

结论 耐药菌感染的重症糖尿病患者合并多种病原体感染风险高，合理使用 TDM 指导可促进此类患者好转。

模型引导下西他沙星对目标病原菌药动学 / 药效学界值的制定及给药方案评价

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目的 本研究旨在制定西他沙星对目标病原菌的药动学 / 药效学（PK/PD）界值，以支持建立抗菌药物药敏试验的临床折点。

方法 本研究基于 342 例受试者的数据建立群体 PK（PopPK）模型，计算西他沙星在不同给药方案（50mg q12h、100mg q24h 和 100mg q12h）下感染患者的 PK 参数，结合体外药效学数据和 PK/PD 靶值，通过蒙特卡洛模拟计算西他沙星不同给药方案对肺炎链球菌、金黄色葡萄球菌、大肠埃希菌、肺炎克雷伯菌和铜绿假单胞菌的达标概率（PTA）和累积响应百分率（CFR），最终制定 PK/PD 界值和评价给药方案。

结果 PopPK 模型显示西他沙星的 PK 特征符合二房室线性消除模型。蒙特卡洛模拟结果显示，基于动物感染模型靶值（fAUC24h /MIC=11.56），西他沙星 3 个给药方案对肺炎链球菌分别在 MIC ≤ 0.06mg/L、MIC ≤ 0.06mg/L、MIC ≤ 0.125mg/L 时 PTA 达 95% 以上，CFR 为 98.2%~99.3%；当以临床研究的 fAUC24h/MIC ≥ 30 为靶值时，3 个给药方案对肺炎链球菌分别在 MIC ≤ 0.03 mg/L、MIC ≤ 0.03 mg/L 和 MIC ≤ 0.06mg/L 时 PTA > 95%，CFR 为 89.2%~97.3%。西他沙星各给药方案对金黄色葡萄球菌、大肠埃希菌、肺炎克雷伯菌和铜绿假单胞菌的 PK/PD 界值均分别为 0.06 mg/L、0.06 mg/L 和 0.125 mg/L，CFR 为 56.3%~76.9%。

结论 本研究建议西他沙星对目标病原菌的 PK/PD 界值为 S ≤ 0.06mg/L 和 R > 0.125 mg/L。根据 PK/PD 界值和 CFR 值预期西他沙星 50mg q12h、100mg q24h 和 100mg q12h 给药方案下对治疗肺炎链球菌引起的呼吸道等相关感染有效，但对铜绿假单胞菌相关感染的疗效不佳。

Development, validation and application of an LC-MS/MS method for the simultaneous quantification of four triazole antifungal concentrations in human plasma

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Abstract Content We developed a method for the simultaneous quantification of four triazole antifungal agents in plasma by liquid chromatography-tandem mass spectrometry to support clinical therapeutic drug monitoring of fluconazole, voriconazole, posaconazole, and isavuconazole.

Methods The method used the stable isotopes voriconazole-d3 and posaconazole-d4 as internal standards (IS), and the four substances to be measured and the IS were extracted from plasma samples by protein precipitation. The mass spectrometer was operated in positive electrospray ionisation mode, and the mass-to-charge ratios of the parent ions and daughter ions of the test substances and IS were monitored using a multiple ion reaction monitoring scheme.

Results Inter-batch accuracy and precision of plasma samples ranged from 90.00% to 117.05% and 0.49% to 11.28%, respectively. Intra-batch accuracy and precision ranged from 92.28% to 111.48% and 0.17% to 3.00%, respectively. Matrix factors ranged from 0.83 to 1.04. The results of clinical samples showed that the mean fluconazole Cmin was 19.05 mg/L, mean voriconazole Cmin was 3.08 mg/L, mean posaconazole Cmin was 1.47 mg/L and mean isavuconazole Cmin was 4.26 mg/L.

Conclusion The advantages of this method are that it is the first time to propose the simultaneous quantification of four antifungal agents, namely, fluconazole, voriconazole, posaconazole and isavuconazole, and the method has strong specificity, simple sample processing, short analysis time, and the methodological validation of each parameter conforms to the industry standard. The method was also successfully applied to quantify 770 clinical plasma samples, which provides a reliable method for guiding the rational use of antifungal drugs and monitoring drug concentrations in the clinic.

PBPK study of contezolid in the central nervous system

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Abstract Content Contezolid, an oxazolidinone, is a structurally improved version of linezolid, substantially reducing haematotoxicity and the inhibition of monoamine oxidase. Two cases of successful treatment of tuberculous meningitis with contezolid have been reported, but there have been no studies of contezolid in the central nervous system.

Methods Physiologically based pharmacokinetic (PBPK) modelling was performed using GastroPlus®. The model was built based on our established human PBPK model of contezolid. Cerebrospinal fluid (CSF)/brain tissue to plasma partition coefficients (KpCSF/brain) were obtained from animal studies. A dose of 84 mg/kg was used, and the experiments were conducted using gavage administration to rats. Food intake was prohibited 12 hours prior to drug administration, but free access to water was allowed. CSF, blood and brain tissue samples were collected before and 0.5, 1, 1.5, 2, 3, 4, 8, 12 and 24 hours after drug administration. The drug content of the samples was determined using a high-performance liquid chromatography-mass spectrometry technique, and Kp was calculated. Information on clinically infected patients was collected, and the model's accuracy was assessed by quantifying the drug concentration in CSF and plasma samples.

Results The KPCSF of contezolid was 0.050, and KPbrain was 0.052 in rats. Statistical analysis was carried out, and it was found that there was a consistent trend of change in the concentration of contezolid in plasma, CSF and brain tissue of the rats after a single dose of the drug. There was no significant difference in drug concentration in brain tissue and CSF at all time points. Plasma and CSF samples were collected after contezolid application from 2 patients. Patient A's kpCSF = 0.0496 after 5.5 h of drug administration was consistent with the results of animal experiments and supported the direct use of 0.05 as the human Kp value. Patient B's pathological and physiological information was entered into the established PBPK contezolid model and loaded with the Kp (0.05). The patient's plasma and CSF drug concentrations were simulated, and measured values were loaded. The predicted drug-time curves fit the measured values well.

Conclusion The results of animal experiments showed that the drug concentrations of contezolid in brain tissue and CSF were essentially the same, so the brain tissue drug concentration could be replaced by monitoring the drug concentration in the CSF. The Kp obtained from animal experiments of contezolid

were consistent with the results of clinical samples. The pedicted curve form the established PBPK model fitted well with the clinical measured values, and the model can be used to predict the pharmacokinetic behaviours of contezolid in the human central nervous system.



微生物

FOCUS—PDCA 在降低感染科住院患儿血培养污染率中的应用

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目的 探讨 FOCUS—PDCA 管理方法在降低感染科住院患儿血培养污染率中的应用效果。

方法 对本科室 2016 年 1 月 -2021 年 12 月住院患儿血培养标本进行数量及污染率统计，并对污染原因进行分析，随后采用 FOCUS—PDCA 管理方法对住院患儿血培养标本进行持续性质量改进，并比较对策实施前后的血培养标本污染率。

结果 通过实施 FOCUS—PDCA 管理方法后我科住院患儿血培养标本污染率明显降低，由对策实施前的 1.1% 降为对策实施后的 0.1%，下降了 1.0%，在后期的效果确认和维持阶段，血培养标本污染率仍然维持在较理想水平（污染率为 0.62%）。

结论 采用 FOCUS—PDCA 管理方法可有效降低住院患儿血培养标本污染率，可有效保证检验分析前阶段标本质量，提高检验结果准确性。

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

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

Methods We analysed clinical outcomes of 46 haematological 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. colonisation. Colonised 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 colonising 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 colonisation to bloodstream infection, with minimal changes in virulence genes. Homology analysis suggested that CRA BSI originated from colonising 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.

A training program for Improving the capacity of infection high-throughput sequencing and Diagnosis in China

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Abstract Content Infectious diseases are a serious threat to human especially since the COVID-19 outbreak has proved the importance and urgency of their diagnosis and treatment again. Metagenomic next-generation sequencing (mNGS) has been widely used and recognized in clinical and carried out localized testing in hospitals. Increasing the training of mNGS detection technicians can enhance their professional quality and more effectively realize the application value of the hospital platform.

Methods Based on the initial theoretical understanding and practice of the mNGS platform for localization construction, we have designed a training program to enhance the ability of technicians to detect pathogens by utilizing mNGS, and hence to conduct training practices nationwide.

Results Until August 30, 2022, the page views of online classes have reached 51,500 times and 6 of offline small-scale training courses have been conducted. A total of 67 trainees from 67 hospitals have participated in the training with a qualified rate of 100%. After the training course, the localization platform of 1 participating hospital has been put into use, 2 have added the mNGS localization platform for admission, among which 3 have expressed strong intention of localization.

Conclusion This study focuses on the training procedures and practical experience of the project

which is the first systematic standardized program of mNGS in the world. It solves the training difficulties in the current industry, and effectively promotes the localization construction and application of mNGS in hospitals. It has great development potential in the future and is worth further promotion.

以腹泻为首发表现的 C 群沙门菌全身侵袭性肝脓肿 1 例

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目的 探讨 C 群沙门菌全身侵袭性肝脓肿的临床特点与诊断、治疗要点。

方法 回顾性分析 1 例以腹泻为首发表现的 C 群沙门菌全身侵袭性肝脓肿患者的临床资料，并对相关文献进行复习。

结果 本例患者，男，52 岁，急性起病无明确诱因出现腹泻，伴发热。便培养、引流液培养、血培养均为 C 群沙门菌。确诊为侵袭性肝脓肿。经皮肝穿引流后联合美罗培南抗感染治疗后体温恢复正常，炎症指标较前明显下降。

结论 侵袭性 C 群沙门菌肝脓肿临床较为少见，因以腹泻为首发表现容易误诊延误治疗时机，对抗生素敏感，规范治疗后可获得良好效果。

抗菌肽 Aurein 1.2 衍生物的设计、合成和活性评价

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目的 抗菌肽 (AMP) 是治疗多重耐药菌感染的有前途药物。Aurein 1.2 是一种含有 13 个氨基酸的天然 AMP，对革兰氏阳性细菌具有较强的抗菌活性，但其抗菌活性仍需进一步提升。

方法 在本研究中，我们设计了 3 种新型 Aurein 1.2 衍生物：Aurein M1，Aurein M2 和 Aurein M3，分析了色氨酸取代和增加正电荷对 Aurein 1.2 活性的影响。利用多种生物信息学工具对其理化性质、二级和三级结构以及两亲性结构进行预测。合成后对衍生物进行抗菌活性、溶血活性、细胞毒性和结构分析。

结果 预测结果与我们的实验结果一致，与 Aurein 1.2 相比，带净正电荷的 Aurein M2 和 M3 对革兰氏阳性菌和革兰氏阴性菌的选择性分别提高了 11.30 倍和 8.00 倍。Aurein M2 的溶血活性低于 Aurein 1.2 和 Aurein M3，并且 Aurein M3 对人成纤维细胞的存活率影响较小。Aurein M3 对金黄色葡萄球菌和大肠杆菌的最低抑菌浓度为 16 μg/ml，推荐作为临床研究的候选物。在三个衍生物中，含有赖氨酸和色氨酸残基的 Aurein M3 比单独氨基酸替换的衍生物更有效。圆二色谱分析表明，在 10 mM SDS 存在下，衍生物具有类似于 Aurein 1.2 的 α 螺旋结构。

结论 增加正电荷可以成功地作为提高抗菌肽效价和选择性的方法。Aurein M3 具有广谱抗菌活性，且效力高于 Aurein 1.2。此外，Aurein M3 的选择性和耐盐性使其成为一种有前景的 AMP，可进行包括序列优化等实验在内的进一步研究。

鲍曼不动杆菌碳青霉烯耐药代谢变化及逆转效应代谢物功能的研究

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目的 解析碳青霉烯耐药鲍曼不动杆菌（CRAB）耐药的代谢机理，验证逆转耐药代谢组的效应代谢物，调控 CRAB 对碳青霉烯的敏感性。

方法 采用气相色谱质谱法代谢组学检测方法，比较鲍曼不动杆菌碳青霉烯敏感与耐药代谢组学差异，结合通路富集和正交偏最小二乘判别分析获得关键代谢通路和候选效应代谢物，通过外源添加代谢物联合美罗培南进行细菌生存率试验、持留菌和生物膜细菌杀菌试验和动物感染模型试验，优选逆转 CRAB 耐药的效应代谢物。

结果 CRAB 最显著的代谢变化是三羧酸（TCA）循环和嘌呤代谢通路下调，胞内腺嘌呤核苷酸水平降低。CRAB 中 TCA 循环酶活性和质子动力势降低验证了 TCA 循环的下调，通路基因 qRT-PCR 结果证实嘌呤代谢通路下调是由于 TCA 循环受限所致。外源性添加三磷酸腺苷（ATP）或一磷酸腺苷（AMP）可以提高美罗培南对 CRAB 的杀菌效率，并具有物质浓度、抗菌药物浓度和作用时间梯度依赖性。有效性验证中发现，ATP 联合美罗培南降低 CRAB 持留菌和生物膜细菌的生存率，降低脓毒症和肺部感染小鼠内脏组织细菌载量，提高小鼠感染后的存活率。

结论 本研究提示 CRAB 的耐药状态存在代谢组学差异，外源性代谢物可调控抗菌药物敏感性，效应代谢物联合抗菌药物是治疗多重耐药菌感染的潜在可行方法。

全靶向宏基因组二代测序技术对脓毒症病原体诊断价值及临床评估治疗研究：一项多中心前瞻性观察研究

原浩、刘玲
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目的 在脓毒症患者中，通过全靶向宏基因组二代测序技术辅助病原体诊断及指导抗感染治疗对患者临床预后的影响。

方法 本研究为多中心前瞻性观察研究，对 4 个重症医学中心的患者进行筛查，纳入符合 Sepsis 3.0 诊断标准、怀疑血流感染，在使用抗感染治疗前留取血液标本进行全靶向宏基因组二代测序，当测序结果与血培养结果不一致时则应用 PCR 对病原体进行验证。联合血培养和 RT-PCR 结果，分析全靶向 mNGS 对脓毒症患者病原体的诊断阳性率的情况，观察全靶向 mNGS 指导抗感染治疗对脓毒症患者入组后第 3、7 天的序贯器官衰竭评分（SOFA）的变化情况，分析全靶向 mNGS 指导抗感染治疗对患者病情严重程度的影响。

结果 2022 年 4 月至 2022 年 11 月共纳入 184 例怀疑血流感染的脓毒症患者。中位年龄 66(56,74) 岁，其中男性 124 例 (67.4%)。以 RT-PCR 证实全靶向 mNGS 的病原体的阳性率显著高于血培养 (51.6% vs 17.4%， P<0.001)，以血培养联合 PCR 验证结果为参考标准，靶向 mNGS 诊断脓毒症病原体的阳性率为 91.8%(169/184) 。不同病原体引起的脓毒症患者预后不同，本研究中金黄色葡萄球菌引起的血流感染病死率最高 (60.0%)。全靶向 mNGS 检测结果回报后，64 名（34.8%）患者调整了抗感染方案，对 41 名（22.3%）产生了临床正向影响，即在入组后 SOFA 评分下降 2 分。

结论 在脓毒症患者中，全靶向 mNGS 病原体阳性率显著高于血培养，根据全靶向 mNGS 指导抗感染治疗可以降低部分患者的 SOFA 评分而产生临床正向影响。

质谱鉴定联合直接快速药敏试验在细菌血流感染中的应用

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目的 评估质谱快速鉴定联合直接药敏试验在革兰阴性细菌血流感染诊断中的临床应用价值。

方法 对2021年8月2022年3月我院133瓶血培养阳性标本经SDS沉淀离心富集细菌后，使用基质辅助激光解吸电离飞行时间质谱（MALDITOF MS）直接鉴定，对阳性血培养液进行直接快速药敏试验（RAST），同时对培养后的菌落进行质谱鉴定和VITEK2Compact药敏分析，比较两种方法的一致性。

结果 对2021年8月2022年3月我院133瓶血培养阳性标本经SDS沉淀离心富集细菌后，使用基质辅助激光解吸电离飞行时间质谱（MALDI TOF MS）直接鉴定，对阳性血培养液进行直接快速药敏试验（RAST），同时对培养后的菌落进行质谱鉴定和VITEK2Compact药敏分析，比较两种方法的一致性。

结论 5% SDS沉淀法联合MALDI-TOF MS直接鉴定细菌菌种准确性高，RAST的CA比例高，8h可作为革兰阴性细菌RAST药敏判读的最佳时间点，对于及时指导临床用药及改善患者预后具有重要意义。

某三级医院耐碳青霉烯铜绿假单胞菌的临床分布及其检出率与碳青霉烯类抗菌药物使用频度 DDDS 的相关性研究

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目的 了解某三级医院耐碳青霉烯铜绿假单胞菌 (carbapenem resistant Pseudomonas aeruginosa, CRPA) 的临床分布情况，及其检出率与碳青霉烯类抗菌药物 DDDS 相关性，为临床治疗、院感防控及合理用药提供参考依据。

方法 梳理 2017-2021 年本院分离的临床菌株，采用 WHONET 5.6 及 SPSS 23.0 软件对数据进行分析。

结果 显示本院 2017 年至 2021 年间分离铜绿假单胞菌（PA）622 株，其中 CRPA91 株，检出率为 14.63%。CRPA 科室分布以呼吸与危重症医学科（31.87%）、重症医学科（23.08%）、神经外科（18.68%）为主。标本类型中，以痰和肺泡灌洗液为主，占 81.32%，其次为伤口分泌物和尿液，分别占 6.59% 和 5.49%。年龄分布以 >80 岁（25.27%）和 60 ~ 80 岁（29.67%）人群最多见。碳青霉烯类抗菌药物使用频度 DDDS 分析结果显示，2017 年至 2021 年 CRPA 检出率与碳青霉烯类抗菌药物 DDDs 呈高度正相关（r=0.82 P=0.086）。临床科室中，神经外科 CRPA 检出率与碳青霉烯类抗菌药物 DDDS 呈正相关（r=0.78 P=0.122）。

结论 本院所分离 CRPA 检出率与碳青霉烯类抗菌药物 DDDS 呈正相关，近年有大量文献报道抗菌药物使用情况与细菌耐药率的相关性，但研究结果差异较大，尤其是不同医疗机构 CRPA 检出率与碳青霉烯类抗菌药物 DDDs 相关性分析结果不尽相同。因此，本文通过了解本院 CPRA 的临床分布特点，重点分析近年本院 CPRA 检出率变化趋势，同时以检出率排名较高的科室为亚组研究对象，探究 CPRA 检出率与碳青霉烯抗菌药物 DDDs 相关性，从而为遏制抗菌药物耐药性提供更为精细化的管理思路。

Quorum sensing coordinates phage defense mechanisms in Pseudomonas aeruginosa

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Abstract Content Quorum sensing (QS) plays a crucial role in regulating key traits, including the upregulation of phage receptors, leading to heightened phage susceptibility in Pseudomonas aeruginosa. Consequently, elevated cell densities usually escalate the likelihood of phage invasions. This observation has sparked speculation that bacteria might have evolved multiple antiphage defense mechanisms to offset the cost of increased phage receptor expression during the prolonged coevolution or cohabitation with phages.

Methods The role of QS in defense strategies employed by P. aeruginosa to fight against phages phipa2 and phipa10's predation was determined by comparing phage inhibition, adsorption, and resistance assays between ZS-PA-35 and its QS mutants (ΔlasR, ΔrhlR, ΔlasI, ΔrhlI, ΔlasR ΔrhlR, and ΔlasI ΔrhlI) at low- and high-cell-densities.

Results The Las system increases phage adsorption rates by upregulating the expression of Type IV pilus and O-antigen receptors, which subsequently leads to accelerated bacterial lysis. Moreover, the Las system, apart from mediating receptor mutations, orchestrates an additional intracellular defense mechanism to suppress the production of both phage phipa2 and phipa10, resulting in a reduction of over 2 logs in high cell density cultures of strain ZS-PA-35 and phipa10. These flexible regulatory systems optimize the function of various defense strategies, particularly when bacterial communities are most susceptible to phage invasion.

Conclusion Bacteria employ QS to finely tune various defense strategies, both mutational and non-mutational defense mechanisms, highlighting the intricate nature of phage-host interactions and the challenges associated with the potential clinical use of phages as therapeutic agents.

Synergistic Effect of N-acetylcysteine and Ambroxol Hydrochloride in Combination with Phage against Pseudomonas aeruginosa and Klebsiella pneumoniae

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Abstract Content N-acetylcysteine (NAC) and ambroxol hydrochloride (AMB) are commonly prescribed to alleviate sputum retention in lower respiratory tract infections, frequently provoked by multidrug-resistant bacteria. With the escalating threat of antibiotic resistance, phage therapy has surfaced as a promising alternative approach against these resilient strains found in sputum. Surprisingly, no studies have delved into the potential interplay between phages and NAC or AMB, even though they are often administered concurrently during phage therapy. Therefore, exploring the dynamics of phage-host interactions in the presence or absence of NAC or AMB could improve clinical approaches to phage treatment for bacterial infections in the lower respiratory tract.

Methods We explored the effectiveness of NAC or AMB in combination with characterized phages utilizing three distinct receptors against their corresponding multidrug-resistant bacteria, Pseudomonas aeruginosa ZS-PA-35 (phipa2-type IV pili, phipa10-o antigen) and Klebsiella pneumoniae Kp36 (phage 117-capsular polysaccharide). Accordingly, we conducted a series of in vitro experiments, including liquid inhibition assays, quantification of phage production, phage adsorption studies, assessment of twitching motility, analysis of receptor gene expression, and biofilm inhibition assays, to investigate potential synergies between phages and NAC or AMB.

Results Phipa10 exhibited synergy with NAC, while phipa2 showed synergy with AMB in LB medium. Although the release of phage progenies in P. aeruginosa was hindered, phipa10 demonstrated synergistic effects with NAC and AMB, whereas phipa2 and 117 exhibited synergies with NAC and AMB in cell culture medium, respectively. Furthermore, we observed that NAC significantly reduced phage stabilities in LB medium but not in cell culture medium, emphasizing the influence of media composition on the phage-host interactions.

Conclusion Together these results showed synergistic effect between phage and airway mucus hypersecretion drugs are more likely to be phage dependent, suggesting a number of factors must be carefully considered during the combination treatments, and our study will further help clinicians predict the outcome of clinical prescriptions, ultimately aiming to optimize their efficacy for potential clinical applications.

脓肿分枝杆菌致婴幼儿迁延性肺炎 1 例并文献复习

梁嘉慧、陈洁琳、王双杰、李林霖、刘敏雪、张欢
广西壮族自治区妇幼保健院 (广西壮族自治区儿童医院广西壮族自治区妇产医院广西壮族自治区出生缺陷预防控制研究所)

目的 探讨婴幼儿感染脓肿分枝杆菌的临床特征和诊疗要点，以加深实验室及临床医生对该菌的认识。

方法 回顾 1 例脓肿分枝杆菌致婴幼儿迁延性肺炎的临床特征及诊疗过程，并以“Mycobacterium abscessus”“children/infant”为英文检索词，在 PubMed 数据库检索，以“脓肿分枝杆菌”“儿童 / 婴幼儿”为中文检索词，在中国知网和万方数据库检索，将获取的国内外报道的婴幼儿感染脓肿分枝杆菌病例资料进行分析。

结果 患儿，男，3 月 17 天，2 个月内先后两次就诊于广西壮族自治区妇幼保健院，主要临床表现为发热、反复咳嗽。实验室检查显示白细胞反复升高；CT 提示肺部团块状病灶，有空洞伴坏死；纤支镜下可见气道管腔内肉芽组织增生及填塞；肺泡灌洗液抗酸染色阳性、培养阳性，质谱仪鉴定为脓肿分枝杆菌；病原宏基因组学检测示脓肿分枝杆菌。诊断为脓肿分枝杆菌感染。给予亚胺培南、复方新诺明、阿奇霉素及头孢西丁联合治疗两个月后好转出院。检索出符合条件的文献共 20 篇 25 例，加上本病例，共纳入 26 例，最常见的症状为咳嗽、发热；最常见的感染部位是肺部；26 例确诊病例中，16 例直接涂片抗酸染色阳性，12 例通过分子诊断技术检出；14 例肺部感染患儿中，有 9 例从肺泡灌洗液检出；22 例可获得用药资料病例均为联合用药。

结论 3 岁以下尤其是无免疫缺陷的健康婴幼儿，罹患脓肿分枝杆菌感染相对较为罕见；怀疑肺部感染脓肿分枝杆菌的患儿，抗酸染色直接涂片、肺泡灌洗液行 NGS 检测及培养 , 是重要且有效的检查方法；多药联合治疗方案疗效好，治愈率高达 95.8%。

Comparison of metagenomic next-generation sequencing and conventional culture for the diagnostic performance in febrile patients with suspected infections

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Abstract Content Background Timely and accurate identification of pathogens is crucial for appropriate treatment and prognosis of infectious diseases. As an increasingly popular pathogen detection method, the performance of metagenomic next-generation sequencing (mNGS) in detecting pathogens in febrile patients with suspected infection requires further exploration.

Methods This study included 368 febrile patients with suspected infections who were admitted to the Infectious Disease Department of Qilu Hospital, Shandong University between January 5, 2021 and April 14, 2023. Both mNGS testing and conventional culture were performed in all patients. Clinical data of enrolled patients were collected, and the diagnostic performances of mNGS and culture were compared.

Results Of the 368 enrolled patients, 231 were finally diagnosed with infection and 137 were with diseases other than infection. The sensitivity (58.01% vs. 21.65%, $p<0.001$) and negative predictive value (54.67% vs. 42.9%) of mNGS were superior to those of culture. In contrast, the culture exhibited higher specificity (99.27% vs. 85.40%, $p<0.001$) and positive predictive value (98.84% vs. 87.01%) than mNGS. Among infected patients with positive mNGS results, 64 received adjusted antibiotic therapy including treatment transitions, antibiotic downgrading, and combination therapy. Among them, 9 had additional antifungal drugs and 21 patients had a treatment turning point based on the mNGS results and these patients recovered and discharged due to timely antibiotic adjustment. Both positive rates of puncture fluid mNGS and tissue mNGS were higher than those of culture in the patients who had prior antibiotic use, and this difference was statistically significant ($p=0.000$).

Conclusion mNGS is more sensitive and accurate than traditional culture, making it ideal for identifying pathogens and screening infectious diseases, especially for those with uncultivated or difficult-to-cultivate species. Early diagnosis allows for prompt treatment with targeted antibiotics, and mNGS is recommended when samples are limited.

Highly sensitive SERS platform for pathogen analysis by cyclic DNA nanostructure@AuNP tags and cascade primer exchange reaction

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Abstract Content The capacity to identify small amounts of pathogens in real samples is extremely useful. Herein, we proposed a sensitive platform for detecting pathogens using cyclic DNA nanostructure@AuNP tags (CDNA) and a cascade primer exchange reaction (cPER). This platform employs wheat germ agglutinin-modified Fe3O4@Au magnetic nanoparticles (WMRs) to bind the E. coli O157:H7, and then triggers the cPER to generate branched DNA products for CDNA tag hybridization with high stability and amplified SERS signals. It can identify target pathogens as low as 1.91 CFU/mL and discriminate E. coli O157:H7 in complex samples such as water, milk, and serum, demonstrating comparable or greater sensitivity and accuracy than traditional qPCR. Moreover, the developed platform can detect low levels of E. coli O157:H7 in mouse serum, allowing the discrimination of mice with early-stage infection. Thus, this platform holds promise for food analysis and early infection diagnosis.

Methods Herein, we proposed a sensitive platform for detecting pathogens using cyclic DNA nanostructure@AuNP tags (CDNA) and a cascade primer exchange reaction (cPER). This platform employs wheat germ agglutinin-modified Fe3O4@Au magnetic nanoparticles (WMRs) to bind the E. coli O157:H7, and then triggers the cPER to generate branched DNA products for CDNA tag hybridization with high stability and amplified SERS signals.

Results It can identify target pathogens as low as 1.91 CFU/mL and discriminate E. coli O157:H7 in complex samples such as water, milk, and serum, demonstrating comparable or greater sensitivity and accuracy than traditional qPCR. Moreover, the developed platform can detect low levels of E. coli O157:H7 in mouse serum, allowing the discrimination of mice with early-stage infection.

Conclusion Thus, this platform holds promise for food analysis and early infection diagnosis.

Study on the Detection and Infection Distribution of Multidrug-Resistant Organisms in Different Specimens

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Abstract Content Study on the Detection and Infection Distribution of Multidrug-Resistant Organisms in Different Specimens

Objective To analyze the infection and distribution of multidrug-resistant organisms (MDRO) in different clinical specimens, thereby providing a reference for clinical diagnosis and treatment and prevention and control.

Methods Patient and Methods 2314 strains of MDRO isolated from clinical specimens in the First Affiliated Hospital of Nanjing Medical University from January to December 2020. MDRO were collected by Information System. The detection rate of MDRO, infection rate, the proportion of infection, and detection rate of MDRO infection in different specimens were analyzed.

Results The top three specimens in the detection rate of MDRO were BALF (60.71%), sputum (33.68%), and blood (28.79%). The top three specimens in the proportion of MDRO infection were blood (97.74), other sterile body fluids (90.35%), and BALF (90.20%). The top three specimens in the MDRO infection rate were BALF (9.75%), sputum (3.07%), and secretions (2.90%). The top three specimens in the detection rate of MDRO infection were sputum (0.63‰), other sterile body fluids (0.13‰), and secretions (0.11‰).

Conclusion The detection and infection distribution of MDRO vary greatly in different specimens. The submission of sterile body fluids for examination should be strengthened and the standard of sample collection should be highlighted.

2012-2022 年某综合医院门诊男性患者人乳头瘤病毒感染状况和基因型分布

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目的 分析某综合医院门诊男性患者人乳头瘤病毒感染状况和基因型分布。

方法 收集 2012 年 1 月 _x0002_2022 年 12 月解放军总医院第一医学中心门诊送检的 5078 例男性首次就诊标本，采用荧光定量聚合酶链式反应 (PCR) 方法对 HPV 进行检测，分析其亚型分布及感染特征。

结果 受检男性患者共检出 HPV 阳性 1737 例，总 体阳性率 34.21%。按 亚 型 频 次 分 布，低 危 型 HPV6/11 是 最 常 见 的 感 染 亚 型，占 53.83%，其 次 是 高 危 型 以 HPV16、52、51、58 为主，分别占 13.58%、10.02%、9.15% 和 8.35%；按感染状态分析，单纯高危型感染占比 45. 60%，高低危混合型感染占比 20.26%；单一感染 1198 例，占 68.98%；多重感染 539 例，占 31.03%；多重感染中，二重、三重、四重感染的感染率较高，分别为 21.13%、6.10% 和 2.53%，且多重感染中的高低危混合型占比均高于 单纯低危型和单纯高危型 ($P<0.05$)；按年龄分布，>20~30 岁感染阳性率最高，达 38.57%。就诊患者疾病呈现 多样化，尖锐湿疣和泌尿系感染位居前两位，占比 51.01% 和 13.47%。

结论 1 年间 HPV 总体感染率整体呈下降趋势，单纯低危感染率呈下降趋势，但高危型感染率整体呈上升趋势。为预防 HPV 感染，应重视男性 HPV 检测和治疗意识，推荐男性接种 HPV 疫苗。

Tracing the Possible Evolutionary trends of Morganella morganii: Insights from Molecular Epidemiology and Phylogenetic Analysis

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Abstract Content Morganella morganii, which encompasses two subspecies, subsp. morganii and subsp. sibonii, was considered as a common opportunistic pathogen, notable for intrinsic resistance to multiple antimicrobial agents and an extensive array of virulence factor. Despite its significance, there remains a paucity of research delving into the potential evolutionary dynamics of M. morganii. To address this gap, an extensive analysis was undertaken, leveraging molecular epidemiology and genomics to elucidate the potential evolutionary trajectory of this species.

Methods This study involved the analysis of genome 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 A diverse array of antimicrobial resistance genes (ARGs) was identified in M. morganii isolates, including mcr-1, tet(X4), tmexCD-toprJ, and various carbapenemase genes. Additionally, a novel blaKPC-2-bearing plasmid with demonstrated conjugative capability was discovered in M. morganii. The majority of virulence-related genes (VRGs), except for the hlyCABD gene cluster, were found in almost all M. morganii. Three novel genospecies of M. morganii were identified, designated as M. chanii, M. variant1, and M. variant2. Compared to M. sibonii, M. chanii genospecies possessed a greater number of flagellar-related genes, typically located within mobile genetic elements (MGEs), suggesting potential for better environmental adaptability. Phylogenetic analysis further disclosed that M. morganii was divided into 12 sequence clusters (SCs). Particular, SC9 harbored an elevated abundance of ARGs and VRGs, mainly toxin-related genes, and was associated to a higher presence of MGEs compared to non-SC9 strains.

Conclusion The collective findings suggest that M. morganii undergoes evolution driven by the influence of MGEs, thereby significantly enhancing its adaptability to selective pressures of environmental changes and clinical antimicrobial agents.

应用定量测序技术评估呼吸机相关下呼吸道感染患者的早期微生物反应

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目的 发生 VA-LRTI（Ventilator-associated lower respiratory tract infections, 呼吸机相关下呼吸道感染）会导致机械通气患者死亡率增高。及时准确分析治疗前后的病原体负荷变化，即早期微生物反应，对于判断初始治疗方案的有效性十分关键，并为后续抗感染药物的合理使用提供重要依据。

方法 本研究建立了 QtNGS（Quantitative targeted amplicon-based next-generation sequencing，定量靶向二代测序）技术，即通过在靶向二代测序技术（tNGS）基础上引入内参基因以实现同步对目标病原体定性与定量检测的方法。本团队共纳入了 23 名以鲍曼不动杆菌为主要病原体的呼吸机相关下呼吸道感染患者，分析治疗后病原体负荷改变与临床结局间的关联。

结果 在本研究中，我们为了准确描述治疗后病原学负荷量的变化，定义了 RQR（Relative Quantification Ratio，相对定量比）这一指标，具体计算方式为治疗后测得的病原体定量值 / 治疗前的定量值。通过对研究的样本进行了微滴式数字 PCR 复测确定这两种方法测得的 RQR 之间的显著一致（$p = 0.0161$）。在后续的 28 天随访期中，死亡组 RQR 显著增加（中位数 2.872；$p = 0.0156$）；而存活组治疗后 RQR 显著降低（中位数 0.1098；$p < 0.0001$）。ROC 曲线分析显示，RQR ≥ 1.41 预测死亡结局的曲线下面积（AUC）为 0.9375（0.8377-1）。

结论 本研究证明了应用 QtNGS 技术获得的治疗后相对定量比（RQR）这一指标可以用于定量描述 VA-LRTI 患者治疗早期的微生物反应；其数值与患者预后相关。

Whole genome sequence of Porphyromonas pogonae PP01-1, ahuman strain harboring blaOXA-347 and tet(Q)with chromosomal location

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Abstract Content Porphyromonas pogonae (P.pogonae) is an anaerobic gram-negative coccobacillus which associated with diseases in many species, including lizards, Pogona vitticeps, rats, and human beings, causing acute sinusitis, soft tissue infection, septicaemia, aortic prosthesis infection and abscesses. P. pogonaehave the ability to grow under both anaerobic and micro aerophilic conditions, is the 16th species of the genus Porphyromonas [2]. P. pogonae could be differentiated from most of the other species of the genus Porphyromonas due to the strong β-hemolytic colony(except P. catoniae and P. gingivalis) . Human infections caused by P. pogonae were quite rarely reported, with only five cases published in the PubMed database. The drug resistance phenotype of P. pogonae is rarely reported, and the genetic basis of resistance in P. pogonae is still understudied. Since P. pogonae was officially named and confirmed in 2015, no whole genome sequence of P. pogonae has been reported so far. The aim of this study was to characterise the first complete genome of Porphyromonas pogonae strain PP01-1 of human origin in China.

Methods Illumina NovaSeq 6000 (200X coverage) and Nanopore MinION platform (100X cover age) were used for genome sequencing. The de novo hybrid assembly of short Illumina reads and long MinION reads was performed using Unicycler (v.0.5.0). Genome annotation of PP01-1 was performed using the prokaryotic gene prediction tool Prokka1.14.6.The genome was further analysed using several bioinformatics tools, including ResFinder, VFDB, VirulenceFinder,TYGS, AntiSMASH, PathogenFinder, MobileElementfinder, CRISPRFinder, and IslandViewer.

Results The assembled circular genome of Porphyromonas pogonae strain PP01-1 was 2,916,423 bp in length with a GC content of 41.0%, and no plasmid sequence was detected. A total of 2399 coding sequences were predicted by Prokka. PP01-1 harbors antimicrobial resistance genes blaOXA-347 (beta-lactamase resistance), tet(Q) (tetracycline) and floR (chloramphenicol and florfenicol)

Conclusion Here we first report the complete genome of Porphyromonas pogonaestrain PP01-1 of human origin. In this strain, we firstly identified blaOXA-347 and tet(Q) in Porphyromonas pogonae, which will paves the way of further analysis that would aim to identify the potential mechanism of ARGs and virulence factors in Porphyromonas pogonae.

Performance of Disk Diffusion Method for Aztreonam in Combination with Avibactam against Enterobacteriales

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Abstract Content The global spread of carbapenem-resistant Enterobacteriales poses significant challenges for clinical anti-infective treatment, especially the strains that produced the metallo-β-lactamases (MBLs). Combination of aztreonam with avibactam has been proved to be one of the potential therapeutic approach for treating infections related with MBL-producing isolates, and specially recommended by the Infectious Diseases Society of America (IDSA) .To evaluate the performance of in-house developed disk diffusion method for aztreonam in combination with avibactam against Enterobacteriales.The in vitro antibacterial activity of aztreonam with avibactam against 204 carbapenemase-producing Enterobacteriales was determined by disk diffusion method, with broth microdilution method as a reference.

Methods A total of 204 non-duplicated Enterobacteriales were collected from 16 hospitals in 31 provinces or municipalities across China in 2021, and all strains were identified using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) system (bioMérieux, France).The MICs for aztreonam, ceftazidime/avibactam, and aztreonam/avibactam were determined for all Enterobacteriales isolates using broth microdilution method according to CLSI M07 of 2018. And the disk diffusion testing was performed according to CLSI M02 of 2018,7 in parallel with BMD method using the same 0.5 McFarland inoculum tubes.Diffusion breakpoints for aztreonam/avibactam were estimated by the the model-based approaches using the dBETS software. The susceptibility and resistance rates of Enterobacteriales to aztreonam/avibactam obtained by every method were calculated based on the corresponding breakpoints. According to the CLSI M52, compared to the reference method, if the categorical agreement (CA) $\geqslant$ 90%, major error (ME) $\leqslant$ 3%, and very major error (VME) $\leqslant$ 1.5%, indicating that the tested method had been validated as an acceptable method.

Results of the broth microdilution susceptibility testing indicated that 96.1% (196/204) and 3.9% (8/204) of Enterobacteriales were susceptible and resistant to aztreonam/avibactam, respectively. Estimated by the model-based approaches of the dBETS software, the estimated optimal S/R breakpoints for aztreonam/avibactam disks of 30/20 μg and 10/4 μg were $\geqslant$ 22/ $\leqslant$ 21 mm and $\geqslant$ 12/ $\leqslant$ 11mm; and based on the breakpoints, the susceptibility rates of Enterobacteriales to aztreonam/avibactam of two types were 97.1% (198/204) and 97.1% (198/204), while the resistance rates were 2.9% (6/204) and 2.9% (6/204),

respectively. Compared with the broth microdilution method, the CA of aztreonam/avibactam disk diffusion method results for 30/20 μg and 10/4 μg concentrations against 204 Enterobacteriales were both 98.0% (200/204), and the ME and VME were both 0.5% (1/196) and 37.5% (3/8), respectively.

Conclusion This study was the first to evaluate the susceptibility testing results of two different concentrations of aztreonam/avibactam disks, 30/20 μg and 10/4 μg.Compared with the BMD results, the CA and ME of two types of disk were all in the acceptable range, but both VMEs were high, suggesting that false susceptible results may occur when using the disk diffusion method to determine the susceptibility of aztreonam/avibactam. If the aztreonam/avibactam disks were available in the laboratories, the calculated breakpoints determined by dBETs could be used to evaluate the susceptibility of aztreonam/avibactam against Enterobacteriales, but the susceptible results should be further confirmed by BMD to avoid the false susceptible report.

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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Abstract Content 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, 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.

微生物

基于 Nanopore 技术的宏基因组测序在肺炎患者 Balf 病原诊断价值的临床观察研究

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目的 肺炎是全世界感染性疾病死亡的主要原因之一，致病微生物在早期常不明确，准确识别致病微生物有助于肺炎的诊断及治疗。宏基因组二代测序技术（mNGS）可以覆盖几乎所有病原体，敏感性明显高于培养。牛津纳米孔技术（ONT）即利用纳米孔测序技术为基础的宏基因组测序技术，较二代测序技术读长更长、速度更快。目前还没有专门的文献评价 ONT 在肺部感染患者中的病原检测性能。这项大规模多中心前瞻性研究，评估 ONT 在肺部感染病原体诊断中的价值。

方法 纳入 2021 年 7 月至 2022 年 5 月浙江大学医学院附属第一医院等 7 家医院就诊临床诊断为肺部感染患者，收集完整资料，将获取的 Balf 同时送检 CMTs、mNGS、ONT 进行病原体检测并比较，评估 ONT 检测结果对病原微生物检出及临床诊断效能。

结果 本研究纳入 91 例患者，对 CMTs、mNGS、ONT、病理等结果及临床病历资料综合分析。将 ONT 结果与 CMTs、mNGS 比较，评估 ONT 结果对微生物检出及临床诊断的影响。发现 ONT 比 CMTs 检测出更多的病原微生物，能检测出 CMTs 遗漏的病原微生物。ONT 与 mNGS 相比，两者在病原微生物的检出各有优势，ONT 在病毒的检出优于 mNGS，mNGS 在细菌的检出优于 ONT。在临床诊断效能方面，ONT 在肺部感染病例的病原诊断敏感性优于 CMTs，两种方法在诊断的特异性没有明显差异；mNGS 和 ONT 在临床诊断的灵敏度、特异度、阳性预测值及阴性预测值无差异。在混合感染病例中，ONT 在致病微生物的检出高于 CMTs；而与 mNGS 相比，mNGS 致病微生物检出更多致病微生物但不存在统计学差异。

结论 支气管肺泡灌洗液 ONT 检测结果相对 CMTs 对肺部感染患者病原诊断具有积极影响，但与 mNGS 敏感性相仿；ONT 因其长读长、全基因测序及实时数据分析可作为肺部感染病原诊断的可靠方法。

KPC-2 和 NDM-1- 共携带含 IncR 质粒的弗劳地柠檬酸杆菌在中国的出现和克隆传播

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Abstract Content We report the largest cohort to date of 8 KPC-2- NDM-1-CRCFs isolates from children with urinary tract infections.

Methods Whole-genome sequencing (WGS), and comparative genomics, was conducted for the KPC-2- NDM-1-CRCF clinical isolates.

Results 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 46,050bp IncR plasmid, transferable via mediation by other binding transfer elements.

Conclusion 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.

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。

新型 β－内酰胺酶抑制剂 FL058 提高亚胺培南抗脓肿分枝杆菌活性

谭至立[1,2]、徐丽云[1,2]、樊峻晟[1,2]、贾亚平[1,2]、张哲民[1,2]、李冰[1,2]、褚海青[1,2,3]

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目的 β－内酰胺类药物是抗脓肿分枝杆菌复合群（Mycobacterium abscessus complex，MABC）感染治疗的关键。由于脓肿分枝杆菌生成 A 类 β－内酰胺酶（BlaMab）来分解 β－内酰胺类药物，从而导致耐药性，因此治疗 MABC 感染具有挑战性。二氮杂双环辛烷（DBO）β－内酰胺酶抑制剂（BLI）可以抑制 BlaMab。FL058 是一种新型 DBO BLI，其与 β－内酰胺类药物联用的抗 MABC 活性尚不清楚。

方法 本研究通过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、头孢地尼、头孢呋辛和阿莫西林）分别联合 3 种 DBO BLIs（FL058、阿维巴坦和瑞来巴坦）对 2 株 MABC 标准菌的活性。此外，还评估了亚胺培南分别联合 FL058、阿维巴坦或瑞来巴坦对 193 株临床分离菌株的抗 MABC 活性。进一步测试了亚胺培南联合 FL058 在巨噬细胞内 的抗 MABC 活性。最后，在模拟肺 MABC 感染的中性粒细胞减少小鼠模型中测定了亚胺培南联合 FL058 的抗菌效力。

结果 结果显示FL058、阿维巴坦和瑞来巴坦能显著提高 β－内酰胺类药物（尤其是亚胺培南）对标准菌株和临床分离菌株的抗 MABC 活性。FL058 促进亚胺培南抗 MABC 活性的能力优于与阿维巴坦或瑞来巴坦。亚胺培南联合 FL058 显著减少巨噬细胞内和中性粒细胞减少小鼠肺组织的细菌载量。

结论 亚胺培南与 FL058 联用表现出的较高抗 MABC 活性，这可能是治疗 MABC 感染的潜在新方案。

新型 InhA 还原酶抑制剂 NITD-916 对脓肿分枝杆菌的体内外活性研究

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目的 脓肿分枝杆菌对临床大多数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。本研究旨在探索脓肿分枝杆菌对新型烯酰 ACP 还原酶（InhA）抑制剂——NITD-916 的体内外活性。

方法 采用微量肉汤滴定法检测 NITD-916 对 12 株 NTM 标准菌株和从上海市肺科医院系列收集并分离鉴定的 194 株脓肿临床分离株的最小抑菌浓度（MIC）。通过棋盘试验检测 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。此外，还评估了 NITD-916 对巨噬细胞内脓肿分枝杆菌的胞内活性。最后，建立急性脓肿分枝杆菌肺部感染的小鼠模型以测定 NITD-916 在体内的抗菌效力。

结果 NITD-916 对脓肿分枝杆菌具有抑菌活性，大量临床分离株的 MIC50 为 0.125 mg/L，MIC90 为 1mg/L，并且相较于 R 型对 S 型更敏感。NITD-916 和克拉霉素在 40% 的脓肿亚种马赛分枝杆菌菌株中具有协同作用。此外，NITD-916 能够抑制细胞内脓肿分枝杆菌生长 (0.7；2.6 Log10CFU)，这导致脓肿分枝杆菌肺部感染小鼠的中性粒细胞减少。100mg/kg NITD-916 连续给药 14 天后小鼠肺组织的脓肿负荷显著减少 (3；5.6 Log10CFU)，疗效优于 100mg/kg 的利福布汀和 200mg/kg 的克拉霉素。

结论 NITD-916 对脓肿分枝杆菌具有较强的体内外活性，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可能性，强调 InhAMAB 是抗脓肿分枝杆菌的有力靶点。

A Simple Disk Stacking Plus Micro-Elution Method for Rapid Detection of the Synergistic Effect of Aztreonam and Ceftazidime/Avibactam Against Metallo-β-Lactamase Producing Enterobacterales

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Abstract Content Purpose To establish and evaluate a simple disk stacking plus micro-elution (DSE) method that can be routinely performed to rapidly detect the synergistic effect between aztreonam (ATM) and ceftazidime/avibactam (CZA) against metallo-β-lactamase (MBL)producing carbapenem-resistant Enterobacterales (CRE). Methods: The DSE method was established, and a total of 32 MBL-producing CRE isolates collected from multiple centers were tested for ATM-CZA synergy. The results obtained after 8 h of incubation were compared with those obtained by a reference checkerboard assay (CBA) after 18~24 h. Reproducibility experiments were completed on three separate days. Results: The reproducibility study showed that the results of the DSE method were precise. Compared with CBA, the DSE method exhibited excellent performance, with 92.8% sensitivity, 100.0% specificity 93.8% categorical agreement, 0.0% very major error, 0.0% major error, and 6.2% minor error over three days of testing. Conclusion: The DSE method is a simple, rapid and practical method for ATM-CZA combination testing. Further evaluation should be completed to improve its clinical application. Keywords: aztreonam, ceftazidime/avibactam, metallo-β-lactamases, Enterobacterales, antimicrobial combinations, clinical method

Methods The DSE method was established, and a total of 32 MBL-producing CRE isolates collected from multiple centers were tested for ATM-CZA synergy. The results obtained after 8 h of incubation were compared with those obtained by a reference checkerboard assay (CBA) after 18~24 h. Reproducibility experiments were completed on three separate days.

Results The reproducibility study showed that the results of the DSE method were precise. Compared with CBA, the DSE method exhibited excellent performance, with 92.8% sensitivity, 100.0% specificity 93.8% categorical agreement, 0.0% very major error, 0.0% major error, and 6.2% minor error over three days of testing.

Conclusion The DSE method is a simple, rapid and practical method for ATM-CZA combination testing. Further evaluation should be completed to improve its clinical application.

2021－2022监测年度枣庄市乙型流感病毒Victoria系全基因组测序分析

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目的 为了解山东省枣庄市2021-2022监测年度乙型流感病毒Victoria系的流行情况，分析病毒全基因组遗传特征，了解病毒进化变异特点，分析与疫苗株的相似程度，为流感的防控提供参考依据。

方法 从枣庄市流感监测网络实验室分离的流感毒株中随机选取10株B/Victoria系毒株，以WHO推荐的B/Victoria流感疫苗株B/Washington/02/2019（2020-2022北半球疫苗代表株）为参考进行全基因序列测定，利用生物信息学软件构建进化树，并分析分子进化特征。

结果 2021年4月-2022年3月，枣庄市流感病毒监测阳性率为17.03%（202/1186），均为B/Victoria系流感。将枣庄市分离的10株B/Victoria系毒株序列与北半球疫苗代表株B/Washington/02/2019相比血凝素（Hemagglutinin，HA）基因核苷酸同源性为99.5%~100%，HA基因氨基酸同源性为99.7%~100%；HA进化树分析中，该10株B/Victoria系毒株与疫苗代表株B/Washington/02/2019同属于1A分支；但发现已有5处抗原表位突变，均发生在120-loop区122位、133位，150-loop区144位、150位，190-loop区197位；神经氨酸酶（NA）未发现关键氨基酸位点变异。NA抑制剂耐药位点均未发生变异，奥司他韦等药物治疗流感敏感。

结论 枣庄市2021-2022监测年度流行的流感病毒均为乙型Victoria系，与疫苗推荐株相比HA发生了抗原漂移，提示B/Victoria系疫苗株与本地区流行株的匹配度有所降低。枣庄地区流行的乙型流感病毒对药物奥司他韦和扎那米韦依然敏感。

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。

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

宏基因组测序诊断鹦鹉热衣原体肺部感染

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目的 探讨宏基因组二代测序在鹦鹉热衣原体肺炎早期诊治中的意义以及了解鹦鹉热衣原体肺炎患者的临床特点。

方法 本文回顾性分析了 2021 年 1 月至 2023 年 06 月在常州市第三人民医院宏基因组二代测序（Metagenomic next-generation sequencing,mNGS）检测的 433 个肺泡灌洗液样品。回顾性分析鹦鹉热衣原体肺炎患者的临床资料，包括流行病学特征、临床表现、实验室检测结果、治疗及预后。

结果 常州市第三人民医院 2021 年 1 月至 2023 年 06 月 mNGS 检测的 10 个肺泡灌洗液样品（10/433，2.3%）呈鹦鹉热衣原体阳性。8 例患者为男性（8/10,80%），平均年龄为 58 岁。鹦鹉热患者有明确的禽类接触史占 80%（8/10），以发热（10/10,100%）、乏力（9/10，90%）、头痛（6/10,60%）、咳嗽（6/10，60%）和纳差（4/10,40%）为主。CRP、IL-6、SAA、中性粒细胞百分比升高、GGT 升高；白细胞计数、降钙素原（PCT）仅有 1 例升高；淋巴细胞百分比降低。CT 显示患者以肺部单个肺叶实变、斑片状模糊影为主。10 例患者肺泡灌洗液 mNGS 均检测到鹦鹉热衣原体，以多西环素联合莫西沙星或奥玛环素治疗，10 例患者治愈、好转。

结论 鹦鹉热临床表现多样，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。

耐碳青霉烯类肺炎克雷伯菌 ST11 的分子流行病学特征

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目的 分析本院临床耐碳青霉烯类肺炎克雷伯菌菌株 ST11 临床特点、耐药性、碳青霉烯酶基因型及危险因素。

方法 收集常州市第三人民医院住院患者临床标本分离的 CRKP 83 株，采用全自动微生物鉴定和药敏仪检测 CRKP 的药敏结果，胶体金方法分析产碳青霉烯酶情况；通过多位点序列分型分析菌株分型；多因素 logistic 回归分析 CRKP 感染的潜在危险因素。

结果 CRKP 菌株在重症医学科检出率最高，为 44 株（53.01%），主要来源于痰液 52 株（62.65%）CRKP 菌株对头孢菌素、氨曲南、喹诺酮类和碳青霉烯类药物不敏感，耐药率高达 95%，对阿米卡星敏感率达 57.14%，对替加环素和头孢他啶/阿维巴坦的敏感率是高达 100% 以上。32 株 CRKP 均产 KPC-2 酶。多位点序列分析 83 株肺炎克雷伯菌为同一个分型 ST11。多因素回归分析结果显示机械通气和患者≥ 70 岁是 CRKP 感染的独立危险因素。

结论 加强对重点科室和重点人群的病原菌药敏结果的监测和分析，减少导致感染 CRKP 的相关性操作。

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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目的 近年来，纹带棒状杆菌在临床上引起的感染频发，特别是在免疫力低下或者接受有创性操作的住院患者，但目前关于纹带棒状杆菌引起的呼吸机相关性肺炎（VAP）的临床研究较少，本研究目的是分析纹带棒状杆菌所致 VAP 的临床特征以及确定其预后危险因素与死亡率之间的关系。

方法 本研究为一项回顾性病例对照研究，纳入 2022 年 1 月 1 日至 2023 年 8 月 31 日期间纹带棒状杆菌所致的 VAP 患者共 90 例。

结果 根据出院时的临床转归情况，分为生存组和死亡组，其中死亡组所占比例为 30%。两组患者的中位年龄分别为 71 岁、76 岁，因手术治疗入院的分别为 41.3%、18.5%。在痰培养阳性的初次血清学结果中，两组淋巴细胞水平分别为 0.85*109/L、0.50*109/L,C- 反应蛋白 (CRP) 水平分别为 44.37mg/L、76.43mg/L, 天冬氨酸氨基转移酶（AST）分别为 27.30U/L、40.70U/L，肌酐水平分别为 71.80 μ mol/L、83.15 μ mol/L，白蛋白水平分别为 33.40g/L、29.15g/L；总的住院时间分别为 43 天、15 天 , 机械通气（MV）天数分别为 20 天、8 天，气切率分别为 63.5%、33.3%，确诊 VAP 前青霉素类抗生素的使用率分别为 28.6%、7.4%、确诊 VAP 后抗生素治疗用药时间分别为 10 天、6 天。二元 logistic 回归分析显示，住院期间进行气管切开，确诊 VAP 前使用青霉素类抗生素，痰培养阳性时初次血清学 AST 水平，肌酐水平均是院内死亡的独立预测因素。

结论 高龄、CRP 比例升高、白蛋白水平降低、不及时进行气管切开、确诊 VAP 前未使用青霉素类抗生素、治疗用药持续时间较短等因素可能与纹带棒状杆菌感染预后不佳相关。住院期间进行气管切开、确诊 VAP 前使用青霉素类抗生素、AST 和肌酐水平是院内死亡率的独立预测因子。

In vitro activities of the essential antimicrobial including aztreonam/avibactam, eravacycline, colistin, and other comparators against carbapenem-resistant organisms: a multicenter study in China, 2021

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Abstract Content Objective Carbapenem-resistant organisms (CRO), including carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Pseudomonas aeruginosa (CRPA), and carbapenem-resistant Enterobacterales (CRE), have posed a considerable threat to public health in China. Eravacycline, aztreonam/avibactam, and colistin are important antimicrobial agents for the treatment of serious infections caused by CRO. The objective of this study is to evaluate the prevalence and susceptibility of commonly used clinical antimicrobial drugs against the clinical CRO strains.

Methods We collected 7,194 gram-negative bacteria (GNB) strains from different regions of China and identified 924 carbapenem-resistant strains. All the collected strains were from the organisms that have caused definite infections. Antimicrobial susceptibility testing, which coverd 21 antimicrobial agents including aztreonam/avibactam, eravacycline, colistin, and other comparators, was performed by broth microdilution method. Carbapenemase genes blaKPC, blaNDM, blaOXA, blaIMP, and blaVIM were screened by PCR and confirmed by DNA sequencing. All statistical analyses were performed using Statistical Package for the Social Sciences version 23.0 software.

Results The isolation rates of CRE, CRAB, and CRPA were 6.31% (332/5265), 62.95% (440/699), and 15.20% (152/1000), respectively. The main type of carbapenemase-producing in carbapenem-resistant Escherichia coli （CRECO) is NDM, while in CRKP is KPC. All CRAB produced OXA and 85.52 % of CRPA did not produce any of the carbapenemase including NDM, KPC, VIM, IMP and OXA. Aztreonam/avibactam, colistin, and eravacycline exhibited high antimicrobial activity against different species producing various carbapenemases. Compared to ceftazidime/avibactam, aztreonam/avibactam showed higher antimicrobial activity, particularly pronounced in CRECO and strains producing metallo-beta-lactamases (MBLs). In a comparison of antimicrobial activity between tigecycline and eravacycline, eravacycline maintained higher antimicrobial activity in different species. Antimicrobial drugs exhibited varying antimicrobial activities when against strains with different resistance mechanisms. For instance, in CRPA, MBLs-producer and KPC-producer tended to have higher resistance rates to many drugs compared to strains that do not produce carbapenemases.

Conclusion Our results support the fact that using aztreonam/avibactam, eravacyline, and colistin to treat infections caused by CRO offers significant advantages. These data will guide clinical practice and optimize antibiotic administration.

Involvement of Tn3 Transposon in Formation and Transmission of Hypervirulent and Carbapenem-resistant Klebsiella pneumoniae

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Abstract Content Hypervirulent and carbapenem-resistant Klebsiella pneumoniae poses a severe threat to public health for its high pathogenicity, transmissibility, and drug resistance. This study aims to explore the evolutionary path and the role of Tn3 transposon in the virulence and carbapenem resistance transmission of K. pneumoniae. Bioinformatics analysis and some experimental tests, such as plasmid conjugation experiments, antimicrobial susceptibility testing and virulence-associated tests were performed to explore the virulence and drug resistance transmission. The complete genome sequencing, S1 nuclease pulsed-field gel electrophoresis (S1-PFGE), and bioinformatics analysis were used to investigate their transmission mechanism medicated by Tn3 transposons. Three hypervirulent and carbapenem-resistant K. pneumoniae isolates, which were obtained from different patients at different time points in the same ward, harbored a virulence plasmid and a carbapenem resistance plasmid. They were confirmed to have first evolved from hypervirulent isolates and then acquired a blaKPC-positive plasmid (CR-hvKp evolutionary pattern). The non-conjugative virulence plasmid pVir could be transferred to other bacterial strains via mobilization by the conjugative IncN/U-type plasmid pKPC, as well as by fusing with the conjugative pKPC plasmid (mediated by the Tn3-based homologous recombination) to be self-transmissible, thus transferring drug resistance and virulence. The cointegration, pVir/KPC fusion plasmid, was further resolved into pVir and pKPC between the duplicated copies of the Tn3 transposon resolution site mediated by site-specific recombination. Therefore, Tn3 transposons can mediate hypervirulent and carbapenem-resistant K. pneumoniae strains transferring drug resistance and virulence to other bacteria. We must be vigilant to emerging transposon-mediated hypervirulent and carbapenem-resistant pathogens.

Methods None

Results None

Conclusion None

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 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。

Analysis of the Spectrum of Common Pathogens and the Resistance of Mycoplasma in Sialidase-Positive Bacterial Vaginosis

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Abstract Content The objective of this study is to understand the characteristics of the common spectrum of pathogen and the resistance of Mycoplasma in Sialidase-positive bacterial vaginosis

Methods The vaginal secretion specimens collected from August 2018 to October 2018 for the analysis of bacterial vaginosis (BV) were subjected to various techniques. These included routine leukorrhea examination, bacterial vaginosis sialidase testing, routine culture for common pathogens, mass spectrometry identification, and Mycoplasma resistance testing.

Results A total of 238 patients with BV were identified. The cleanliness grading was mostly clean (+) and clean (2+), accounting for 38.24% and 30.67%, respectively. The bacterial vaginosis test for vaginal secretions showed leukocyte esterase positivity in 220 cases, resulting in a positivity rate of 92.44%. The spectrum of routine culture was analyzed and divided into four groups: A, B, C, and D. Group A consisted of Candidal vaginitis (13.45%); group B consisted of Gardnerella vaginalis vaginitis (32.77%); group C consisted of gram-negative bacillus vaginitis (46.22%); and group D consisted of Streptococcus agalactiae vaginitis (7.56%). The identification and antimicrobial susceptibility testing results for Mycoplasma showed a high detection rate of BV, with a positivity rate of 86.13%. There was a high sensitivity to tetracyclines for Ureaplasma urealyticum and Mycoplasma hominis, but a high resistance to macrolides and quinolones.

Conclusion Bacterial vaginosis existed in various complex forms, including Candida, Gardnerella vaginalis, Gram-negative bacillus, and Streptococcus agalactiae types. Moreover, there was an increasing trend of multi-drug resistance in Mycoplasma hominis. Therefore, it is crucial to pay attention to this condition and make accurate judgments based on the etiological characteristics and common antimicrobial susceptibility tests. This will enable the implementation of effective therapeutic interventions.

59 例咽峡炎链球菌群感染脑脓肿患者临床特征分析

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目的 分析咽峡炎链球菌群（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），差异具有统计学意义（t=2.614，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（t=4.174，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（分别为 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（t=14.257，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（分别为 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。

The peripancreatic microbiota is associated with the severity of acute pancreatitis

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Abstract Content Infectious pancreatic necrosis (IPN) is associated with the prognosis of acute necrotizing pancreatitis (ANP). The correlation of microbial diversity in the peripancreatic region with the severity of AP remains unclear. The objectives of this study are to analyze the microbial composition of peripancreatic necrosis in IPN patients by 16S ribosomal RNA (16S rRNA) and internal transcribed spacer (ITS) sequencing.

Methods Patients with acute pancreatitis who met the clinical diagnostic criteria for IPN were prospectively included. These patients were subsequently divided into sepsis group and non-sepsis group. Samples of peripancreatic necrotic fluid were collected by percutaneous puncture drainage, followed by 16S rRNA sequencing and internal transcribed spacer (ITS)

Results There was no significant difference between the sepsis and non-sepsis groups in terms of bacterial Alpha diversity, and there was a significant difference in Beta diversity analysis by Welch's t-test ($P < 0.001$), Adonis analysis ($P=0.037$) and Anosim analysis ($P = 0.032$). The relative abundance of Klebsiella differed significantly between the two groups (2.79% vs. 34.14%, $P = 0.0093$) and correlated with the length of hospital stay ($r = 0.422$, $P = 0.025$).

Conclusion The peripancreatic microbiota is associated with the severity of acute pancreatitis, with Klebsiella being the dominant microflora in patients with IPN combined with sepsis.

抗心律失常药物决奈达隆通过抑制 LuxS 发挥增强多粘菌素抗菌活性的机制研究

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目的 从已有抗儿茶酚胺类药物中筛选多粘菌素增效剂并鉴定其机制

方法 多粘菌素增效剂的高通量筛选，热蛋白组实验，重组蛋白的表达纯化，表面等离子共振，转录组测序，动物实验

结果 抗心律失常药物决奈达隆可显著增强多粘菌素 B 的抗菌活性，热蛋白组及小分子蛋白质相互作用实验结果表明决奈达隆可与自诱导剂 -2 合成酶 LuxS 直接结合并抑制其介导的细菌自诱导剂 -2 的合成。动物实验表明决奈达隆可明显升高多粘菌素 B 耐药肺炎克雷伯菌肺部感染小鼠的存活率。

结论 决奈达隆可通过抑制 LuxS 功能而发挥增强多粘菌素 B 抗菌活性的作用。体内实验表明决奈达隆 + 多粘菌素的联合用药具有良好的应用前景。

Global epidemiology and evolutionary trajectory of mcr-positive Klebsiella pneumonia from 2000 to 2023

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Abstract Content 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 pneumonia worldwide is 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 These 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 (STs) 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 showed a relatively high frequency of 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 Continuous surveillance is imperative for effectively controlling the global dissemination of mcr-positive K. pnenmoniae.

从 ST11 新突变株识别耐碳青霉烯肺炎克雷伯菌的多种潜在耐药基因靶标

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目的 本研究的目的是鉴定来自耐碳青霉烯肺炎克雷伯菌（CR-KP）中 ST11 新突变株的耐药基因，为进一步的耐药机制研究提供依据。

方法 采用 RNA 测序 (RNA-Seq) 比较了 CR-KP 及 ST11 突变型 CR-KP 之间基因表达的差异，采用 qRT-PCR 验证了差异表达基因（DEGs）在临床样本中的表达情况。

结果 8 个临床分离株的总 RNA 被用于构建文库，每个样本平均产生 3.14GB 干净读数，这些数据被组装成 5751 个 mRNA 基因。DESeq2 分析结果显示 DEGs 共计 274 个（差异倍数 >2，$P < 0.05$），其中 109 个上调，165 个下调。此外，差异表达前 20 位的 DEGs 均通过 qRT-PCR 进行了验证，该方法检测了 60 株临床分离的 CR-KP，7 株临床分离的 ST11 突变型 CR-KP。此外，16 个 DEGs 显示 $2^{-\Delta\Delta Ct}$ 的相对表达水平，并具有统计学意义（$P \leq 0.05$）。GO 分析和 KEGG 通路的功能富集分析表明，7 个 DEGs 具有 β - 内酰胺酶活性，5 个具有孔蛋白活性，3 个具有跨膜转运蛋白活性，1 个具有毒力作用，这些 DEGs 可能与 ST11 突变型 CR-KP 耐药和致病十分相关。

结论 寻找耐药相关基因是进一步研究病原菌高发病率和抗菌素耐药性（AMR）的必要条件，尤其是在广谱耐药 CR-KP 基础上突变的耐药株，更值得警惕。此外，该研究为 ST11 突变型 CR-KP 耐药机制研究提供了新的方向。

Dissemination of clinical Escherichia coli strains harboring mcr-1, blaNDM-7 and siderophore-producing plasmids in a Chinese hospital

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Abstract Content Background Carbapenem-resistant E. coli (CREco) pose a significant public health threat due to their multidrug resistance. Colistin is often a last-resort treatment against CREco; however, the emergence of colistin resistance gene mcr-1 complicates treatment options.

Methods Two E. coli strains (ECO20 and ECO21), recovered from hospitalized patients in distinct wards, exhibited resistance to carbapenems and colistin. Whole-genome sequencing and phenotypic characterization were employed to study resistance patterns, plasmid profiles, transferability of resistance and virulence genes, and siderophore production capabilities. Comparative genome analysis was used to investigate the genetic environment of mcr-1, blaNDM-7, and virulence clusters.

Results Both E. coli strains exhibited thr presence of both mcr-1 and blaNDM-7 genes, showing high resistance to multiple antibiotics. Genomic analysis revealed the clonal transmission of these strains, possessing identical plasmid profiles (pMCR, pNDM, and pVir) associated with colistin resistance, carbapenem resistance, and virulence factors. Conjugation experiments confirmed the transferability of these plasmids, indicating their potential to disseminate resistance and virulence traits to other strains. Comparative genomic analyses unveiled the distribution of mcr-1 (IncX4-type) and blaNDM (IncX3-type) plasmids across diverse bacterial species, emphasizing their adaptability and threat. The novelty of pVir indicates its potential role in driving the evolution of highly adaptable and pathogenic strains.

Conclusion Our findings underscore the co-occurrence of mcr-1, blaNDM-7, and siderophore-producing plasmids in E. coli, which poses a significant concern for global health. This research is crucial to unravel the complex mechanisms governing plasmid transfer and recombination and to devise robust strategies to control their spread in healthcare settings.

Transmission of non-conjugative virulence plasmid of ST65 carbapenem-resistant and hypervirulent Klebsiella pneumoniae strains

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Abstract Content Background The escalating global incidence of infections caused by hypervirulent and carbapenem-resistant Klebsiella pneumoniae poses a threat to public health. This study focuses on the evolutionary trajectory and dissemination patterns of ST65 carbapenem-resistant hypervirulent K. pneumoniae strains (CR-hvKp) in a Chinese hospital, delving into their genomic attributes and transmission mechanisms.

Methods We identified two clinical K2-ST65 hypervirulent K. pneumoniae strains (P6 and P10) harboring KPC-producing plasmids. Plasmid conjugation experiments were performed to explore the dis semination of virulence plasmid. Resistance and virulence phenotypes were determined by antimicrobial susceptibilities and several virulence assays, such as serum resistance, siderophore production, and G. mellonella larvae infection models. Bioinformatic analyses were also performed to investigate the genome evolution.

Results Genomic analysis shows that both P6 and P10 carry a non-conjugative virulence plasmid, a conjugative untyped KPC plasmid, and a conjugative IncM2 plasmid. P6 and P10 exhibited extensive resistance profiles and multiple virulence phenotypes. However, they cannot maintain hypervirulence and carbapenem resistance for a long time. The conjugative plasmid (IncM2 plasmid) is confirmed to be essential for the transfer of non-conjugative virulence plasmid. Transmission mechanisms were further elucidated, including IS26-mediated plasmid fusion and the role of IncM2 plasmids in mobilizing non-conjugative virulence plasmids. Additionally, these transconjugants exhibit multidrug resistance, altered capsule production and increased siderophore production.

Conclusions This research provides insights into the dynamics of ST65-CR-hvKp strains and elucidates mechanisms involving IS26-mediated plasmid fusion and the role of IncM2 plasmids in mobilizing non-conjugative virulence plasmids. Understanding these mechanisms is crucial for developing effective strategies in managing and preventing the spread of these clinically challenging strains.

人源性非伤寒沙门菌感染中由质粒介导的阿奇霉素耐药性

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目的 非伤寒沙门菌对阿奇霉素的耐药机制很少有报道。在这里，我们调查 10 株对阿奇霉素耐药非伤寒沙门菌的流行特点和基因组特征。

方法 我们从广州一家三甲医院收集 457 株非伤寒沙门菌，采用药敏实验、质粒接合实验、外排泵抑制剂实验、qPCR 外排泵定量实验、全基因组测序和生物信息学分析等方法探究非伤寒沙门菌对阿奇霉素的耐药机制。

结果 10 株非伤寒沙门菌（2.8%）对阿奇霉素耐药，其最小抑菌浓度（MIC）值范围为 128-512 mg/L，并且都为多重耐药表型。系统发育树显示 5 株伦敦沙门菌（AR1-AR5）在不同时间和科室检出但基因组高度相似（3-74 SNPs），2 株鼠伤寒沙门菌相隔三个月检出（AR7 和 AR8）是克隆株（<3 SNPs），存在多重耐药非伤寒沙门菌垂直传播现象。定位于不同质粒上的 mph(A) 基因主要导致了对阿奇霉素的耐药性，包括 IncFIB、IncHI2、InFII、IncC 和 IncI 质粒。其中，IncFIB、InFII 和 IncHI2 质粒携带不同的 IS26-1 类整合子排列模式介导多重耐药性的传播。可接合转移的 IncC 质粒携带对环丙沙星、头孢曲松和阿奇霉素的耐药性。此外，质粒系统发育树表明与本研究携带 mph(A) 基因质粒亲缘关系密切的质粒主要分布在非伤寒沙门菌、大肠杆菌、肺炎克雷伯菌和荷蒙氏肠杆菌中。10 株非伤寒沙门菌中 mph(A) 基因的遗传环境是 IS26-mph(A)-mrx(A)-mphR(A)-IS6100/IS26，它与 1 类整合子共同组成多重耐药基因区域定位于多种质粒上。

结论 mph(A) 基因是 10 株非伤寒沙门菌对阿奇霉素高水平耐药的主要原因，以基因簇 "IS26-mph(A)-mrx(A)-mphR(A)-IS6100/IS26" 与携带多种耐药基因的 1 类整合子共同定位于不同质粒流行于肠杆菌科细菌中，需要进一步监测这些携带多种耐药基因质粒在不同地区的流行趋势，对公共卫生安全具有重要意义。

Epidemiology of Meyerozyma guilliermondii species complex isolated from invasive fungal diseases: a multicenter study in China

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Abstract Content Meyerozyma guilliermondii is an important opportunistic pathogen in invasive fungal infections, ranking the fourth among non-albicans Candida species and showing an increasing isolation trend in recent years. This study aims to analyze the current epidemiology of Meyerozyma guilliermondii species complex causing invasive infections in China.

Methods A total of 461 non-duplicate clinical isolates were collected from 63 surveillance centers of the China Hospital Invasive Fungal Surveillance Network (CHIF-NET) between 2009 and 2021. All isolates were accurately identified by matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF) and ITS sequencing. The antifungal susceptibility profile of Meyerozyma guilliermondii was accessed by the commercial Sensititre YeastOne plates (SYO; Thermo Fisher Scientific, Waltham, MA, USA).

Results Three species, Meyerozyma caribbica, Candida carpophila, and Meyerozyma guilliermondii were identified, of which Meyerozyma guilliermondii was the most (96.5%). A total of 461 isolates were isolated from 452 patients from 63 hospitals, with a higher proportion of male patients (64.6%) than female patients (35.4%), and 62.9% of the patients were older than 50 years. The isolates were mainly collected from general surgery (41.2%), ICU (26.5%), and general medical departemnt (12.1%). Blood was the predominant specimen type (65.3%), followed by ascites (11.9%), and catheters (8.0%). The echinocandin resistance rate was 1.52% (7/461). The proportion of non-WT (non-wild type) isolates of the four azoles were 104/461 (22.6%) for fluconazole, 17.1% for voriconazole, 7.4% for itraconazole, and 10.8% (50/461) for posaconazole. The percentage of isolates non-WT for all four azoles reached 7.4%, and the cross-non-WT rates between 5-fluorocytosine with azole antifungals was as high as 7.6%.

Conclusion Invasive infections of Meyerozyma guilliermondii species complex in China are dominated by Meyerozyma guilliermondii, and bloodstream infections are the most common infection type. In addition to amphotericin B, Meyerozyma guilliermondii species complex is resistant to all types of antifungal drugs, and even the phenomenon of cross-resistance exists, which should be emphasized in clinical practice.

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。

Complex evolutionary trajectories in vivo of two novel KPC variants conferring ceftazidime-avibactam resistance

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Abstract Content Background More and more ceftazidime-avibactam resistant KPC-producing K. pneumoniae have been reported with its widespread use, and the detection rate of KPC variants has increased dramatically. However, the evolutionary mechanism and fitness effects during KPC mutation remained unknown.

Objective Here, we report the complex in vivo evolutionary trajectories of two novel KPC variants, KPC-155 (L169P/GT242A) and KPC-185 (D179Y/GT242A), from Klebsiella pneumoniae in the same patient.

Result The novel variants were shown to confer ceftazidime-avibactam resistance but restore carbapenem susceptibility based on the results of plasmid transformation assays, cloning experiments, and enzyme kinetic measurements. In vitro competition experiments highlighted the adaptive advantage conferred by strains carrying these KPC variants, which could lead to the rapid spread of these ceftazidime-avibactam resistant strains. The growth curve indicated that blaKPC-185 had better growth conditions at lower avibactam concentration compared to blaKPC-155, which was consistent with ceftazidime-avibactam use in vivo. In addition, replicative transposition of the IS26-flanked translocatable unit (IS26-ISKpn6-blaKPC-ISKpn27-IS26) also contributes to the blaKPC amplification and formation of two copies (blaKPC-2 and blaKPC-185), conferring both carbapenem and ceftazidime-avibactam resistance. However, strains with double copies showed reduced competitive advantage and configuration stability. The comparative plasmid analysis of IS26 group (IS26-blaKPC-IS26) and Tn1721 group (Tn1721-blaKPC-IS26) revealed that IS26-insertion could influence the distribution of resistance genes and ability of self-conjugation.

Conclusion The dynamic changes in blaKPC configuration highlight the need for consistent monitoring including antimicrobial susceptibility testing and determination of blaKPC subtypes—during clinical treatment, especially when ceftazidime-avibactam is administered.

A novel KPC-179 variant conferring ceftazidime-avibactam resistance in a carbapenem-resistant Klebsiella pneumoniae isolate

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Abstract Content

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. Ceftazidime–avibactam (CZA) is currently one of the few effective antibiotics for CRKP strains. In this study, we aim to explore the resistance mechanism of CZA.

Methods Phenotypic test, conjugation experiment 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 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. 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) and aztreonam-avibactam (MIC＝1 mg/L).The phenotypic test for carbapenemase was negative, and the transferability of CZA resistance was confirmed through a conjugation experiment with E. coli EC600.

Conclusion Our study highlights the importance of monitoring susceptibility during CZA treatment and accurately detecting of KPC variants. It is crucial to develop appropriate dosage and course of CZA for critically ill patients.

Blood-rsCDM: a New Rapid and Simplified Carbapenemase Detection Method for Detecting Carbapenemases in Enterobacterales Directly from Positive Blood Cultures

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Abstract Content Objective We aim to validate and evaluate a new rapid and simplified method, called Blood-rsCDM, for the detection and characterization of carbapenemase using 3-aminophenylboronic acid (APBA) and ethylenediaminetetraacetic acid (EDTA) β-lactamase inhibitors from positive blood cultures.

Methods We utilized a panel of 172 Enterobacterales strains, including blaKPC (77), blaNDM (48), blaIMP (9), blaVIM (2), blaOXA-181 (2), blaKPC and blaNDM (6), as well as 28 carbapenem-susceptible Enterobacterales isolates, to assess the performance of Blood-rsCDM and the EDTA-carbapenem inactivation method (eCIM). Carbapenemase class was determined using specific inhibitors at 4 h and 6 h by Blood-rsCDM.

Results Blood-rsCDM exhibited a sensitivity of 97.9% at both time points, with a specificity of 100%, regardless of the culture duration. The sensitivity of eCIM was 94.4%, with a specificity of 100%. Blood-rsCDM accurately characterized KPC-producing isolates as 77/77, metallo-β-lactamases (MBLs) as 58/59, and KPC and NDM carbapenemases as 6/6 at 4 h. There was no difference in results between the 4 h and 6 h time points. However, Blood-rsCDM could not differentiate OXA-181-producing strains. For eCIM, the characterization numbers for KPC-, OXA-181-, and MBLs-producing strains were 77/77, 2/2, and 57/59, respectively, but it failed to detect the coproduction of KPC and NDM isolates.

Conclusion Blood-rsCDM accurately discriminates carbapenemase within 4 h and is capable of directly differentiating multi-enzyme (KPC and NDM) presence from positive blood culture broths. Therefore, Blood-rsCDM represents a rapid, simple, easy-to-read, and accurate tool that can be utilized in resource-limited settings.

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

凌勇
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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（ χ^2=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（ χ^2=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。

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。

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。

Genome sequencing unveils blaKPC-2-harboring plasmids as drivers of enhanced resistance and virulence in nosocomial Klebsiella pneumoniae

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Abstract Content The threat posed by Klebsiella pneumoniae in healthcare settings has worsened due to the evolutionary advantages conferred by blaKPC-2-harboring plasmids (pKPC-2). However, the specific evolutionary pathway of nosocomial K. pneumoniae carrying pKPC-2 and its transmission between patients and healthcare environments are not yet well understood.

Methods Between August 1st and December 31st, 2019, 237 ST11 KPC-2-producing-CRKP (KPC-2-CRKP) were collected from patient or ward environments in an ICU and subjected to Illumina sequencing, of which 32 strains were additionally selected for Nanopore sequencing to obtain complete plasmid sequences. Bioinformatics analysis, conjugation experiments, antimicrobial susceptibility tests and virulence assays were performed to identify the evolutionary characteristics of pKPC-2.

Results The pKPC-2 plasmids were divided into three subgroups with distinct evolutionary events, including Tn3-mediated plasmid homologous recombination, IS26-mediated horizontal gene transfer and dynamic duplications of antibiotic resistance genes (ARGs). Surprisingly, the incidence rates of multicopy blaKPC-2, blaSHV-12 and blaCTX-M-65 were quite high (ranging from 27.43% to 67.01%), and strains negative for extended-spectrum β-lactamase tended to develop multicopy blaKPC-2. Notably, the presence of multicopy blaSHV-12 reduced sensitivity to ceftazidime/avibactam (CZA), and the relative expression level of blaSHV-12 in the CZA-resistant group was 6.12 times higher than that in the sensitive group. Furthermore, a novel hybrid pKPC-2 was identified, presenting enhanced virulence levels and decreased susceptibility to CZA.

Conclusion This study emphasizes the notable prevalence of multicopy ARGs, and provides comprehensive insight into the intricate and diverse evolutionary pathways of resistant plasmids that disseminate among patients and healthcare environments. These evidences highlight the threat of pKPC-2 to CRKP treatment and control. Thus, surveillance and timely disinfection in clinical settings should be practiced to prevent transmission of CRKP carrying threatful pKPC-2. And rational use of antibiotic should be called for to prevent inducing of pKPC-2 evolution, especially the multicopy ARGs.

Excellent performance of XGBoost in predicting bloodstream infections

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Abstract Content Background Efficient detection and timely intervention in bloodstream infections (BSI) are pivotal for enhancing prognosis, given their strong correlation with elevated mortality. Although blood culture stands as the current gold standard for BSI, its time-consuming nature limits its applicability in rapid clinical diagnosis. Machine learning has the potential to combine multiple indicators and achieve early diagnosis of BSI.

Methods This study encompassed 2,678 patients diagnosed with BSI within a hospital setting from January 2021 to June 2022. A retrospective analysis scrutinized clinical and microbiological attributes of individuals with BSI, and machine learning models were deployed for BSI prediction.

Results Gram-negative bacteria constituted the majority of pathogenic organisms (56.50%), followed by Gram-positive bacteria (34.43%) and yeast (6.91%). Staphylococcus aureus, Escherichia coli, and Candida parapsilosis were the most prevalent among Gram-positive, Gram-negative, and fungal pathogens, respectively. Yeast exhibited the lengthiest median time from sample collection to reporting, followed by Gram-positive and Gram-negative bacteria. Univariate analysis identified 43 laboratory indicators displaying substantial inter-group differences, with Area Under the Curves (AUCs) for BSI surpassing 0.6. Procalcitonin, a widely recognized infection indicator, exhibited an AUC of 0.71. Thrombomodulin, previously unknown in its association with BSI, also displayed elevated diagnostic efficacy with an AUC of 0.70. The XGBoost model demonstrated superior predictive performance for BSI, achieving an AUC of 0.80. In contrast, other models, including generalized additive models, radial kernel support vector machines, elastic net, logistic regression, random forest, and linear kernel support vector machines, all had AUCs below 0.78. Variable importance analysis in each model unveiled several infrequently used indicators for BSI, notably direct bilirubin and hydroxybutyrate dehydrogenase.

Conclusions This study identified several novel laboratory indicators potentially linked to BSI, which deserve further research and validation. Furthermore, it established a high-performance machine learning model for predicting BSI, introducing fresh perspectives and possibilities for BSI diagnosis.

Dynamic evolution of ceftazidime-avibactam resistance from a single patient through the IncX3_NDM-5 plasmid transfer and blaKPC mutation

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Abstract Content Background The rapid dissemination of carbapenem-resistant Enterobacterales (CRE) especially carbapenem-resistant K. pneumoniae (CRKP) poses a great threat to global public health. Ceftazidime-avibactam, a novel b-lactam/b-lactamase inhibitor combination, has been widely used due to its excellent antibacterial activity against KPC-producing K. pneumoniae. However, several resistance mechanisms have been reported since its use.

Objective Here, we conducted a series of in vitro experiments to reveal and demonstrate the dynamic evolution of ceftazidime-avibactam resistance including interspecies IncX3_NDM-5 plasmid transfer between E. cloacae and K. pneumoniae and blaKPC mutation from blaKPC-2 to blaKPC-33.

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 increasing ceftazidime-avibactam concentration, the conjugation frequency remained at 10-3-10-5, while the mutation frequency of K. pneumoniae 5298 was 10-6-10-8 at the same concentration. Further plasmid analysis (the IncX3_NDM plasmid from this study and other 658 plasmids from the NCBI database) 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 of genetic environment detected in IncX3 plasmids, the dominant structures (168/258, 65.1%) were identified: ISKox3-IS26-blaNDM-5-IS5-ISAba125-Tn3000-Tn3. In additon, several structural variations were found in the core gene structure.

Conclusion The high fitness and transmissibility of the IncX3_NDM-5 plasmids were noteworthy. More importantly, the diverse ceftazidime-avibactam resistance mechanisms including blaNDM-5 tranfer and blaKPC-2 mutation highlighted the importance of the continuous monitoring of antimicrobial susceptibility and carbapenemases subtype during ceftazidime-avibactam treatment.

A large-scale surveillance revealed that KPC variants mediated ceftazidime-avibactam resistance in clinically isolated Klebsiella pneumoniae

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Abstract Content To monitor the resistance rate and gain a deeper understanding of the resistance mechanisms, we conducted over a two-year surveillance focusing on the Klebsiella pneumoniae associated with the clinical usage of ceftazidime-avibactam (CZA) in a teaching hospital.

Methods A total of 4641 K. pneumoniae isolates were screened to identify the CZA-resistance through antimicrobial susceptibility testing. Comprehensive analyses, including homology analysis, conjugation experiments, clone assays, and whole genomic sequencing (WGS), were further performed on the CZA-resistant strains.

Results In total, four CZA-resistant K. pneumoniae (CZA-R-Kp) strains were separated from four patients, with three of them received CZA treatment during the hospitalization, accounting for a 4% (3/75) resistance development rate of K. pneumoniae under CZA stress. All CZA-R-Kp 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 of KPC enzyme.

These mutations were found to impact the amino acid sequence and spatial structure of the enzyme's active center, consequently affecting KPC carbapenemase activity.

Conclusion This study underscores the importance of active surveillance to monitor the emergence of resistance to CZA, highlighting the need for ongoing research to develop effective strategies for combating 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.

In vivo divergent evolution of cross-resistance to new β-lactam/β-lactamase inhibitor combinations in Pseudomonas aeruginosa following ceftazidime/avibactam treatment

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Abstract Content To describe and characterize the cross-resistance mechanisms to ceftazidime/avibactam, ceftolozane/tazobactam and imipenem/relebactam of a carbapenem-resistant P. aeruginosa (CRPA) 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 CRPA strains developed high-level resistance to ceftazidime/avibactam and cross-resistance to ceftolozane/tazobactam or imipenem/relebactam through two distinct evolutionary pathways, clustering into clade A and clade B. In both clades, the overexpression of AmpC was crucial to ceftazidime/avibactam resistance, which was driven by AmpD deficiency in clade A and DacB mutation in clade B, respectively. In clade A, mraY mutation and a new allele of AmpC (blaPDC-575) elevated resistance to ceftazidime/avibactam, with blaPDC-575 also conferring resistance to ceftolozane/tazobactam. In clade B, mexB mutation was associated with the resistance to both ceftazidime/avibactam and imipenem/relebactam. In addition, the overexpression of both MexAB-OprM and AmpC contributed to the resistance to imipenem/relebactam. Moreover, the fitness costs of P. aeruginosa strains typically increased with the higher 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 .

IS26 mediated recombination poses contribution to the formation of blaKPC and blaNDM hybrid plasmid

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Abstract Content 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).

Methods 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.

Results 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.

Conclusion 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

The Novel, Unprecedented Photodynamic Therapy of Ionic Aggregation-induced Emission Compounds for the Treatment of Superbug Candida auris Infections

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Abstract Content Disseminated infections caused by Candida auris pose a global threat to human healthhence novel therapeutic drugs with high efficiency, low physiological toxicity and low drug resistance through new antimicrobial strategies are urgently needed. The aggregation of charged aggregation-induced emission (AIE) molecules in physiological environment of aqueous medium is conducive to the increase of fluorescence intensity and photodynamic (PDT) effect, wherein the introduction of charge is expected to promote the balance of hydrophilicity and improve the phototoxicity and dark toxicity simultaneously, consequently achieving good penetration to the fungal membranes and killing them more efficiently. Based on such considerations, we designed and synthesized a new ionic AIE molecule OTFPy. It was found that OTFPy exhibited highly efficient antimicrobial activity and biofilm barrier penetration efficiency , achieving therapeutic efficacy against drug-resistant Candida auris infections, which provides a new way of thinking about the study of therapeutic drugs for Candida auris infections.

Methods The same search was done to find the AIE photosensitizer OTFPy nanoparticles with antibacterial effect against Candida ear. Laser scanning confocal microscopy was used to observe the binding of OTFPy nanoparticles with Candida otitis, fluorescent probe 2',7'-dichlorofluorescein diacetate (DCFH-DA) was used to detect the ability of OTFPy nanoparticles to produce ROS in Candida otitis, and the morphology of Candida auris after co-cultivation with the AIE photosensitizer was observed by field emission scanning electron microscopy. Cytotoxicity assay and hemolysis assay were then used to assess the biosafety of OTFPy. In addition, biofilm inhibition and eradication experiments were carried out by incorporating the drug-resistant properties of Candida auris, and the effect of OTFPy nanoparticles on Candida auriculata biofilm was observed using the CLSM technique. For the biosafety and antimicrobial effect, not only in vitro experiments but also in vivo experiments in a mouse wound infection model were conducted to verify the biosafety and antimicrobial effect simultaneously.

Results The AIE photosensitizer OTFPy nanoparticles with antimicrobial effect against Candida auriculata were successfully searched.The MIC90 of OTFPy nanoparticles against Candida auriculata was 4 μmol/L and MIC 16 μmol/L under dark condition, and its antimicrobial effect was enhanced after combined with photodynamic force, and the MIC90 of OTFPy nanoparticles was 2 μmol/L and MIC 4 μmol/L. Although the in vitro biosafety assessment showed a narrower safety range, the mouse wound infection model demonstrated the antimicrobial effect against Candida auriculata from in vivo experiments. in vitro biosafety assessment indicated a narrow safety range, the mouse wound infection model demonstrated experimentally in vivo that the AIE photosensitizer OTFPy nanoparticles had better therapeutic efficacy against Candida auris than the conventional antibiotic fluconazole, as well as that they did not cause any damage to vital organs in mice after use. It was also found that the two AIE photosensitizers kill pathogenic bacteria through the photodynamic generation of ROS and the destruction of pathogenic bacteria cell membranes; OTFPy nanoparticles can also play an antimicrobial effect through the inhibition and eradication of Candida auris biofilm.

Conclusion The studies searched for AIE photosensitizers that are antimicrobial and safe and efficient against Candida auris, respectively, and provide a new direction for synthesizing next-generation antimicrobial drugs, which are expected to be used in the clinical treatment of multidrug-resistant bacterial infections.

头孢他啶－阿维巴坦压力下 KPC 突变的体外模拟：表型、分子机制、遗传结构和动力学研究

申思权、唐成康、杨维维、丁丽、韩仁如、施清喻、郭燕、尹丹丹、胡付品
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Methods This study attempts to simulate the in vivo process in the form of in vitro induction with different concentrations of CZA against strains containing KPC-2 as well as carbapenems against strains containing KPC variants.

Methods We conducted in vitro simulations of in vivo blaKPC mutations using CZA. Four pre-therapy KPC-Kp isolates (K1, K2, K3, and K4) were evaluated, all initially exhibited susceptibility to CZA and produced blaKPC-2.

Results Findings suggest that the resistance of KPC-KP to CZA primarily results from the emergence of KPC variants, complemented by increased KPC expression.

Conclusion Clinical use of carbapenems to treat KPC variant strains increases the risk of infection, as the gene can mutate back to blaKPC-2, rendering the strain even more cross-resistant to carbapenems and CZA.

肺炎链球菌感染研究进展

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目的 本文旨在分析肺炎链球菌（S. pneumoniae）的病原学、黏附和侵袭方式、毒力因子，以及现有的实验室诊断方法和防治手段，为深入理解肺炎链球菌和寻找有效的防治措施提供参考。

方法 文章通过文献综述的方式，对肺炎链球菌的病原学特性、流行病学特点、黏附和侵袭机制、毒力因子进行了系统的梳理。同时，对 PCR、基因测序等基因组领域的新实验室诊断方法进行了阐述，并探讨了肺炎链球菌感染的防治策略。

结果 研究发现，肺炎链球菌的荚膜多糖（CPS）是其主要的毒力因子，并且肺炎链球菌通过多种机制参与人体多种疾病的发生。肺炎链球菌可通过黏附、侵袭皮肤黏膜、入血和侵入其他部位等方式引起感染。实验室诊断方法包括传统的病原学检查、免疫学检测和分子检测等，其中，基于 qPCR 的新靶标检测和全基因组测序（WGS）为诊断提供了新的视角。在防治方面，抗生素治疗和疫苗接种是主要手段，但耐药性的出现对治疗构成挑战。

结论 随着肺炎链球菌毒力和耐药性的不断增强，开发新的诊断技术和防治策略显得尤为重要。未来的研究需要关注新型抗菌药物的发现、疫苗的开发以及血清型变化带来的挑战，以减少肺炎链球菌对社会的负担。

Xpert Carba-R 技术在 CRE 耐药基因快速检测中的应用及其诊断效率

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目的 本研究旨在评估 Xpert Carba-R 检测技术在肠杆菌科细菌碳青霉烯酶基因诊断中的应用及其诊断效率，为临床提供快速准确的诊断方法，以应对日益严峻的碳青霉烯类抗生素耐药问题。

方法 通过回顾和归纳 Xpert Carba-R 方法应用于 CRE 诊断的相关研究，本文分析了 Xpert Carba-R 检测技术的原理、样本类型、准确性以及其在不同临床样本中的应用情况。Xpert Carba-R 基于实时荧光 PCR 技术，能够快速准确地检测 CRE 中的碳青霉烯酶类基因家族 KPC、NDM、VIM、IMP 和 OXA-48。

结果 研究表明，Xpert Carba-R 在高危和低风险人群中的诊断特异性和灵敏度分别为 0.98、0.99 和 0.99、0.96，显示出良好的准确性。该技术在多种样本类型中均取得了较好的诊断效果，包括直肠拭子、痰样本、尿液和人工支气管抽吸物等。此外，Xpert Carba-R v2 和 Xpert Carba-R NxG 作为技术的延伸，进一步提高了检测的敏感性和特异性。

结论 Xpert Carba-R 检测技术为 CRE 的快速诊断提供了一种高效率和高准确性的方法，有助于早期发现和治疗碳青霉烯耐药肠杆菌科细菌，对于控制和预防 CRE 的传播具有重要意义。随着技术的不断改进和更新，Xpert Carba-R 在简化操作步骤、缩短检测时间以及提高对罕见基因型的检测能力方面展现出巨大潜力，有望为全球性 CRE 感染的控制提供更有效的工具。

多粘菌素耐药性：机制、挑战与防控策略

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目的 本文旨在综述多粘菌素耐药机制的研究进展，并探讨耐药菌传播的防控措施，以期为多粘菌素的安全使用和耐药性的控制提供参考。

方法 首先概述了多粘菌素的历史背景和抗菌机制，随后详细分析了多粘菌素耐药性的多种机制，包括染色体突变、质粒介导的耐药性、外排泵机制和异质性耐药。以及多粘菌素耐药性的全球传播情况以及我国在农业和临床中采取的防控措施。

结果 研究发现，多粘菌素耐药性主要通过 LPS 修饰减少负电荷、mcr 基因家族介导的质粒传播、外排泵机制以及异质性耐药等方式产生。mcr-1 基因的发现及其在动物、人类、环境和食品中的广泛检出，揭示了多粘菌素耐药性的快速传播。我国禁止多粘菌素作为动物饲料添加剂后，mcr-1 基因的流行性显著下降，表明合理使用抗生素的措施能有效地影响耐药基因的流行。

结论 多粘菌素耐药性是一个日益严峻的全球性问题，需要从多个层面采取措施进行防控。在动物饲养中减少多粘菌素的使用，以及在临床中优化多粘菌素的使用策略，对于控制耐药性的传播至关重要。同时，加强医院感染管理、提高手卫生依从性和无菌操作，以及进一步研发新的抗菌药物，是应对多粘菌素耐药性挑战的重要策略。

基于 MALDI-TOF MS 与机器学习快速检测热带念珠菌氟康唑耐药性研究

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目的 本研究旨在构建采用基于机器学习结合基质辅助激光解吸电离飞行时间质谱（MALDI-TOF MS）的抗真菌药物敏感性试验（MS-AFST），并评估 MS-AFST 快速检测念珠菌抗真菌药物耐药性的临床应用潜能。

方法 回顾 2018 年至 2021 年四川大学华西医院血流感染中热带念珠菌检出情况，利用念珠菌显色培养基和 MALDI-TOF MS 鉴定热带念珠菌临床分离株，进行 Sensititre YeastOne 显色抗真菌药物敏感性试验和 CLSI 微量肉汤稀释法（BMD）抗真菌药物敏感性试验检测热带念珠菌临床分离株的氟康唑最小抑菌浓度（MIC）并判读耐药性。采用常见的机器学习分类模型（Logistics 回归、线性判别分析和随机森林模型）分析热带念珠菌 MALDI-TOF 质谱图预测氟康唑耐药性，包括对两种不同来源的质谱图（暴露于 0-256 μg/mL 氟康唑系列浓度的热带念珠菌质谱图，无药物暴露的菌种鉴定的热带念珠菌质谱图）分别构建机器学习模型，并与 CLSI BMD 参考方法和 Sensititre YeastOne 结果比较，评估其分类预测性能。

结果 器学习预测热带念珠菌氟康唑耐药性方面，对来自基于氟康唑暴露的 MS-AFST 的质谱图，随机森林模型的表现最好，平均准确度为 74.52%，AUC 为 0.8530，敏感性 73.33%，特异性 82.17%；对来自于菌种鉴定的 MALDI-TOF 质谱图而言，线性判别分析预测分类效果最好，平均准确度为 66.33%，AUC 为 0.7986，敏感性 69.23%，特异性 72.73%。

结论 机器学习结合不同条件下的 MALDI-TOF 质谱图，用于预测念珠菌抗真菌药物耐药性是值得探索的方法，机器学习可能将会给抗菌药物耐药性预测带来新的转变。

Antimicrobial application of multimodular functional materials constructed based on alkyne amine click reaction against carbapenem-resistant gram-negative bacilli

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Abstract Content Organ and tissue damage caused by bacterial infections poses a major threat to global health, while the emergence of carbapenem-resistant Gram-negative bacteria has led to an increasingly critical global multi-drug resistance situation and an urgent need for new antimicrobial strategies. In order to develop novel therapeutic drugs with high efficiency, low toxicity and less resistance, we designed photosensitizer MTPABP-pyo with activated alkyne moiety and cholesterol lipid molecule Chol-yne using AIE materials, and modified them through click reaction, and finally synthesized PEI-MTPABP-Chol nanoparticles.PEI-MTPABP-Chol is anchored to the molecules with the help of cholesterol lipid molecule. molecule anchoring effect not only to achieve the binding of molecular materials for Gram-negative bacteria, but also to achieve rapid imaging and efficient killing effect at low concentration.PEI-MTPABP-Chol obtained photodynamic activity through the modification of PEI to achieve simultaneous enhancement of fluorescence and ROS.PEI-MTPABP-Chol nanoparticles possessed highly efficient antimicrobial activity and biofilm barrier penetration efficiency, achieving effective treatment of multidrug-resistant bacterial infections, and providing new ideas for the study of therapeutic drugs for carbapenem-resistant Gram-negative bacterial infections.

Methods The AIE photosensitizer PEI-MTPABP-Chol nanoparticles with antibacterial effects on carbapenem-resistant gram-negative bacilli (CR-GNB) were found, and the effects of PEI-MTPABP-Chol on carbapenem-resistant Klebsiella pneumoniae (CRKP) and carbapenem-resistant Klebsiella pneumoniae (CRKP) were observed by plate colony counting. The MICs of carbapenem-resistant Escherichia coli (CREC), carbapenem-resistant Acinetobacter baumannii (CRAB) and carbapenem-resistant Pseudomonas aeruginosa (CRPA) were determined.

The binding of PEI-MTPABP-Chol nanoparticles to CR-GNB was observed by laser scanning microscopy (CLSM), and the fluorescent probe 2' was used. 7'-Dichlorofluorescein diacetate (DCFH-DA)

was used to detect the ability of PEI-MTPABP-Chol nanoparticles to produce ROS in bacteria, and the morphological changes in bacteria cocultured with nanoparticles were observed by continuous dehydration with absolute ethanol under a field emission scanning electron microscope (SEM). Cytotoxicity and hemolysis assays were then used to evaluate the biosafety of PEI-MTPABP-Chol.

Results The AIE photosensitizer PEI-MTPABP-Chol nanoparticles with antibacterial effects against carbapenem-resistant gram-negative bacilli and the AIE photosensitizer OTFPy nanoparticles with antibacterial effects against Candida auris were successfully found. PEI-MTPABP-Chol nanoparticles had no antibacterial effect on CRKP, CREC, CRAB or CRPA under dark conditions, but their antibacterial effects were significantly enhanced after photodynamic treatment, with an MIC90 of 1 μg/mL and an MIC of 2 μg/mL for CRKP and 1μg/mL for CREC, CRAB and CRPA.

Conclusion The studies searched for AIE photosensitizers that are antimicrobial effective and safe and efficient against carbapenem-resistant gram-negative bacilli, respectively, which provide a new direction for synthesizing the next-generation antimicrobial drugs and are expected to be used in the clinical treatment of multidrug-resistant bacterial infections.

A case report of elbow joint cyst caused by Nocardioides zeae infection

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Abstract Content Background: In recent years, the detection rate of Nocardia spp. bacteria in the clinic is gradually increasing, which should attract the attention of clinicians and laboratory doctors.Nocardioides zeae is a rare bacterium first separated from healthy stems of maize by German microbiologists in 2014 and identified as the Nocardia genus based on 16S rRNA gene sequence similarity while naming it Nocardioides zeae, which currently has no clear Chinese translation and will be tentatively referred to as Nocardioides zeae according to the translation. It is a strictly aerobic gram-positive rod-shaped bacillus (0.9-1.5×1.5-2.5 μm), nonmotile. Colonies growing on blood plates are round, raised, and yellow, and the optimal temperature for growth is 28°C[1]. There are currently no reports of human infection with Nocardioides zeae at home and abroad, and only one case of Nocardioides zeae separated from a healthy rootstock of maize has been reported. Methods: A rare strain was separated and cultured for the first time from the joint cavity fluid of a patient in our laboratory.We identified the strain by Gram staining and 16S RNA sequencing. The authors will present the case review analysis, bacterial identification process and results demonstration, and discussion of the following aspects to report the new clinical discovery of rare pathogenic bacteria and review the literature for Nocardia spp. bacteria in conjunction with the case.Results: The strain separated from the joint cavity fluid was identified as Nocardioides zeae by 16S RNA sequencing. Conclusion:This case report have newly discovered a genus of Nocardia bacteria that can infect humans, which provides new ideas for the diagnosis of rare clinical pathogenesis.

Methods A rare strain was separated and cultured for the first time from the joint cavity fluid of a patient in our laboratory.We identified the strain by Gram staining and 16S RNA sequencing. The authors will present the case review analysis, bacterial identification process and results demonstration, and discussion of the following aspects to report the new clinical discovery of rare pathogenic bacteria and review the literature for Nocardia spp. bacteria in conjunction with the case

Results The strain separated from the joint cavity fluid was identified as Nocardioides zeae by 16S RNA sequencing.

Conclusion This case report have newly discovered a genus of Nocardia bacteria that can infect humans, which provides new ideas for the diagnosis of rare clinical pathogenesis.

The rapid transform of blaKPC variant within ST11 carbapenem-resistant and hypervirulent Klebsiella pneumoniae contributed to ceftazidime/avibactam resistance during in vivo severe infection

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Abstract Content Ceftazidime-avibactam (CAZ/AVI) hypervirulent Klebsiella pneumoniae has emerged, the dynamic within-host evolution and competitive features of which were unclear.

Methods Thirty-nine Kp strains were isolated from a single patient with osteomyelitis during intermittent CAZ/AVI-based treatments for 2 years. To identify genetic features, a combination of short- and long-reads whole-genome sequencing analysis was performed. The copy number and expression of blaKPC was further investigated by qPCR. Microbiological characteristics were examined through antimicrobial susceptibility testing, plasmid transformation assay, plasmid stability assay, growth curves, in vitro competition assay, and Galleria mellonella larvae lethality assay. The process of resistance evolution was reconstructed under CAZ/AVI pressure in vitro to elucidate the mechanisms of resistance evolution.

Results Among all clinical Kp isolates, 37 were CRKP, including 25 CAZ/AVI resistant Kp. All isolates belonged to ST11-K47, with SNP distances ranging from 1 to 64. CAZ/AVI resistant strains presented different MICs ranging from 16 to >256 μg/mL. WGS analysis revealed that twenty-four isolates harbored a novel blaKPC variant gene, blaKPC-144. qPCR revealed that increased expression of blaKPC-2 contributed to CAZ/AVI resistance in one blaKPC-2-harboring isolate. The growth of isolates showed no significant differences in the presence of different KPC subtypes (blaKPC-144, blaKPC-2, or without blaKPC). The competition assay indicated that PE271024 (carrying blaKPC-144) exhibit a distinct competitive advantage compared to 21P693 (carrying blaKPC-2) and PE311195 (without blaKPC). Plasmid stability assay indicated that after 10 days of passages, both blaKPC-144 and blaKPC-2 had a plasmid retention rate above 80%. During in vivo evolution, the dual copy of blaKPC-2 and blaKPC-144 emerged. Similarly, under the selective pressure of CAZ/AVI in vitro, the copy number of blaKPC increased at low concentrations. while at higher concentrations (4/1 mg/L), the blaKPC copy number increased significantly accompanied by blaKPC variants, which was caused by plasmid duplication and recombination.

Conclusion BlaKPC-144-positive Kp isolates conferring resistance to CAZ/AVI exhibited rapid adaptability and competitive advantage during in vivo evolution. The variation in the copy number and mutation of blaKPC is crucial during CRKP evolution, and more attention should to paid to the recombination after plasmid amplification.

新型分子技术用于非结核分枝杆菌菌种鉴定的效能比较分析

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目的 快速、精准诊断非结核分枝杆菌（NTM）感染至关重要。现代分子生物学技术不断发展，如宏基因组高通量测序和靶向高通量测序技术。本研究旨在比较分析多种新型分子技术对 NTM 菌种的鉴定效能，从而为 NTM 感染的诊断提供参考依据。

方法 从 2018 年至 2022 年复旦大学附属中山医院疑似 NTM 感染患者中收集 141 例临床标本，利用多种方法进行直接鉴定，如多重PCR技术（multi-PCR）、宏基因组二代测序技术（mNGS）、靶向二代测序技术（tNGS）和靶向三代测序技术（tNanopore）。

结果 在 NTM 感染的诊断中，mNGS、tNGS 和 multi-PCR 的敏感度分别为 36.5%、42.6% 和 35.7%，三者联合的敏感度达 53.1%。mNGS、tNGS 和 multi-PCR 的特异度分别为 96.2%、100% 和 96.2%，三者联合的特异度为 92.3%。对于三种方法均阳性的 28 例标本，mNGS、tNGS 和 multi-PCR 的 NTM 菌种鉴定结果一致率为 78.6%（22/28），其中 32.1%（9/28）标本在 NTM 菌种亚种水平完全一致。本研究还选取了 30 例标本进行 tNanopore，结果发现 tNanopore、tNGS 和 mNGS 在 NTM 菌种水平的鉴定一致率为 73.3%（22/30），其中 40%（12/30）标本在 NTM 菌种亚种水平完全一致。

结论 新型分子技术能准确高效地从临床标本中直接鉴定 NTM，具有较大的临床应用前景，为快速诊断并及时治疗 NTM 感染提供指导。

微滴式数字 PCR 检测淋病奈瑟菌方法的建立

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目的 成人淋病奈瑟菌感染通常导致阴道炎和急性尿道炎，新生儿产道感染可导致急性新生儿结膜炎。鉴于染色镜检法淋病奈瑟菌漏检率高、细菌培养法耗时长、灵敏度有限、普通 PCR 法无法绝对定量等因素。有必要建立一种替代方法。

方法 我们选择 pgi1 基因作为检测淋病奈瑟菌的靶基因。建立一种绝对定量、高特异性、高稳定性、准确的淋病奈瑟菌 ddPCR 检测系统。

结果 ddPCR 反应扩增效率高，整个检测过程可在 94 min 内完成。灵敏度可达 5.8pg/μL。本实验 9 种阴性对照病原体均未检测到阳性微滴，特异性高。此外，淋病奈瑟菌的 ddPCR 检测具有良好的重复性，计算 CV 为 4.2%。

结论 ddPCR 检测技术对淋病奈瑟菌具有绝对定量、高稳定性、高特异性和高准确性的特点。可提高淋病奈瑟菌检测的准确性，为临床诊断和治疗提供更科学的依据。

微滴式数字 PCR 检测阴道加德纳菌方法的建立及应用

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目的 阴道加德纳菌（Gardnerella vaginalis，GV）是引起的细菌性阴道病（BV）的病原菌。阴道加德纳菌还可以引起女性宫颈炎，流产，术后感染，尿道感染等，男性可引起前列腺炎。鉴于染色镜检鉴定法漏检率高，细菌培养法耗时长、灵敏度有限且无法绝对定量等因素。有必要建立一种替代方法。

方法 我们选择 23S rRNA 基因作为检测阴道加德纳菌的靶基因。建立一种绝对定量、高特异性、高稳定性、准确的阴道加德纳菌 ddPCR 检测系统。

结果 ddPCR 反应扩增效率高，整个检测过程可在 93 min 内完成。灵敏度可达 4.4pg/μL，生物芯片阅读仪 CS7 读数为 0.35copies/μL。本实验 8 种阴性对照病原体均未检测到阳性微滴，特异性高。此外，阴道加德纳菌的 ddPCR 检测具有良好的重复性，计算 CV 为 1%。

结论 ddPCR检测技术对阴道加德纳菌具有绝对定量、高稳定性、高特异性和高准确性的特点。可提高阴道加德纳菌检测的准确性，为临床诊断和治疗提供更科学的依据。

杭州市某三级医院 2015-2020 年院内鲍曼不动杆菌耐药性及种群特征分析

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目的 探究该院 2015-2020 年分离的鲍曼不动杆菌院内分布、耐药情况和分子流行特征，为制定针对性院感策略以更有效控制耐药菌的传播和流行提供依据。

方法 收集杭州市某三级医院 2015 年至 2020 年鲍曼不动杆菌 190 株，采用肉汤稀释法测定 8 种抗菌药物的 MIC，利用全基因组测序、MLST 和泛基因组分析等生物信息学的方法来分析碳青霉烯类药物的耐药机制、分子流行和种群特征。

结果 共纳入非重复菌株 190 株，菌株的科室分布主要来自于康复医学科（60.5%）和 ICU（11.6%），碳青霉烯耐药率高达 77.9%。148 株 CRAB 主要的碳青霉烯耐药机制为携带碳青霉烯酶编码基因 blaOXA-23（91.2%）；其次为携带 blaNDM-1（4.1%），其中 2 株 CRAB 同时携带 blaOXA-58 和 blaNDM-1。系统发育树显示 190 株菌株分为 3 个簇，分别命名为 Cluster1，Cluster2 和 Cluster3。各簇的占比在 6 年间保持稳定的状态，而各簇的分子分型和耐药情况各不相同。Cluster1 菌株占比最低仅 3.2%，包含的 ST 型有 ST279Pas、ST1264Pas 等；Cluster2 的菌株流行克隆单一为 ST2Pas（70.5%），属于国际克隆 2（Global Clone 2，GC2）且广泛存在克隆传播现象；而 Cluster3 包含的 ST 型较分散（26.3%）。其中，Cluster2 碳青霉烯耐药率高达 98.5%，其 blaOXA-23 携带率为 99.3%，环丙沙星耐药率高达 99.25%，而 Cluster3 碳青霉烯耐药率较低为 26.0%。另外对 ST2 菌株进行 SNP 分析发现，该院内可能存在多起空间和时间克隆传播现象。

结论 杭州市该三级医院院内 CRAB 耐药率较高。携带 blaOXA-23 是 CRAB 碳青霉烯耐药的主要机制；该院菌株的种群结构在 2015-2020 年间保持稳定；Cluster2 中存在克隆传播现象。

基于基因组序列分析 ST11-KL10 CRKP 的进化路径

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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，包含前述的 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。

SSK2 基因影响 VG Ⅰ型格特隐球菌对两性霉素 B 药物治疗敏感性的研究

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目的 VG Ⅰ型格特隐球菌临床菌株 G4 和 G24 在对抗真菌药物两性霉素 B 的敏感性方面表现出显著的差异，本研究拟探讨其潜在机制。

方法 通过全基因组测序比对 VG Ⅰ内部在两性霉素 B 药物敏感性表型差异最为明显的 G4 与 G24 两株菌的 DNA，以寻找差异基因; 利用 CRISPR/Cas9 技术进行差异基因的敲除，对野生型、突变株以及基因回补后的菌株进行表型验证；此外，通过鼻吸感染小鼠模型，分析小鼠的菌载量、肺部病理破坏情况、生存预后以在体内验证差异基因对于两性霉素 B 药敏感性的影响。 通过转录组分析，探索差异基因导致 G4 和 G24 在对两性霉素 B 的敏感性方面表现出显著差异的机制。

结果 与 G24 相比，耐两性霉素 B 药物的 G4 菌株发生了 SSK2 基因点突变（HGVS.c c.793A>G）。ssk2Δ 菌株荚膜变大、黑色素产生增多、抗氧化应激和细胞壁压力减弱以及对于两性霉素 B 和 5- 氟胞嘧啶药物敏感性增强。回补点突变后，菌株表型恢复。小鼠实验中，与野生型对照组相比，野生型治疗组的菌载量显著降低，与野生型对照组相比，突变株治疗组的菌载量减少的差异性更为显著，突变株对照组与野生型对照的治疗效果无差异（$P>0.05$）。 经过两性霉素 B 药物治疗后，突变株治疗的生存明显好于野生型治疗组（$P < 0.01$）。转录组测序分析表明 SSK2 参与调控氧化应激、细胞分裂以及细胞壁合成等通路。

结论 SSK2 点突变影响了 VG Ⅰ型格特隐球菌对 AMB 药物的敏感性。SSK2 可能通过影响氧化还原、细胞分裂以及细胞壁合成途径来影响 VG Ⅰ型格特隐球菌表型。SSK2 可作新的潜在药物靶点，用于开发增强对两性霉素 B 药物的敏感性的新药协同治疗格特隐球菌感染。

利用宏转录组学对肺炎患者下呼吸道样本病原体鉴定的案例报告

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目的 肺炎的病原体种类和药敏鉴定有助于早期诊断和有效治疗。宏转录组学（MTS）作为新兴技术用于多种微生物研究，但其用于肺炎病原体鉴定领域较为少见。本研究意欲通过使用MTS 和宏基因组学（MGS）对同一样本进行分析，并将结果同临床微生物培养及药敏结果进行比较，旨在初步了解 MTS 在鉴定下呼吸道样本中病原体种类和耐药基因方面的准确性。

方法 选择临床诊断为肺炎的患者，对其进行下呼吸道样本采集，并对其同时进行微生物培养及药敏研究、去宿主基因后 DNA 提取、RNA 提取。使用 Illumina 平台对 RNA 及 DNA 样本进行测序，使用自编写脚本对其进行种类及耐药基因鉴定。

结果 MTS 共获得了 34,827,920 条序列，其中非人源序列以肺炎克雷伯杆菌（KPN）为主（592 条），这一结论同宏基因组学结果（68 条 KPN 序列）相同（表 1），同时培养结果也提示为 KPN 感染。MTS 和 MGS 结果对抗菌药物的鉴定方面无明显差别。但药敏结果仅显示对四环素耐药，对其他抗生素表现敏感（表 2）。

结论 我们成功对下呼吸道样本进行了 MTS 鉴定。MTS、MGS 和临床培养在病原体种类鉴定方面表现一致。但 MTS 和 MGS 较临床药敏鉴定结果获得了更多的耐药型。如何通过 MTS 和 MGS 进行快速耐药表型鉴定还需进一步研究。

微滴式数字 PCR 检测解脲支原体方法的建立及应用

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目的 人类感染解脲支原体主要表现为非淋球菌性尿道炎，可导致女性宫颈炎、胎膜早破、流产，男性不育，成为临床诊断和治疗的一大难题。目前，实时荧光定量 PCR 和培养是检测解脲支原体的两种主要方法。实时荧光定量PCR方法无法对核酸进行绝对定量，而培养法则存在灵敏度低、耗时等局限性。本研究旨在建立一种快速、准确的微滴式数字 PCR(ddPCR) 检测解脲支原体的方法。

方法 设计解脲支原体 ParC 基因引物。提取解脲支原体标准株核酸，采用 ddPCR 进行检测，包括引物筛选试验、特异性试验、灵敏度试验、重复性试验和临床样本验证试验，以评价 ddPCR 的检测性能。

结果 92 min 即可完成检测。灵敏度可达 3.8 pg/μL。8 种阴性对照病原菌均未检出阳性微滴，特异性高。ddPCR、SAT 和实时荧光定量 PCR 结果一致。此外，ddPCR 检测解脲支原体具有良好的重复性，计算 CV 为 2.1%。

结论 ddPCR 检测技术对解脲支原体具有绝对定量、高稳定性、高特异性和高灵敏度的特点。可提高解脲支原体的检测准确性，为临床诊断和治疗监测提供更科学的依据。

深圳市人民医院 2019—2023 年铜绿假单胞菌的临床分布及耐药性分析

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目的 回顾性分析 2019-2023 年我院黏液型铜绿假单胞菌（MPA）和非黏液型铜绿假单胞菌（NMPA）的临床分布情况及其对不同抗生素的敏感性，以更好地指导临床用药，并为院感防控工作提供合理的科学依据。

方法 收集 2019-2023 年深圳市人民医院患者送检标本中分离的铜绿假单胞菌数据资料，使用 WHONET 5.6 软件对检出 MPA 和 NMPA 的标本类型、科室分布情况及抗生素耐药率进行统计分析。

结果 2019—2023 年我院共分离出铜绿假单胞菌 1995 株，包含 389 株 MPA 和 1606 株 NMPA。感染铜绿假单胞菌的患者中：男性占 60.21%，女性占 39.79%；年龄分布以大于 65 岁患者比例最高（46.60%），17 岁以下患者比例最低（1.62%）。MPA 主要来自呼吸内科（66.84%），其次是日间手术中心（6.43%）、泌尿外科（4.37%）；标本类型主要分离自呼吸道（91.01%）、尿液（3.60%）、胆汁（2.31%）。NMPA 主要来自 ICU（14.25%），其次是呼吸内科（10.77%）、呼吸重症监护室（8.97%），标本类型主要分离自呼吸道（40.84%）、分泌物（15.94%）、尿（14.45%）。我院检出的 MPA 对左氧氟沙星和哌拉西林的耐药率最高，分别为 23.70% 和 13.47%，对哌拉西林 - 他唑巴坦和阿米卡星的敏感性最高，分别为 86.36% 和 90.42%；NMPA 对左氧氟沙星和亚胺培南的耐药率最高，为 19.15% 和 18.67%；对阿米卡星和妥布霉素敏感性最高，分别为 98.69% 和 96.50%。

结论 2019—2023 年我院 MPA 检出率呈下降趋势，NMPA 检出率呈上升趋势。MPA 感染主要来自呼吸内科，NMPA 感染主要来自重症医学科，二者均主要分离自呼吸道标本。虽然 MPA 对临床常用的抗生素耐药率并不高，但 MPA 容易形成生物膜，治疗时需考虑联合用药。

疥疮 638 例的临床特征分析

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目的 了解疥疮感染的临床特点，期望能丰富本地区的临床流行病学资料，为该病的预防及早期诊疗提供依据。

方法 回顾性分析本院 2020 年 1 月至 2024 年 4 月经显微镜镜检确诊疥疮患者的临床资料，从患者类型、发病季节、年龄和性别等方面进行分析。

结果 共收集到 638 例疥疮患者的临床资料，其中门诊病人 629 例（98.59%），住院病人 9 例（1.41%）。在这些患者中，男性 487 例（76.33%），女性 151 例（23.67%）。从年龄方面看，以青少年（13~18 岁）居多（189 例，29.62%），其次为大于 60 岁的老年（148 例，23.20%）和 19~30 岁的青年（141 例，22.10%），此外，中年患者（31~60 岁）有 130 例（20.38%），而婴幼儿（0~3 岁）及儿童（小于 12 岁）疥疮感染少见。发病季节以春季居多（190 例，29.78%），其次为秋冬季节，分别为 169 例（26.49%）和 179 例（28.06%），夏季较少（100 例，15.67%）。所有患者表现为瘙痒症状且夜间加重，皮损广泛，表现为红斑、丘疹或丘疱疹、结节等，可见隧道样皮损和抓痕，亦可伴有湿疹样变和继发感染而造成误诊或漏诊。皮损部位多见于皮肤薄嫩和褶皱部位，如手指缝、四肢屈侧、胸腹部和腋窝等，亦可累及生殖器部位（如阴囊）并伴有结节。

结论 疥疮感染多以瘙痒、皮疹等自觉症状到门诊就诊居多，好发于青少年、青年及老年患者，男性多于女性，且该病具有季节性，多见于春季，其次为秋冬季。感染处皮损广泛、形态多样，临床医师需结合临床特点和流行病学调查以提高诊断率。

头孢他啶－阿维巴坦耐药相关肺炎克雷伯菌 blaKPC-90 的鉴定及 IS26 介导的耐药基因易位和截短

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目的 本研究以携带 blaKPC-90 的肺炎克雷伯菌为研究对象，研究其耐药表型、blaKPC-90 基因及其编码的 β－内酰胺酶的遗传环境和动力学参数，以探讨其对头孢他啶－阿维巴坦的耐药机制。

方法 1、临床菌株收集

2、肉汤微量稀释法药敏试验、碳青霉烯酶表型试验检测

3、质粒转化试验

4、细菌全基因组提取及生信分析

5、分子克隆试验

6、蛋白纯化及酶促反应动力学参数测定

7、实时荧光定量 PCR

8、外排泵抑制试验

9、膜孔蛋白 SDS-PAGE 电泳

结果 在本研究中，我们从一株肺炎克雷伯菌临床分离株中发现了 blaKPC-90，与野生型 KPC-2 相比，该菌株插入了两个氨基酸 (Thr180_Ser181 ins Tyr Thr)。药敏试验和 KPC-90 动力学参数结果显示，KPC-90 可提高头孢他啶－阿维巴坦的 MIC，恢复碳青霉烯类抗菌药物敏感性，降低碳青霉烯类抗菌药物的水解活性，提高阿维巴坦的 IC50。基因特征分析显示，IS26 可介导耐药决定区分子内倒位和易位。此外，在携带 blakpc -90 的质粒中，我们发现 blaTEM-1 被 IS26 截短，这解释了转座元件的功能多样性。在本研究中，我们强调了 blaKPC-90 在头孢他啶－阿维巴坦耐药中的重要作用，并解释了 IS26 在耐药基因易位和截短方面的功能多样性。

结论 我们描述了 1 例感染携带 blakpc -90 肺炎克雷伯菌的病例，并研究了 blaKPC-2 及其变异株对碳青霉烯类和头孢他啶－阿维巴坦的耐药机制。我们还重点研究了与抗菌药物耐药性相关的 IS26 的功能多样性。未来应关注 blaKPC 基因的进化和水平传播。

A novel COE-D8-Fosfomycin conjugate effectively against first line antibiotic resistant uropathogenic E.coli.

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Abstract Content Urinary tract infection affects millionsof patients yearlyin world wide.In last decay,the misusingantibioticprescriptionrapidly increases the risk ofantibioticresistantbacteria,such asChina. However, the innovation of antibiotic developmentneed to be addressed urgently. Here, wetesteda type of mMembrane-intercalating conjugated oligoelectrolytes (COEs), namely COE-D8，inuropathogenic Escherichia coliwas used to accompare it'shieve enhancedantimicrobial efficacytoclinicalfirst-line antibiotics.Among 95patients'single clonesof uropathogenicEscherichia,four first-lineantibiotics hadover 50%resistant rate at MIC32, inworstcase,Sulfanilamidereached 75%resistant rate atMIC over 512.COE-D8 effectivelyrestricted resistant rate within 50% at MIC 32 and less than 5% at MIC 512,muchbetter performance than Fosfomycin,Cephalothinand Sulfanilamide. Exposure time window assay further confirmed that COE-D8 had at least 4 fold efficiency upon uropathogenic Escherichia within 1 hour exposure than 4 first-line antibiotics.Indeed, COE-D8 penetrated bacterial membrane and caused bacteriallysiswithin 1 hour.Furthermore,drug resistant evolution assay foundthe maximum resistantevolving rateis less than 32foldandbarely seenconsistentlost or gainaccessory genesout ofgenome. Unfortunately, COE-D8 hadhightoxicity in mammalian cells at 2μM IC50and also lead to hemolysisover 322μM in vitro.To further explore the possibilitytodecrease toxicity, we screened the combination between COE-D8 and first-line antibiotics.Interestingly,COE-D8 has a shorter molecular length and is typical of effective antimicrobial COE molecules, presumably due to its prominent membrane disrupting function. In contrast, sulfanilamide andnegative chargedfosfomycin neutralizedat least 4 foldtoxicitylevelof COE-D8 in cell viabilityassay.In miceexperiment,15mg/kg COE-D8 significantly increased ALT, AST andBUN, and 25mg/kg lead to 50% of death rate;strikinglyCOE-D8-fosfomycin cotreatment not only rescued the death rate of 25mg/kg COE-D8 but alsotoxicity.Collectively, wefounda potential antibiotic solutionupon first lineantibiotic resistant uropathogenic Escherichia.exhibits lower efficacy against bacteria and lower toxicity toward mammalian cells. Surprisingly, after supplementing 8μM COE-D8, the minimum inhibitory concentration (MIC) of COE-D8 against Escherichia coli K12 was showed, but sulfanilamide not. Furthermore, COE-D8 and sulfanilamide or fosfomycin were combined to achieve decrease toxicity toward mammalian cells.No increased toxicity toward mammalian cells was observed by the combination of COEs, as indicated by cytotoxicity measurements using the 3T3 cell line.The application of a combined mixture of COEs further demonstrates their promising potential as a new class of antimicrobial agents with high efficacy and selectivity.

Methods We first preliminarily classified bacteria obtained from collaborating medical units, then performed 16S rRNA sequencing to select E. coli, as this study primarily investigates urinary tract infections caused by UPEC. After obtaining confirmed UPEC strains, we conducted a series of in vitro experiments, such as MIC, MTT, hemolytic activity tests, and time kill assays, to assess the bactericidal activity and biocompatibility of COE-D8. To elucidate the bactericidal mechanism of COE-D8, we induced resistance in UPEC treated with D8 and discovered mutations in membrane-associated genes. Additionally, utilizing an outer membrane permeability assay, we observed that D8 indeed disrupts the outer membrane. Finally, we performed toxicity testing of COE-D8 in mice and found that phosphomycin effectively neutralizes the toxicity of COE-D8 to living organisms. Moreover, our in vitro experiments revealed that, based on this foundation, the effectiveness of COE-D8 remains consistent and can still match first-line antibiotics in killing UPEC.

Results Compared the antibacterial activity and cytotoxicity between clinical antibiotics and SOE-D8, it was found that except the three clinically preferred antibiotics for treating urinary tract infections, namely Nitrofurantoin, Fosfomycin, and Cephalothin, as well as four antibiotics that have been on the market for many years for alleviating urinary tract infections, namely Sulfanilamide, Ofloxacin, Kanamycin, and Ampicillin, two membrane-intercalating conjugated oligoelectrolytes D8 exhibited significant antimicrobial activity against all 93 UPEC strains, including UTI89, a characteristic uropathogenic strain, in both in vivo and in vitro experiments, the addition of 512 μg/ml fosfomycin supplement did not induce additional toxicity and even helped increase the IC50 of COE-D8 by approximately 3 times. Furthermore, COE-D8 is anti-UPEC and targets the bacterial envelope.

Conclusion Given that previously published conjugated oligoelectrolytes (COEs) are a novel class of antibiotics, whose mechanism of action is not fully understood, further development is needed to fully realize their widespread potential applications. Here, we continue to investigate their efficacy against Gram-negative bacteria, specifically uropathogenic strains from patients in the southwestern region of China. The treatment mechanism involves the synergistic use of COE with the first-line antibiotic, phosphomycin, to combat UPEC strains. COE-D8, due to its effective membrane disruption potentially caused by mismatched dimensions with the lipid bilayer, is a potent antibacterial molecule. While phosphomycin shows unclear efficacy against UPEC, experimental results indicate its non-toxicity, and its combined use with COE-D8 effectively reduces in vitro and in vivo cytotoxicity without compromising the antibacterial efficacy of COE-D8. Following whole-genome sequencing, computer analysis revealed that the efficient antagonism of IPEC by COE-D8 is related to the membrane protein MarA, which inhibits biofilm formation by regulating the ycgZ-ymgABC operon, thereby compromising membrane integrity to achieve UPEC killing.

2021–2023 年西北地区某中医医院多重耐药菌感染检出情况调查分析

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目的 对 MDROs 感染在西北地区中医医院的发病特点进行探索。指导多重耐药菌（MDROs）感染防控，强化抗菌用药规范，从而使多种耐药菌的传播及感染得到有效控制。

方法 对 2021 年 1 月至 -2023 年 12 月住院患者检出的 MDROs 菌株的种类及科室分布情况进行回顾性调查和分析。

结果 2825 株特定细菌中检出位于前三位的 334 株 MDROs 菌株，阳性率为 11.8%，其中前三位的是产超广谱 β - 内酰胺酶（ESBLs）细菌最多 263 例（占比 78.74%），其次依次是耐甲氧西林金黄色葡萄球菌（MRSA）41 例（12.28%）、耐碳青霉烯类抗菌药物鲍曼不动杆菌（CR-AB）30 例（8.98%）。科室分布以重症医学科、呼吸内科、康复中心为前 3 位。

结论 该院MDROs以重症医学科、呼吸内科、康复中心检出较多，必须加强抗菌药物合理使用，加强 MDROs 及中医诊疗技术医院感染预防与控制措施，以降低医院感染发生率。

Microbial community of municipal drinking water in Hangzhou using metagenomic sequencing

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Abstract Content 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. 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. 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.

Methods

2. Materials and methods

2.1. Sample collection and preparation

Five DW samples were collected, including three municipal tap water samples from distinct families, i.e., JY, LJF, LW, one water sample (SYS) from municipal tap water in the experimental laboratory of a hospital, and one sample (ZJX) from a university. While the exact departure time and date of municipal tap water samples from the water treatment plant (WTP) are not available, the detailed locations and dates of all samples are listed in Fig. S1. All municipal tap water faucets were flushed for 10 min prior to collecting 3000 ml of water within six sterile sampling bags (Hopebio, Qingdao, China). To prevent changes in the microbial community, tap water samples were transported to the laboratory in a cooler box containing ice. The samples were then promptly processed within 1 h of collection. Each sample with 500 ml water was continuously filtered by the fully automatic microbial rapid enrichment system Concentrating Pipette Select™ (InnovaPrep, Drexel, MO, USA) with 0.1 μm PES Flat Filter Concentrating Pipette Tips and 0.05 μm PS Hollow Fiber Filter Concentrating Pipette Tips (InnovaPrep, Drexel, MO, USA) to concentrate bacteria and viruses, respectively. The filter membranes of individual samples were rinsed and preserved at −80 °C until the DNA extraction for metagenomic sequencing. Total residual and free residual chlorines were in line with the national standards of the People's Republic of China “Standards for Drinking Water Quality” (GB5749-2022) (Han et al., 2023).

2.2. Bacterial culture and virus detection

A total of 2500 ml tap water of each sample within five sterile sampling bags was subjected to a heterotrophic plate count, involving filtration onto a 0.45 μm pore size Durapore® polyvinylidene fl uoride (PVDF) membranes (Millipore, Billerica, MA, USA), followed by incubation on tryptone soy agar (TSA) or Pseudomonas isolation agar (PA), and identification by mass spectrometry as previously described (Ballesteros et al., 2021). Colony enumeration was conducted at 24-h intervals to ascertain the plate counts at both 30 °C and 37 °C. Rotavirus, coxsackievirus, and human enterovirus were detected by the corresponding immune kit with the colloidal gold technique (Bioneovan Co., Ltd, Beijing, China). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), was detected using real-time fluorescence quantitative polymerase chain reaction (RT–qPCR) assays with kits obtained from Easy Diagnosis Biomedicine Co., Ltd. (Wuhan, China), which was approved by the China Food and Drug Administration (CFDA).

2.3. DNA extraction and metagenomic sequencing

DNA eluted from filter membranes was extracted using a DNeasy PowerSoil Pro Kit (QIAGEN, Hilden, Germany), and its degradation degree and potential contamination were monitored on 1% agarose gels. The purity and concentration of the extracted DNA samples were determined with a Nanodrop 2000 (Thermo Scientific, Waltham, USA) and Qubit 4 Fluorometer (Thermo Scientific, Waltham, USA),

respectively. A total of 1 μg DNA per sample was used as input material for the DNA sample preparations. Sequencing libraries were generated using the TIANSeq Fragment/Repair/Tailing module and TIANSeq Fast Ligation module (TIANGEN) following the manufacturer's recommendations, and index codes were added to attribute sequences to each sample. Briefly, the DNA sample was fragmented by the interruption enzyme to a size of 300 bp. DNA fragments were end-polished, A-tailed, and ligated with the full-length adaptor for Illumina sequencing with further PCR amplification. Finally, PCR products were purified (AMPure XP system), and libraries were analyzed for size distribution by Fragment Analyzer and quantified using real-time PCR. After cluster generation, the library preparations were sequenced on an Illumina NovaSeq platform, and 150 bp paired-end reads were generated. To extract high-quality clean reads, quality control measures were adopted, including removing low-quality bases (Q < 15 per read 30%) and ambiguous bases (N >5% per read), and eliminating the five base pairs that overlapped with adapter sequences. Clean data from each sample were then assembled to produce scaffolds using MEGAHIT v1.1.2 software. Scaffolds were divided into scaftigs without gaps (N). Gene prediction and annotation were performed with scaftigs longer than 500 bp. Metagenomic sequencing generated approximately 7.57 × 107 reads per sample across raw sequence libraries and yielded approximately 7.32 × 107 high-quality clean sequences after removing low-quality reads; detailed information is listed in Table S1.

2.4. Metagenomic sequencing analyses and statistical analysis

Scaftigs (≥ 500 bp) from each sample were used for open reading frame (ORF) prediction with MetaGeneMark (version 3.26). The predicted ORF (≥ 100 nt) redundancy was removed using the Cluster Database at High Identity with Tolerance (CD-HIT (version 4.6)) program to achieve an initial nonredundant gene catalog (nrGC). The reads from the individual samples were realigned to the nrGC using SoapAligner (Version 2.21). The abundance calculation of nonredundant genes (unigenes) involved mapping their read numbers to the nrGC. The relative abundance of unigenes among samples was multiplied by the maximum read number mapping to the nrGC. Exclusive and shared genes were identified by core/pan analysis.

The unigene phylogenetic information was obtained by blasting sequencing reads against the NCBI NR database (including bacteria, fungi, archaea, and viruses, version 17 June 2019) using BLASTP of DIAMOND (version 0.8.1) with E-value ⩽ 1 × 10−5. Sunburst visualizations of organism-specific k-mer relative abundances (percentages) for each sample were generated using Krona (Ondov et al., 2011). The relative abundance for each taxonomic rank involves summing the relative abundance values of all members. The clustering tree structure of bacteria at different classification levels was based on the Bray–Curtis distance. Unigenes were blasted with the Virulence Factor Database (VFDB) to identify virulence factors with a parameter identity >90% and an E-value <1 × e−10. Unigenes were blasted to the NCBI to identify antimicrobial resistance genes with a parameter identity >90% and coverage >60%. The corresponding hosts were identified by blasting the unigenes filtered with the Pathogen Host

Interactions (PHI) database with more than 90% identity. Kyoto Encyclopedia of Genes and Genomes (KEGG) annotation of each gene was performed using BLASTP of DIAMOND against the KEGG database with E-value ≤1 × 10−5.

Results

3. Results

3.1. Detection of microorganisms and viruses in DW

All water sample membranes were inoculated on TSA culture medium, and no known bacteria were collected after 24 h of culture at 30 and 37 °C. None of the DW samples yielded growth, even after incubation for up to 48 h at 30 and 37 °C (Fig. S2). The indicator organisms, Pseudomonas aeruginosa and Escherichia coli, were not found in any samples by selective culture medium and identification with mass spectrometry (Fig. S3). Viruses, i.e., rotavirus, coxsackievirus, or human enterovirus, were not detectable in any of the water samples with the antigen detection kit employing the colloidal gold method (Fig. S4). RT–qPCR was performed to detect the SARS-CoV-2 genes, and all samples also showed negative results.

3.2. General microbial diversity patterns

To comprehensively and intuitively display the number of genes at different classification levels in each sample, Krona software was used to visualize the species annotation results. The relative abundance of bacteria, archaea, and viruses was visualized using Krona plots. These plots provide a graphical representation of the composition percentages of microbial species in DW samples. All water samples contained a majority of bacteria within the full species diversity (86%–99%), and a minuscule amount of Archaea (0.04–0.4%), eukaryotes (0.2–0.8%), and viruses (0.01–0.6%) (Fig. 1A–E). Except for the SYS sample, the bacterial content of the other four water samples accounted for more than 90% of the total species diversity, specifically in the LW (Figs. 1B and 99%), LJF (Figs. 1A and 99%), ZJX (Figs. 1C and 98%), and JY water samples (Figs. 1D and 92%).

3.3. Bacterial community composition at the phylum level

As shown in Fig. 2, the top 10 microbial species at the phylum level in the five water samples were roughly the same but exhibited distinct distribution patterns. Proteobacteria had the highest abundance, accounting for over half of the total composition (49.77–90.82%). Candidatus_Melainabacteria accounted for 2.91–23.34%, Planctomycetes accounted for approximately 1.28–13.65%, Firmicutes accounted for 1.28–13.65%, and Actinobacteria accounted for between 0.13 and 4.62%. All these bacteria occupied a prominent position within the top five bacteria at the phylum level. Cluster analysis was conducted to compare the similarity of different samples by constructing a clustering tree based on the Bray–Curtis distance. Here, it was observed that the distribution of microbial relative abundances at the phylum level in the SYS, LJF, and ZJX water samples exhibited similarities, and the JY and LW water samples clustered together.

3.4. Identification of the subclass of the Proteobacteria

Within the phylum Proteobacteria, the bulk of Alphaproteobacteria was identified in all municipal tap waters, ranging from 53% to 65%, except for the LJF sample (35%). Betaproteobacteria accounted for 0.6–4% of all samples (Fig. S5). Gammaproteobacteria vary greatly in distinct water samples, ranging from 0.7% to 20%. The abundance of Deltaproteobacteria was extremely low in all water samples, ranging from 0.09% to 1% (Fig. S5).

3.5. Bacterial community composition at the genus level

Further classification of microorganisms in all samples was conducted at the class, order, family, genus, and species levels. As shown in Fig. 3, the top 10 microbial species at the genus level in the five water samples were roughly the same but exhibited distinct distribution patterns. Methylobacterium was the most abundant (0.23–18.64%) in all water samples, followed by Sphingomonas (2.19–14.31%), Gemmata (0.06–4.44%), Azospirilum (0.03–4.28%), and Mycobacterium (0.02–.92%). Methylobacterium and Sphingomon as belong to the subclass of Alpha-Proteobacteria.

3.6. Virulence and antimicrobial resistance genes

Unigenes were blasted by the VFDB with identity >90% and E-value <1 × e−10, and four virulence genes, including KasB, devR/dosR, Esx-5, and esxN, were found in two of five water samples (Table 1). In particular, sample JY contained all of these virulence genes. Blasting the unigenes against the PHI database showed that four virulence genes only corresponded to the Mycobacterium tuberculosis (Mtb) and Mycobacterium marinum (Mm) hosts. Unigenes were blasted against the antimicrobial resistance gene database of NCBI with the identity >90% and coverage >60%, and only an antibiotic resistance gene (ARG) 'Erm(X)' encoding a 23S ribosomal RNA methyltransferase with an identity 100% and coverage 100% was found in one of the five water samples. However, after blasting this gene against the PHI database, no host was found due to a low identity of less than 40%.

3.7. Archaea community composition and relative abundance

The proportion of Archaea in the complete microbiome was extremely low (0.04–0.4%). Euryarchaeota was the most abundant at the phylum level of the archaea in all DW samples (22–67%), followed by Candidatus Bathyarchaeota (1–9%), Thaumarchaeota (1–5%), Candidatus Lokiarchaeota (0.9–3%), and Crenarchaeata (0.9–3%) (Fig. S6, A-E). The archaeal taxonomic subdivisions encompassed 19 classes, 21 orders, 31 families, and 26 genera. Among these, Methanomicrobia was the most important class of the Euryarchaeota phylum in all samples and had a dominant abundance ranging from 22% to 67%, as detailed in Fig. S7.

3.8. Virus composition and relative abundance

Unigenes were blasted against NCBI, and only two predominant viruses were found. Among them, Ortervirales, a new viral order of reverse-transcribing viruses, occupied 5–34% of the total virus species, and the abundance of Herpesvirales ranged from 11 to 13% in water samples except for the JY sample (Fig.

4, A-E). However, after blasting these two genes against the PHI database, no host was found due to low identity.

3.9. KEGG pathways and functional predictions

Blasting the unigene of each sample against the KEGG pathway database, the relative abundance of KEGG pathways at level 1 in all samples almost exhibited the same distribution. BRITE hierarchies and metabolism were the top two relative abundances of the KEGG pathway, accounting for over 65% (Fig. 5, A). At level 2 of the KEGG pathway, 67931, 67242, and 32285 unigenes were substantially enriched in signaling and cellular processing, genetic information processing, and metabolism of the BRITE hierarchies. Amino acid metabolism, metabolism of cofactors and vitamins, and energy metabolism were the dominant metabolic processes, including 11722, 11099, and 7916 unigenes, respectively (Fig. 5, B). Furthermore, transporters, exosomes, and bacterial motility proteins were among the top three signaling and cellular processes. DNA repair and recombination proteins, transfer RNA biogenesis, and chromosome and associated proteins occupied the top 3 genetic information processing pathways. Peptidases and inhibitors, protein kinases, and lipid biosynthesis proteins were listed as the top 3 metabolic pathways (Fig. 5, C).

Conclusion The combination of traditional culture-dependent methods and metagenomic sequencing coupled with bioinformatics tools presents an effective approach for investigating the autochthonous microbial community within DW during the COVID-19 era. The following conclusions could be drawn from the results of this study:

(1)Although culturable bacteria were not detected using traditional methods, the phyla Proteobacteria a nd Planctomycetes and the genus Methylobacterium were the most predominant bacterial taxa in DW using metagenomics.

(2)Mycobacterium spp., hosts corresponding to virulence factor ‘Esx-5’, was identified by metagenomics.

(3)While viruses were not found in water isolated from the COVID-19 era, a new order of reverse-transcribing viruses Ortervirales was identified in the water using metagenomics.

(4)The identified metabolic pathways reflect the cooperation between different microbial populations in the water.

The results of this study provide insight into bacteria, viruses, virulence-associated factors, and metabolic processes present in DW from various regions, yielding new information on the microbial community structure of tap water and its associated gene functions. In the post-COVID-19 era, effective surveillance of clean and safe sanitation water is very important to the protection of public health.

Assessment of microorganisms in drinking water disinfected by catalytic ozonation with fluorinated ceramic honeycomb and NaClO disinfectants under laboratory and pilot conditions

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Abstract Content While sodium hypochlorite (NaClO) has long been used to disinfect drinking water, concerns have risen over its use due to causing potentially hazardous byproducts. Catalytic ozonation with metal-free catalysts has attracted increasing attention to eliminate the risk of secondary pollution of byproducts in water treatment. Here, we compared the disinfection efficiency and microbial community of catalytic ozone with a type of metal-free catalyst fluorinated ceramic honeycomb (FCH) and NaClO disinfectants under laboratory- and pilot-scale conditions. Under laboratory conditions, the disinfection rate of catalytic ozonation was 3~6-fold that of ozone when the concentration of Escherichia coli was 1 × 10^6 CFU/ml, and all E. coli were killed within 15 s. However, 0.65 mg/L NaClO retained E. coli after 30 min using the traditional culturable approach. The microorganism inactivation results of raw reservoir water disinfected by catalytic ozonation and ozonation within 15 s were incomparable based on the cultural method. In pilot-scale testing, catalytic ozonation inactivated all environmental bacteria within 4 min, while 0.65 mg/L NaClO could not achieve this success. Both catalytic ozonation and NaClO-disinfected methods significantly reduced the number of microorganisms but did not change the relative abundances of different species, i.e., bacteria, viruses, eukaryotes, and archaea, based on metagenomic analyses. The abundance of virulence factors (VFs) and antimicrobial resistance genes (ARGs) was detected few in catalytic ozonation, as determined by metagenomic sequencing. Some VFs or ARGs, such as virulence gene 'FAS-II' which was hosted by Mycobacterium_tuberculosis, were detected solely by the NaClO-disinfected method. The enriched genes and pathways of cataO_3-disinfected methods exhibited an opposite trend, especially in human disease, compared with NaClO disinfection. These results indicated that the disinfection effect of catalytic ozone is superior to NaClO, this finding contributed to the large-scale application of catalytic ozonation with FCH in practical water treatment.

Methods

2. Materials and methods

2.1. The generation of catalytic O_3 under experimental conditions

Catalytic O_3 with a concentration of 0.09 g/h was produced by an ozone generator (Azco Industeried

Ltd, Canada) with or without FCH based on a constant rate of 250 ml/min of pure O_2 provided by Jiande Hangyang Gas Co., Ltd., China. According to the above conditions, the final doses of ozone of the reactor under lab conditions were 0.5 mg/L, 1 mg/L, and 1.5 mg/L at corresponding times of 5 s, 10 s, and 15 s, respectively (Fig. S1). The concentrations of catalytic O_3 referred to the "Guidelines for drinking-water quality" of the World Health Organization (WHO, 2017).

2.2. Evaluation of the disinfection ratio of E. coli by catalytic O_3 and O_3

Catalytic O_3 and O_3 were continuously injected into 240 ml ddH_2O containing initial concentration 1×10^6 or 1×10^8 CFU/ml chloramphenicol-resistant E. coli, FCH, and the Ouyi Environmental Protection Equipment's aeration head (Yixing, China) to kill the bacteria. The post-killed bacterial solution of 100 µl at the corresponding time point (5 s, 10 s, 15 s) was spread on a plate containing 100 µg/ml chloramphenicol and cultured for 16–18 h at 37 °C to count the number of E. coli (Fig. S1) and draw a logarithmic curve of inactivation of E. coli. In cases where the bacteria count is "0", we adopt the "0 + 1" method to create figures, avoiding the situation of "log0".

2.3. Evaluation of the disinfection ratio of E. coli by NaClO

Various concentrations of NaClO (0.65 mg/L, 3.94 mg/L, 24 mg/L) were added to 240 ml ddH_2O containing initial concentration 1×10^8 CFU/ml E. coli to disinfect for 30 min, and then 100 µl of the disinfected bacteria was spread on a plate containing 100 µg/ml chloramphenicol resistance and incubated for 16–18 h at 37 °C to encumber E. coli. The concentrations of 0.65 mg/L and 24 mg/L referred to the parameters of the Jiande Liuwu water factory (13 kg NaClO/kt water) and a study (Hassaballah et al., 2020), respectively. These concentrations form a geometric sequence of "$24/3.94 \approx 3.94/0.65$".

2.4. Detection and identification of species disinfected by catalytic O_3 and NaClO at the pilot scale

2.5. Water sample collection and preparation

The detailed disinfection workflows, including the equipment, disinfection process of catalytic ozonation, actual renderings, and parameters of catalytic O_3 at the pilot scale, are listed in Table S1 and Fig. S2. The reaction equipment under the pilot scale was slightly different from the laboratory catalytic ozonation reaction equipment in which the reaction volume was small. A total of 80 water samples were collected, including 12 raw water samples of drinking water reservoir (3 samples/per time point, 4 time points), 60 catalytic O_3-disinfected water samples (3 samples/per time point, 20 time points), and 8 NaClO-disinfected water samples (4 samples/per time point, 2 time points). All raw waters disinfected by catalytic O_3 or NaClO were from the Liuwu Reservoir. All water faucets were flushed for 10 min before collecting 500 ml of water within sterile sampling bags (Hopebio, Qingdao, China). To concentrate bacteria, each sample with 500 ml water was continuously filtered by the fully automatic microbial rapid enrichment system Concentrating Pipette Select™ (InnovaPrep, Drexel, MO, USA) with 0.45 µm pore size Durapore® polyvinylidene fluoride (PVDF) membranes (Millipore, Billerica, MA, USA). Subsequently, the filter membranes from each sample were preserved at −80 °C until DNA preparation.

2.6. Bacterial culture and identification

Total bacterial heterotrophic plate counts were conducted on tap water samples filtered through 0.45 μm PVDF membranes, which were incubated on tryptone soy agar (TSA) or Pseudomonas isolation agar (PA), as previously described (Ballesteros et al., 2021; Cai et al., 2021). The plates were incubated at 30 and 37 °C, and colonies were counted every 24 h to determine the plate counts. Bacterial species were identified by the matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS; Bruker Daltonik GmbH, Germany) according to the manufacturer's instructions.

2.7. DNA extraction and whole-genome shotgun sequencing

The DNA of three samples, including one mixed sample of catalytic ozonation-disinfected water (from SKCS1-1 to SKCS1-6, SKCS2-1 to SKCS2-4, SKCS3-1 to SKCS3-4, and SKCS4-1 to SKCS4-6, a total of 18 samples in which the DNA concentration was extremely low), one raw water sample (SKRS4-1) and one NaClO-disinfected water sample, was extracted by a DNeasy PowerSoil Pro Kit (QIAGEN, Hilden, Germany) from shredded 0.45 μm PVDF membranes containing bacteria. The concentration of DNA samples extracted is documented in Table S3. To create sequencing libraries, 10 ng of DNA per sample was employed, utilizing the TIANSeq DirectFast Library Kit (TIANGEN). Briefly, the DNA samples underwent fragmentation to achieve a size of 300 bp and then were subjected to end-polishing, A-tailing, and ligation with full-length adaptors. Sequencing was conducted on the Illumina NovaSeq platform, producing 150 bp paired-end reads. The details of the raw reads, clean reads, and scaftigs are listed in Table S3.

2.8. Metagenomic sequencing analyses

Scaffolds with a length of $\geqslant$ 500 bp extracted from individual samples were used for identifying open reading frames (ORFs), which, in turn, contributed to establishing an initial nonredundant gene catalog (nrGC). The count of reads for each nonredundant gene (referred to as unigenes) successfully aligned to the initial nrGC was utilized for abundance calculations. To determine the abundance, the relative abundance of each gene was multiplied by the maximum read count aligning to the nonredundant gene catalog across all samples, resulting in normalized read numbers. The alignment of sequencing reads against the NCBI NR database (including bacteria, viruses, fungi, and archaea, version 17 June 2019) was performed by DIAMOND (version 0.8.1, BLASTP, E-value $\leqslant 1 \times 10^{-5}$) to obtain the phylogenetic information of unigenes. The relative abundance for each taxonomical rank was calculated by summing the relative abundance of all its members. To identify VFs, unigenes were blasted against the Virulence Factor Database (VFDB) with identity >70% and E-value $<1 \times e^{-10}$ (http://www.mgc.ac.cn/VFs). Unigenes were blasted by AMRFinderPlus of NCBI with identity >70% and coverage >60% to identify ARGs (https://www.ncbi.nlm.nih.gov/mailman/listinfo/amrfinder-announce). The corresponding hosts were identified by blasting the unigenes with the Pathogen Host Interactions (PHI) database with more than 90% identity. Kyoto Encyclopedia of Genes and Genomes (KEGG) annotation of each gene was performed by DIAMOND (BLASTP, E-value $\leqslant 1 \times 10^{-5}$) against the KEGG database.

2.9. Statistical analysis

Survival data were expressed as log10 (cfu), where cfu is the number of initial colonies or the number of colonies after disinfection. Unpaired t-tests were performed by Graph Pad Prism 8 between the catalytic ozonation and ozonation groups at the same time points or the same NaClO group at different time points. One-way ANOVA with multiple comparisons was performed for the different concentrations of NaClO at different time points. *represents $P < 0.05$, ****represents $P < 0.0001$, #represents $P < 0.05$, ##represents $P < 0.01$, and n.s represents data of no statistical significance.

Results

3. Results

3.1. The inactivation of E. coli by catalytic O_3, O_3, and NaClO under laboratory conditions

We compared the inactivation of E. coli in different disinfectants under laboratory conditions. Catalytic O_3 and regular O_3 could completely kill all the E. coli within 15 s. The average inactivation rate of catalytic O_3 was 6.15-fold and 3.8-fold higher than that of O_3 at 5 s and 10 s, respectively, when the initial E. coli concentration was 1.4 × 106 CFU ml−1 (Fig. 1A and Fig. S1). Thes area under the inactivation curve reflecting the total disinfection availability by catalytic O_3 and O_3 was significant ($P < 0.05$, $P = 0.0278$). Similarly, catalytic O_3 and O_3 exhibited a similar inactivation trend, with 3.15-fold and 3.12-fold at time points 5 s and 15 s, respectively, when the E. coli concentration reached 1.2×10^8 CFU ml−1 (Fig. 1B). However, neither catalytic O_3 nor O_3 completely eliminated the number of species in the raw water of the reservoir at 5 s, 10 s, and 15 s (Fig. 2A). As shown in Fig. 1C, NaClO concentrations of 0.65 and 3.94 mg/L did not kill all E. coli after 30 min of disinfection unless the disinfection concentration reached 24 mg/L. Collectively, these results demonstrate that disinfection efficiency of catalytic O_3 was higher than O_3 and NaClO in laboratory conditions.

3.2. The content of culturable microorganisms and indicator pathogens of reservoir raw and disinfected water inactivated by catalytic O_3 and NaClO under pilot-scale conditions

To evaluate the disinfecting effect of catalytic O_3 and NaClO on microorganisms in reservoir raw water, different parameters of catalytic O_3 were carried out under pilot-scale conditions (Table S1) after the investigation under laboratory conditions. As shown in Fig. 2 and Table S2, the content of bacteria in raw water from Liuwu Reservoir ranged from 8.0 to 11.2, 6.4–8.8, 8.0–12.0, and 7.2–12.8 cfu/ml during residence times of 4, 6, 8, and 12 min, respectively, under water ingress rates of 0.4, 0.6, 0.8, and 1.2 m^3/h. However, the bacterial colony counts in almost all disinfected water samples were significantly decreased when catalytic O_3 was applied, with most of the colony counts less than 2 cfu/ml. Compared with the short-term (15 s) inactivation of the catalytic O_3 in lab conditions, the content of species of reservoir raw water was rare when the inactivation time was elongated, especially when the disinfection time was extended to more than 4 min under the pilot-scale condition (Fig. 2A and C). However, the quantity of culturable

bacteria was not markedly decreased when the concentration of catalytic O_3 was 6 mg/L under water ingress of 0.6 m^3/h, residence time of 8 min, water ingress of 0.8 m^3/h, and residence time of 6 min (Fig. 2D). The number of culturable bacteria disinfected by NaClO exhibited decreased trends, and the colony count was markedly higher than that upon disinfection by catalytic ozonation (Fig. 2B). Altogether, these results revealed that catalytic O_3 could efficiently inactivate the environmental microorganisms of reservoir raw water. In addition, catalytic O_3 exhibited a more inactivation availability than NaClO under pilot-scale conditions.

3.3. The identification of culturable microorganisms in reservoir raw and disinfected water

Common clinical bacteria, i.e., E. coli, Acinetobacter baumannii, Klebsiella pneumoniae, Streptococcus pneumoniae, Staphylococcus aureus, and Pseudomonas aeruginosa, were not detectable in all raw water or water disinfected by catalytic O_3 and NaClO. As shown in Table S2, a total of 12 different bacteria, including Acinetobacter radioresistens, Bacillus megaterium, Lysinibacillus sphaericus, Bacillus cereus, and Aeromonas veronii, etc, were identified by the mass spectrometer in the raw and disinfected water, Among those, three bacteria from raw reservoir water, i.e, Lysinibacillus sphaericus, Enterobacter asburiae, and Bacillus cereus, which can cause diarrhea and vomiting, were completely removed by catalytic O_3 when the concentration of catalytic O_3 was 4 mg/L under water ingress of 1.2 m^3/h, residence time of 4 min (Table S2 and Fig. 2C). However, there are still several unknown species that were detected by the mass spectrometer. Altogether, these findings establish that catalytic O_3 could inactivate some environmentally harmful bacteria.

3.4. General microbial diversity patterns of raw and disinfected water

Based on the results of the culture of E. coli, catalytic ozonation and NaClO could kill most culturable bacteria; however, the effect of the two disinfectants on microbial communities using metagenomics remains unknown. As shown in Table S3, the DNA concentrations, total content, and average scaftig length of DNA in catalytic ozonation-disinfected water were significantly lower/shorter than those in NaClO-disinfected water and raw water. Bacteria, eukaryotes, archaea, and viruses identified by DNA characterization are shown in Krona plots, representing the relative abundance of total species diversity detected in raw and disinfected water samples. All water samples contained most bacteria within the full species diversity (92.7%–92.9%), a minuscule amount of eukaryotes (4.0–4.2%), archaea (0.7–0.8%), viruses (0.7–0.9%), and other unclassified species (1.6–1.7%) (Fig. 3A–C). These results indicated that catalytic ozonation and NaClO disinfectants exhibited the same inactivation effects on the total microbial diversity patterns.

3.5. Bacterial community composition at the phylum, genus, and species levels

The top 10 most prevalent microbial species at the phylum level in raw and disinfected water were roughly the same. Proteobacteria had the highest abundance, accounting for over half of the composition (58.06–58.22%) followed by Planctomycetes (12.26–12.95%), Bacteroidetes (4.37–6.24%), Actinobacteria

(2.75–4.09%), and Verrucomicrobia (3.50–3.93%) (Fig. 4A and Table S4). Cluster analysis is conducted to compare the similarity of different samples by constructing a clustering tree based on the Bray–Curtis distance. The relative abundance of microbial distribution at the phylum level in the SKRS and SKCS_NaClO water was similar; however, the catalytic O_3 sample clustered far away, and these results indicated that catalytic ozonation exhibited a more significant disinfection effect than NaClO in microecology aspects (Fig. 4A). Among the subclass of Proteobacteria, the majority of Alphaproteobacteria detected in raw and disinfected water by NaClO and catalytic O_3 were 48.1%, 48.2%, and 48.4%, respectively. Betaproteobacteria accounted for 33.8%, 33.8%, and 33.3%, respectively. Gammaproteobacteria ranged from 6.3% to 6.7%. The abundance of Deltaproteobacteria was extremely low in all water samples, ranging from 0.4% to 0.5% (Fig. S3).

Further classification of microorganisms in all samples was conducted at the levels of class, order, family, genus, and species. The top 10 microbial species at the genus level in raw and disinfected water by NaClO and catalytic O3 samples were roughly the same (Fig. 4B and Table S4). Novosphingobium was the most abundant in all waters (5.89–6.80%), followed by Undibactgerium (4.43–5.04%), Sphingomonas (2.03–2.81%), Rhodopseudomonas (1.73–2.24%), and Cupriavidus (1.80–2.23%). Among them, Novosphingobium, Sphingomonas, and Rhodopseudomonas belonged to the subclass Alphap roteobacteria. Undibactgerium and Cupriavidus belonged to the subclass of Betaproteobacteria (Table S4).

The top 10 bacteria at the species level in raw and disinfected water were also roughly the same (Fig. 4C and Table S4). Rhodopseudomonas_palustris was the most abundant bacteria in all waters (1.10–1.46%), followed by Undibacterium_squillarum (0.63–1.01%), Sphingomonas_sp._CCH10–B3 (0.69–0.99%), Nonomuraea_zeae (0.1–0.98%), and Zoogloea_sp._1C4 (0.72–0.95%). Among them, Rhodopseudomonas_palustris, Undibacterium_squillarum, and Sphingomonas_sp._CCH10–B3 belonged to the subclass of Rhodopseudomonas, Sphingomonas, and Undibactgerium genus, respectively (Table S4). Collectively, these results demonstrate that catalytic O_3 and NaClO showed the same inactivation availability in the bacteria construction at phylum, genus, and species levels.

3.6. ARGs

A total of 15 ARGs were detected, including six genes in the raw water of the LiuWu Reservoir, eight ARGs in the NaClO-disinfected water samples, and one ARG detectable in the cataO3-disinfected water (Fig. 5A). There were four corresponding functional mechanisms of eight ARGs in NaClO-disinfected water samples, whereas there were only three and one functional mechanism in raw water and cataO3-disinfected water, respectively (Fig. 5A). Among them, the NaClO disinfection method could decrease the abundances of beta-lactam ARGs; however, the catalytic zone could completely remove these ARGs. The functional mechanism of phenicol, sulfonamide, and aminoglycoside was only increased in the NaClO-disinfected water, however, these observations were lost in the cataO3-disinfected water. The thorough removal of aph(6′)-lb, an APH(6)-I family aminoglycoside O-phosphotransferase, was observed only in the

cataO3-disinfected water. Three genes with 100% identity and coverage 100%, 'sul1, catB3, and aph(6)-ld', were detected, and the detailed information is listed in Table S5; however, their corresponding hosts were not matched in the PHI database. Altogether, these results indicated that catalytic O_3 and NaClO exhibited different inactivation effects on ARGs.

3.7. VFs

A total of 626 virulence genes were detected, including 377 genes in raw water of LiuWu Reservoir, 241 VFs in the NaClO-disinfected water samples, and only 8 VFs in the cataO3-disinfected water. The functional mechanism of these genes corresponding to adhesion and invasion, biofilm formation, stress protein, motility, biofilm formation, efflux pump, secretion system, and toxin all decreased in the NaClO-disinfected water; however, these functional mechanisms rarely existed in the catalytic ozonation-disinfected water (Fig. 5B). Four genes with 100% identity and E-value $<1 \times e^{-10}$, 'colibactin (clbN), T6SS-III (A79E_1985), type 3 fimbriae (mrkB), and sigma (sigA/rpoV)', were detected only in the NaClO-disinfected water. These genes are involved in the process of adhesion, secretion system, and regulation, and detailed information is listed in Table S6. Interestingly, the kasB gene, with an identity of 88.57% and an E-value of $1 \times e^{-87}$, corresponding to VF 'FAS-II' was matched to host 'Mycobacterium_tuberculosis' in the PHI database with an identity of 91.62%. The flaA gene, with an identity of 88.68% and an E-value of $9 \times e^{-21}$, corresponding to VF 'Flagella' was also matched to host 'Mycobacterium_tuberculosis' in the PHI database with an identity of 90.74%. These results indicated that both disinfection methods could significantly inactivate the microorganisms containing VFs, but the disinfection effect of catalytic ozonation was exhaustive. In addition, Mycobacterium tuberculosis containing VFs 'FAS-II' and 'Flagella' was not inactivated by NaClO.

3.8. KEGG pathways and functional predictions

The relative abundance of the KEGG pathway at level 1 of raw and disinfected water samples showed different distributions. The genes of raw water were dominantly enriched in human diseases, organismal systems, and brite; however, the cataO3-disinfected water exhibited an opposite trend compared with the raw water. NaClO-disinfected water clustered nearly with the raw water, enriching the cellular process and metabolites (Fig. 5C). Furthermore, based on further classification annotation of KEGG at level 2, catalytic O_3-disinfected, NaClO-disinfected, and raw water exhibited different trends, among them water translation, amino acid metabolism, cancer, drug resistance, infectious diseases, and cardiovascular disease were significantly enriched in raw water samples, whereas the genes of cataO3-disinfected water were enriched more in lipid metabolism, replication and repair, folding, sorting and degradation, and some unclassified terms (Fig. 5D). Collectively, these results uncovered that both disinfectants could inactivate gene fragments related to human diseases, whereas catalytic O3 exhibited an exhaustive inactivation availability than NaClO.

Conclusion This research provides a comprehensive understanding of the effectiveness of deactivating pathogens and the alteration of microbial communities of catalytic ozonation and NaClO in both laboratory and pilot-scale settings using culture-dependent techniques and metagenomic sequencing. Our findings revealed that catalytic O_3 by FCH improves the disinfection ratio of E. coli by approximately 3~6-fold over O_3. Moreover, catalytic ozonation killed and inactivated more organisms, VFs, and ARGs than NaClO, but both disinfectants did not change the relative abundance of microorganism species (bacteria, viruses, eukaryotes, archaea). Catalytic ozonation could eradicate gene fragments of human diseases and eliminate harmful species, especially in the removal of Mycobacterium tuberculosis containing VFs 'FAS-II' and 'Flagella'. However, NaClO exhibited limited inactivation. All these findings illustrated that catalytic ozonation with FCH exhibited a higher inactivated efficiency than ozone and NaClO, this contributed to the large-scale application of catalytic ozonation in practical water treatment.

Application of Total Laboratory Automation for Direct Rapid Antimicrobial Susceptibility Testing from Enterobacterales-Containing Blood Cultures

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Abstract Content Introduction Currently, EUCAST and CLSI have issued guidelines for direct rapid antimicrobial susceptibility testing (RAST) on blood cultures. Research on RAST mainly focuses on EUCAST RAST, while research on CLSI RAST is limited and there are few reports on total laboratory automation (TLA) for RAST in China. The purpose of this study is to use TLA to evaluate both EUCAST RAST and CLSI RAST methods in Enterobacterales-containing blood cultures.

Methods From April to August 2022, blood cultures positive for Enterobacterales (54 Escherichia coli and 60 Klebsiella pneumoniae) were analyzed. EUCAST RAST (4h, 6h, 8h) and CLSI RAST (8h, 16h) were performed using TLA and compared with Vitek 2 results.

Results CLSI RAST showed lower categorical agreement with Vitek 2 for E. coli (66.7% at 8h, 81.9% at 16h) and K. pneumoniae (72.8% at 8h, 84.0% at 16h), with a higher proportion of resistance judgments. EUCAST RAST's readable inhibition zone increased over time, with high categorical agreement with Vitek 2 (97.1%, 96.2%, 96.1% for E. coli , and 96.1%, 97.1%, 97.9% for K. pneumoniae) and low error rates (VME < 3%).

Conclusion According to the CLSI-M52 standards, the detection performance of EUCAST RAST at 4h, 6h, and 8h was equivalent to that of Vitek 2. Except for ciprofloxacin in E. coli, the readable rates and categorical agreement of all antibiotics are good at 6h. The categorical agreement of CLSI RAST is poor, and the results are more likely to be judged as resistant.

High-fat diet changed salmonella infection pattern associated with increasing intestinal permeability and altering gut microbiota

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Abstract Content The impact of a High-fat diet (HFD) on gut microbiota may influence host susceptibility to pathogen infection. Here we utilized a HFD-induced dysbiosis mice model to investigate how HFD alters gut microbiota, thereby affecting the pattern of Salmonella infection.

Methods The mice was fed with HFD or Grain-based chow (GBC) for 3 weeks, then orally gavaged with 106 CFU S. enteritis to induce colitis. The survival rate, fecal bacterial counting, liver and spleen bacterial burden and cytokine detection were performed to compare the difference of two groups. Moreover, FTIC-Dextran method was used to investigate the intestinal permeability of HFD or GBC feeding mice. Finally, antibiotics cocktail pretreatment was performed to investigate the effect of HFD on gut microbiota.

Results When the mice were performed gavage with 106 CFU S. enteritis, the mortality of HFD mice (100%) was significantly higher than GBC mice (50%) (P=0.0225). Interestingly, the results displayed the fecal colonization amount of mice in GBC group was higher than HFD group. However, the bacterial burden of liver and spleen in HFD group was significantly higher than in GBC group (Fig. 1). The result showed the pro-imflammatory cytokine (TNF-α, IL-6 and IL-1β) concentration of HFD was higher than GBC mice, regardless of serum, spleen and colon (Fig. 2). Using FTIC-Dextran method to investigate the intestinal permeability, the results showed HFD decreased intestinal mucosal permeability. Meanwhile, Western results showed HFD reduced intestinal Occludin expression, which is an important component of the intestinal tight junction (Fig. 3). Finally, Antibiotics cocktail pretreatment was performed to destroy mice gut microbiota, the results showed the survival curve and fecal bacerial counting of group HFD+Antibiotics and GBC+Antibiotics was identical. It is implied that depleting gut microbiota with antibiotics rendered the mice equally susceptible to Salmonella infection, irrespective of their diets (Fig. 4).

Conclusion Our findings reveal a significant increase in Salmonella infection-induced mortality associated with HFD. HFD increased host susceptibility to Salmonella infection maybe due to HFD increasing intestinal permeability and altering gut microbiota.

微滴式数字聚合酶链式反应在临床诊断中的研究进展

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目的 聚合酶链式反应（PCR）是一种分子生物层面的检测技术，具有特异性、敏感性和重复性均较高的优势。目前已经广泛应用在诊断医学的各个领域，尤其是在临床诊断中是一项不可或缺的检测技术。而微滴式数字聚合酶链式反应（ddPCR）在 PCR 基础上进行了改良，在扩展反应结束后可根据泊松分布原理对待测样本进行绝对定量分析。本文主要介绍 ddPCR 的原理以及探讨 ddPCR 在临床诊断中的应用和发展前景。

方法 查阅近 10 年 ddPCR 相关研究，从 ddPCR 的原理优势和临床诊断进行综述分析。

结果 ddPCR 作为新型的分子检测技术，与 qPCR 相比，拥有自己的优势，抗干扰能力强和可绝对定量这两方面尤其突出。因此，其应用范围越来越广泛。

结论 ddPCR 具有可绝对定量、高灵敏度、高特异性的特点，研究人员在多个方面进行了大量研究，并证明其具有良好的诊断性能。但未来仍需对其检测系统进一步优化、细化，成本合理化，也相信 ddPCR 技术发展会越来越成熟，应用方面更加广泛，有望成为临床诊断的手段之一。

不携带 mecA 基因的甲氧西林耐药金黄色葡萄球菌的检出及分子特征

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目的 本研究旨在调查不携带 mecA 基因的甲氧西林耐药金黄色葡萄球菌（MRSA）的检出及分子分型，为临床准确检出 MRSA 提供数据支持，从而避免选择不适当的治疗方案。

方法 采用苯唑西林琼脂稀释法对 2012-2023 年间上海 14 家医院临床分离的金黄色葡萄球菌进行药敏测定。对筛选出的苯唑西林耐药菌株进行全基因组测序，检测 mecA 基因的存在。对不携带 mecA 基因的 MRSA 菌株进行头孢西丁纸片扩散法和苯唑西林肉汤稀释法复核，同时利用 SCCmecFinder 1.2 网站分析葡萄球菌 mec 盒（SCCmec）的存在及型别。采用细菌多位点序列分型（MLST）、agr 分型和葡萄球菌 A 蛋白（spa）分型分析不含 mecA 基因的 MRSA 病原菌分子特征。通过 BLAST 和 Snipp 软件分析与苯唑西林和其他 β－内酰胺耐药基因的存在及突变，以期揭示其潜在的耐药机制。

结果 本研究共收集金黄色葡萄球菌临床病原菌 347 株，苯唑西林琼脂稀释法结果显示 MRSA 检出率为 69.16% (240/347)。全基因组测序发现 4 株苯唑西林耐药菌株不携带 mecA 基因和 SCCmec 元件。头孢西丁纸片扩散法结果显示上述 4 株临床菌株对头孢西丁耐药。其中 2 株来源于血流感染患者的临床菌株在苯唑西林微量肉汤稀释法中仍呈现耐药性，而 2 株来源于肺炎患者的临床菌株则呈现苯唑西林敏感表型。分子特征分析显示，4 株临床菌株中，除 1 株为 agr Ⅱ型，其余 3 株都为 agr Ⅳ型 。尽管 agr 分型相对集中，但这 4 株菌在 MLST 和 spa 分型上呈现显著差异，均属于不常见分型。全基因组测序分析进一步表明，pbp4 相关基因突变以及参与肽聚糖合成的 mur 连接酶突变可能与耐药性相关。

结论 本研究在临床金葡菌中检出了不携带 mecA 基因，但对苯唑西林和头孢西丁耐药的 MRSA 菌株。基因组分析和药敏试验结果提示，pbp4 和 mur 连接酶突变可能与这类菌株的苯唑西林耐药性相关，为进一步的研究提供了新的方向和思路。

Persistent dissemination of β-lactam resistant Streptococcus pneumoniae clones in China linked to distinct Penicillin-Binding-Protein mutational combination

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Abstract Content To understand the prime mover of persistent dissemination of antimicrobial-resistant Streptococcus pneumoniae and pneumococcal serotype distribution in Zhejiang, China in the last decade.

Methods From 2010 to 2023, 996 S. pneumoniae isolates were collected across eight hospitals in Zhejiang, China. The micro broth dilution method was used to test the susceptibility against common antibiotics, penicillin (PEN), ceftriaxone (CRO), tetracycline (TET), and erythromycin (ERY), for treating pneumococcal infections. All isolates were submitted to chromosome extraction and next-generation sequencing (NGS) via the Illumina platform. After assembling, all the genomes were used for phylogenetic construction, multi-locus sequence typing (MLST), and Penicillin-Binding Protein (PBP) type analysis. Among all strains, 777 were also been serotyped via latex and quellung reactions.

Results According to the non-meningitis breakpoint, the insensitivity rates of isolates against PEN, CRO, TET, and ERY were 31.1%, 25.9%, 86.8%, and 94.4%, respectively (Fig.1). Based on whole genome sequence analysis and the antibiotic sensitivity test (AST) results of penicillin, isolates insensitive to penicillin were mainly concentrated in clone complex (CC)271, CC320, CC876, CC81, and CC902. The PBPs (PBP1a-2b-2x) mutational combination type of CC271/S19F is 13-11-33, and the CC320/S19A is 13-11-16 (Fig.2). The dominant serotypes in our study were 19F、3、19A、23F、6B and 14 are all 20-variant pneumococcal conjugate vaccine (PCV20) covered serotypes. The serotype coverages of PCV7, PCV13, and PCV20 were 46.5%, 22.7%, and 4.4%, respectively (Fig.3).

Conclusion The high β-lactam resistance rate in our pneumococcal collection is mainly driven by the dissemination of the predominate clones that carry the combination of PBPs (1a-2b-2x) mutation type of 13-11-33 in CC271 and 13-11-16 in CC320. 19F and 19A are the major serotypes in these two

clones and are covered by PCV13 and 20, indicating vaccination with PCV would benefit the control of resistance dissemination. Our study provides a comprehensive insight into the molecular epidemiology of β-lactam resistance of S. pneumoniae in Zhejiang, China.

急性髓性白血病患者的肠道菌群－宿主代谢物的时间变化及临床预测价值

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目的 分析急性髓系白血病（Acute Myeloid Leukemia, AML）患者肠道菌群、血清及尿液代谢物在纵向时间上的动态变化，探讨与临床特征的相关性和预测价值。

方法 本研究纳入 2022 年 10 月至 2023 年 4 月本中心 29 例初治及复发难治 AML 患者，采用 16s rDNA 测序及广靶代谢组学技术检测肠道菌群及血清 / 尿液代谢物，比较 AML 患者高危风险发生粒细胞减少伴发热时菌群及代谢物的组成及其含量变化。

结果 AML 患者治疗后较治疗前肠道微生物群和血清 / 尿液代谢物的多样性显著下降，直至下一个治疗周期开始前恢复。高风险发生粒细胞减少伴发热（Neutropenic Fever, NF）或使用广谱抗生素的 AML 患者中，菌群多样性显著下降。其中高风险 NF 时 Enterococcus 在肠道中明显扩张，其丰度变化联合 C 反应蛋白（C-Reactive Protein，CRP）增加提示 NF 风险增加，Enterococcus 上调与尿液中胆汁酸代谢物下调密切相关，胆汁酸代谢物也可预测 AML 患者 NF 风险增加。

结论 AML 患者肠道菌群与血清 / 尿液代谢物之间存在密切相关性，Enterococcus 及尿液中胆汁酸代谢物有望对 AML 高危发生 NF 提供预测价值，需进一步探究 AML 患者肠道微生物群—宿主代谢组串扰的机制。

Screening of potential biomarkers involved in Lyme disease infection via bioinformatics analysis with machine learning algorithm

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Abstract Content Lyme disease (LD) presents significant diagnostic challenges due to the absence of a reliable screening method for initial detection. Utilizing bioinformatics, this study aimed to identify potential biomarkers that could enhance clinical diagnostic accuracy.

Methods The gene expression profiles GSE145974 and GSE63085 were procured from the Gene Expression Omnibus (GEO) database. Machine learning algorithms were employed to identify the hub genes from the differentially expressed genes (DEGs). High-throughput data coupled with receiver operating characteristic (ROC) curves were utilized to authenticate the central genes. Function enrichment analysis was employed to investigate the potential molecular mechanisms underlying Lyme disease. The analysis was conducted with CIBERSORT to determine the correlation between the central genes and the immunemicroenvironment. The introduction of clinical data into the Nhanes database further authenticated the correlation between significant immune cell count and insomnia in Lyme disease.

Results The results from the Gene Set Enrichment Analysis (GSEA) indicated that the hub genes were enriched in the circadian rhythm. Through the integration of machine learning algorithms, FCGR1B, MPP1, and HSPA6 were identified as potential central genes in Lyme disease. The immune infiltration analysis of individual genes indicated that Lyme disease infection is frequently associated with the monocyte-macrophage system and humoral immunity.

Conclusion These findings provide a novel direction for the targeted treatment of Lyme disease.



血液

Acinetobacter spp. bloodstream infection in hematological patients: a 10-year single-center study

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Abstract Content 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.

浙江地区健康体检人群血清水平调查

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目的 调查浙江地区健康体检人群血清水平以及性别差异。

方法 选取在 2022 年 1 月至 12 月期间送至本单位进行血清肿瘤标志物又称肿瘤标记物，是指特征性存在于恶性肿瘤细胞，或由恶性肿瘤细胞异常产生的物质，或是宿主对肿瘤的刺激反应而产生的物质，并能反映肿瘤发生、发展，监测肿瘤对治疗反应的一类物质。肿瘤标志物存在于肿瘤患者的组织、体液和排泄物中，能够用免疫学、生物学及化学的方法检测到。

结果 A 组和 B 组比较，意义 (P<0.01)。

结论 本地区人群男女之间血清，且男性的血清含量明显高于女性；本地区的血清含量在男女各年龄段间均有差异，提示应该按性别和年龄分别建立

The pathogenesis of severe aplastic anemia may be influenced by Poxviridae and Retroviridae through metabolic pathways

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Abstract Content Severe aplastic anemia is a bone marrow failure disease resulting from autoimmune abnormalities that cause injury to hematopoietic stem cells, with pathogenic microorganisms potentially playing a crucial role in triggering immune responses.Our aim was to investigate the plasma microbiota of patients with SAA and identify potential pathogenic microorganisms implicated in the etiology of SAA.

Methods In this study, we employed the DNBSEQ™ sequencing platform technology to perform high-depth metagenomic sequencing of plasma samples obtained from patients with SAA and normal controls.

Results Firstly, regarding the distribution of species, the plasma microbiota of SAA patients and normal controls mainly consisted of Proteobacteria, Cyanobacteria, Ascomycota, Firmicutes, Actinobacteria, Nucleocytoviricota, Bacteroidetes, Preplasmiviricota, Uroviricota, Basidiomycota and Artverviricota. Secondly, the relative abundance of the TOP30 species across phylum, class, order, family, genus, and species exhibited significant statistical variations in response to changes in virus abundance, particularly within poxviridae and retroviridae. Specifically for SAA patients' plasma microbiota Pasteurella ceae, Saccharomycetaceae, Poxviridae and Retroviridae were found to have significant influence on specific species. Finally with regards to functional analysis enrichment results from KEGG pathway indicated that pathogenic microorganisms were primarily concentrated in metabolic pathways such as biosynthesis of Alanine,aspartate and glutamate metabolism; C5-Branched dibasic acid metabolism; Pantothenate and CoA biosynthesis.

Conclusion This study provides the first description of the species composition and functional pathways of plasma microbiota in SAA patients, revealing an increased relative abundance of poxviridae and retroviridae species, which exert a significant influence on plasma microbiota. These alterations in plasma microbiota are likely to contribute to the pathogenesis of SAA through metabolic pathways.

血液

基于社会生态系统理论的白血病患者恢复居家生活体验的质性研究

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目的 了解白血病患者化疗结束后的居家生活体验，为制定针对性的护理干预提供借鉴。

方法 以社会生态系统理论为理论框架，采用目的抽样法选取 15 例白血病患者为访谈对象，基于现象学研究对其进行面对面半结构式访谈并收集资料，采用定向内容分析法对资料进行处理与分析。

结果 共归纳出 3 个主题，10 个亚主题，即微观系统 (舒适改变、实际需求未得到满足、持续的负性情绪、就医延迟), 中观系统 (经济负担沉重、角色缺失、家庭关系紧张), 宏观系统 (缺乏信息支持、就医体验及诊疗水平待改善、社会压力)。

结论 白血病患者在化疗结束回归社会后，其社会生态系统状况存在诸多问题，医护人员应重视疾病给患者身心健康带来的改变，采取有效措施以满足患者身心健康需求，维持其社会生态系统的稳定。

血液系统恶性肿瘤患者粒缺发热时期宏基因组二代测序技术分析病原微生物的临床研究

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目的 评估宏基因组二代测序技术（Metagenomic Next-generation Sequencing，mNGS）在血液系统恶性肿瘤(Hematological malignancies，HM）粒细胞缺乏伴发热（Febrile Neutropenia， FN） 患者的病原微生物检出情况，探讨 mNGS 对血液系统恶性肿瘤合并 FN 患者病原微生物的检出优势、 诊断价值及预后意义

方法 回顾性分析 2019 年至 2023 年在解放军总医院住院的血液系统恶性肿瘤出现粒缺发热的共 170 例患者的住院资料及临床标本，分析 mNGS 与传统病原学检测方法对不同种类病原体的诊断优势，并以临床感染作为金标准计算不同方法的诊断效能

结果 1、mNGS 总体检出率为 76.5%，对细菌的检出率为 17.6%; 对真菌的检出率为 5.9%; 对病毒的检出率为 72.9%。 血培养对细菌检出率为 15.3% 其他传统方法对病毒检出率为 12.4%

2、mNGS 检测时间明显短于传统检测血培养（ P<0.001 ） 3、对于致病病原体， mNGS 相较于血培养对革兰阴性杆菌具有明显的检出优势（ 93.5% vs 32.3%， P<0.001 ）； 血培养相较于 mNGS 对革兰阳性球菌检出情况无统计学差异（78.6% vs 28.6%， P=0.092 ）； mNGS 能检出全部致病的真菌，而血培养未检出任一致病真菌

4、共 46 例患者根据 mNGS 结果调整抗感染治疗， 37 例根据传统方法调整抗感染治疗，两者感染死亡率无统计学差异

结论 从检测角度，mNGS 在血液系统恶性肿瘤出现粒缺发热患者中检出病原体的阳性率、检测时间均优于传统方法。mNGS 相较于传统方法检出革兰阴性杆菌、真菌等方面存在优势。从诊断角度，mNGS 可作为传统病原学检测的有效补充方法。从治疗角度，根据 mNGS 调整抗感染治疗可以达到和传统方法近似的临床结局。

结核

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目的 （二）监测承担风险责任。医疗机构应当与经营企业签订协议，经营企业应当与境外生产企业签订协议，明确双方责任，保证药品质量。制定责任风险分担和免责相关规定。在用药前，医生应向患者明确说明病情、用药风险和其他需要告知的事项，并取得书面知情同意；不能或者不宜向患者说明的，应当向患者的近亲属说明，并取得其书面知情同意。

方法 （二）监测记录临时进口药品使用相关的临床诊疗病历及药品安全性、有效性、经济性、依从性、不良反应等信息数据，并应当长期保存。若发生严重不良反应时，及时通报医疗机构所在省份的药品监督管理部门、卫生健康主管部门、国内药品经营企业。省级药品监督管理部门与省级卫生健康主管部门共同研判临床用药风险，必要时采取停止使用等紧急控制措施，并质量。制定责任风险分担和免责相关规定。在用药前，医生应向患者明确说明病情、用药风险和其他需要告知的事项，并取得书面知情同意；不能或者不宜向患者说明的，应当向患者的近亲属说明，并取得其书面知情同意。

结果 （二）监测记录临时进口药品使用相关的临床诊疗病历及药品安全性、有效性、经济性、依从性、不良反应等信息数据，并应当长期保存。若发生严重不良反应时，及时通报医疗机构所在省份的药品监督管理部门、卫生健康主管部门

结论 （二）监测记录临时进口药品使用相关的临床诊疗病历及药品安全性、有效性、经济性、依从性、不良反应等信息数据，并应当长期保存。若发生严重不良反应时，及时通报医疗机构所在省份的药品监督管理部门、卫生健康主管部门、国内药品经营企业。省级药品监督管理部门与省级卫生健康主管部门共同研判临床用药风险，必要时采取停止使用等紧急控制措施，并分别报告上级主管部门。（三）制定完善的安全防范措施和风险监控处置预案。（四）应按规定对临时进口药品合理储存。（五）应按年度对临时进口药品进行评估，并报告省级卫生健康主管部门。（六）按规定选取药品经营企

CD7 CAR-T 桥接 allo-HSCT 显著提高难治 / 复发 T 细胞急性淋巴细胞白血病 / 淋巴瘤的无病生存

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目的 在本研究中探索了 r/r T-ALL/LBL 在 CD7 CAR-T 后桥接 allo-HSCT 的长期结局，分析了接受 allo-HSCT 后的预后相关危险因素。

方法 研究纳入 2018 年 2 月至 2023 年 1 月期间，在本院接受 allo-HSCT 的 90 例 r/r T-ALL/LBL 患者。中位年龄为 14（2~65）岁。移植前通过基因测序检测体细胞和胚系突变。移植前 32 例 CR（A 组），58 例 NR。58 例 NR 中 41 例在 allo-HSCT 前行 CD7 CAR-T 治疗（B 组），17 例 NR 行挽救性移植（C 组）。供者类型包括半相合 60 例、非血缘 16 例和同胞全合 14 例。TBI/FLU 51 例或 BU/FLU 39 例的清髓性预处理方案。

结果 所有患者获得了持久植入。三组患者的 aGVHD、cGVHD 和感染发生率无明显差异。中位随访 25.5(19.6~32)个月，B 组的 2 年 OS 与 A 组相似(P=0.33)，远高于 C 组(P=0.0065)；B 组的 2 年 DFS 与 A 组相似（P=0.24），远高于 C 组（P=0.0029）。B 组、A 组和 C 组的 TRM 无统计学意义（P=0.65）。B 组的 2 年累计复发率（31.7%）与 A 组（29.0%）相似，远低于 C 组（70.5%）。

体细胞 TP53 突变或 MED12 突变的复发和死亡风险更高。胚系突变对移植后的预后无明显影响。

多变量分析显示，CD7CAR-T、TBI 预处理方案和 cGVHD 是 OS 的保护性因素，而 aGVHD 和 TP53 突变是 OS 的危险因素。同时 CD7 CAR-T 和 TBI 的预处理方案对 DFS 保护性影响，而 TP53 突变对 DFS 也有危险影响。

结论 CD7 CAR-T 桥接 allo-HSCT 显著改善了化疗耐药 T-ALL/LBL 的长期 DFS，且治疗的安全性和有效性与接受 allo-HSCT 的化疗敏感患者相当。本研究还揭示了 r/r T-ALL/LBL 的体细胞和胚系基因突变及在这种情况下影响移植预后的一些保护性因素和危险因素。

血液

曲美替尼在 RAS 突变的恶性血液肿瘤维持治疗中可显著降低复发率改善预后生存

李智慧、王先选、王磊、温晓培、王晶晶、吴彤
北京高博博仁医院

目的 本研究回顾性分析了异基因移植后使用曲美替尼维持治疗在 RAS 突变血液恶性肿瘤患者中的疗效和安全性。

方法 研究纳入 2018 年 1 月至 2023 年 1 月在我院接受 allo-HSCT 的 61 例 RAS 突变血液恶性肿瘤患者。疾病诊断包括 AML（37.7%）、BALL（54.1%）、TALL（5.0%）和其他（3.3%）。中位年龄为 15（1-68）岁。移植前，5 例伴有髓外病变，16 例伴有染色体异常。53 例接受了二线治疗。15 例二次移植。移植前完全缓解（68.9%）和未缓解（31.1%）。供者类型包括同胞全相合（8.2%）、非亲缘（18.0%）和单倍型（73.8%）。采用以 TBI/FLU（54.1%）或 BU/FLU（45.9%）的清髓预处理。25 例在移植后接受了曲美替尼维持治疗，36 例在移植后未接受任何维持治疗。两组患者的临床特征无显著差异。曲美替尼治疗开始的中位时间为 94（63-178）天，中位剂量为 1（0.5-2）mg/d。

结果 中位随访 16.5（16.8-24.8）个月，OS 和 PFS 分别为 81.2（68.6-89.1）% 和 73.0（59.7-82.5）%。曲美替尼组 OS 和 PFS 分别为 91.5（70.0-97.8）% 和 88.0（67.3-96.0）%。对照组 OS 和 PFS 分别为 73.9（55.9-85.6）% 和 65.8（47.7-78.9）%。曲美替尼维持治疗可显著改善 OS 和 PFS。曲美替尼组复发率显著低于对照组。曲美替尼维持治疗的中位持续时间为 270（30-630）天。9 例由于副作用暂时停用曲美替尼，12 例调整剂量。曲美替尼治疗期间出现 2 级副作用，未见≥ 3 级副作用。

结论 移植后使用曲美替尼维持治疗 RAS 突变血液恶性肿瘤患者安全有效，且可显著降低复发率，改善 OS 和 PFS。未来需进一步开展更大样本量的前瞻性、随机、对照临床试验。

TP53 突变恶性血液病行异基因造血干细胞移植后应用奥拉帕利的维持治疗

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目的 本研究回顾性分析了 TP53 基因突变的恶性血液病患者行 allo-HSCT 后应用奥拉帕利维持治疗的有效性和安全性。

方法 本研究纳入 2018 年 9 月至 2022 年 11 月期间在本院接受 allo-HSCT 治疗的 71 例 TP53 突变恶性血液病患者。诊断结果包括 AML 17 例、BALL 36 例、TALL/LBL 8 例和 NHL 10 例。

29 例复发患者接受了二线治疗。21 例接受了二次移植。中位年龄为 20.35 岁。移植前 33 例有髓外疾病，27 例染色体异常。移植前 45 例完全缓解，26 例未缓解。移植类型包括 3 例同胞全合，17 例非亲缘和 51 例单倍型。采用以 TBL/FLU 40 例或 BU/FLU 31 例为基础的清髓性预处理。32 例在 HSCT 后接受奥拉帕利维持治疗，39 例患者在移植后没有接受任何维持治疗。两组的临床特征无明显差异。开始奥拉帕利治疗的中位时间为移植后 67（25-496）天，中位剂量为 75（50-150）mg，每周 2 次。奥拉帕尼维持治疗的中位持续时间为 10（0.24-45）个月。

结果 中位随访时间为 12.30 个月，OS 和 PFS 分别为 56.36% 和 51.33%。

奥拉帕利组的 OS 和 PFS 分别为 90.63% 和 84.38%。对照组的 OS 和 PFS 分别为 25.51% 和 23.52%。奥拉帕利维持治疗显著改善 OS 和 PFS.

奥拉帕利组的复发率明显低于对照组。8 例（11.3%）患者暂时停用奥拉帕利，11 例（15.5%）患者因副作用而调整剂量。奥拉帕利治疗期间出现 2 级副作用，但未观察到≥ 3 级副作用。

结论 移植后使用奥拉帕利维持治疗 TP53 突变恶性血液病患者是安全有效的，可以显著降低复发率，改善 OS 和 PFS。未来应进一步开展样本量更大的前瞻性、随机对照临床试验。

血液

PD-1 单抗在治疗移植后早期播散性腺病毒感染中的应用

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目的 我们开创性地尝试用 PD-1 单抗治疗一例对传统治疗无应答的异基因造血干细胞移植后早期播散性腺病毒感染患者。

方法 患者于 2020 年 3 月诊断弥漫大 B 细胞淋巴瘤，接受包含利妥昔单抗在内的 8 个疗程治疗后，疾病缓解。2022 年 10 月诊断急性髓系白血病，3 个疗程化疗后达形态学缓解，接受子供母单倍型造血干细胞移植。移植后 2 月诊断 EBV-PTLD，接受 3 剂利妥昔单抗治疗。移植后 3 月诊断播散性腺病毒感染，累及上呼吸道、消化道、血液。患者接受减停免疫抑制剂及 2 剂西多福韦治疗后，临床症状、多部位腺病毒拷贝数、炎症指标进行性恶化，因此患者接受 PD-1 单抗（信迪利单抗 200mg）作为挽救性治疗，用药后密切监测多部位腺病毒拷贝数、炎症指标、脏器功能、排异情况。

结果 患者在接受 PD-1 单抗治疗后，临床症状、炎症指标明显改善，3 周后多部位腺病毒定量均转阴。且外周血 EBV 在 PD-1 单抗应用 1 周后也转阴。患者在接受 PD-1 单抗治疗后出现肝脏 3 级急性移植物抗宿主病，应用环孢素及巴利昔单抗 3 剂后，肝脏排异指标明显好转，疗效评估达完全缓解。目前为移植后 9 月，患者一般状态良好，无病毒复燃、排异反复表现。

结论 PD-1 单抗对于移植后播散性腺病毒感染，是一种非常有前景的治疗方法。

异基因造血干细胞移植后耶氏肺孢子菌肺炎临床特征分析

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目的 总结异基因造血干细胞移植（allo-HSCT）后合并耶氏肺孢子菌肺炎（PJP）患者的临床特征。

方法 回顾性分析 2018 年 7 月至 2023 年 7 月在苏州大学附属第一医院和苏州弘慈血液病医院诊断的 21 例 allo-HSCT 后 PJP 患者的临床表现、实验室检查、影像学表现及治疗转归。

结果 21 例患者男女比为 2.5：1，中位年龄 36（15-62）岁，移植后并发 PJP 的中位时间为 225 d；临床表现缺乏特异性，主要为呼吸道症状（呼吸困难、咳嗽、咳痰等）和发热；实验室检查发现 15 例外周血淋巴细胞计数降低，19 例 CD4+T 淋巴细胞绝对值 <200/μl，20 例 C 反应蛋白明显升高，14 例乳酸脱氢酶升高，14 例 1,3-β-D 葡聚糖试验升高；胸部 CT 表现分为磨玻璃型、结节型、混合型 3 种，其中磨玻璃型发生率最高 18 例，结节型 2 例、混合型 1 例。通过 mNGS 均检测出耶氏肺孢子菌序列数（15-57570），11 例患者为混合感染。治疗上予以 TMP-SMX、卡泊芬净、甲基强的松龙等治疗，17 例患者获得病情好转，4 例死亡，均死于呼吸衰竭。

结论 PJP 是造血干细胞移植术后危急重症，诊断不易，早期诊断可取得更好的预后。mNGS 诊断 PJP 的敏感性高，为临床提供早期精准诊断可能，值得应用和推广。

宏基因二代测序技术在 allo-HSCT 后 军团菌肺炎的 6 例临床应用观察

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目的 探讨宏基因二代测序（mNGS）技术在异基因造血干细胞移植（allo-HSCT）后军团菌肺炎中的应用。

方法 回顾性病例系列研究。收集 2019 年 9 月至 2023 年 7 月在苏州大学附属第一医院和苏州弘慈血液病医院采用 mNGS 诊断的 6 例 allo-HSCT 后军团菌肺炎患者临床资料，回顾性分析其临床特征及治疗转归，评价 mNGS 在诊断 allo-HSCT 后军团菌肺炎的临床应用价值。

结果 6 例患者中男性 4 例，女性 2 例，中位年龄 40（25~50）岁；临床表现主要为发热及咳嗽、咳痰，胸闷、气促等呼吸道症状；实验室检查表现为淋巴细胞数降低、CRP、IL-6 等炎症指标升高、血钠及血磷降低；胸部 CT 检查发现病变以实变影多见 (5 例，83.3%)，另外 1 例为双侧磨玻璃影；3 例伴有胸腔积液，3 例肺部有空洞改变。通过 mNGS 均检测出军团菌序列数（247-69402 之间），5 例为嗜肺军团菌，1 例为辛辛那提军团菌。6 例经 mNGS 诊断后使用含莫西沙星联合用药，5 例患者临床症状缓解，胸部影像学好转，1 例由于合并巨细胞病毒、肺炎克雷伯杆菌混合感染，后因呼吸衰竭死亡，总体治愈率 83.3%。

结论 军团菌感染是造血干细胞移植术后少见的机会性感染，诊断不易，早期诊断可取得更好的预后。mNGS 检测为临床提供早期精准诊断可能，值得应用和推广。

Clinical Characteristics and Treatment Response of Chronic Disseminated Candidiasis in Patients with Hematological Disorders

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Abstract Content Chronic disseminated candidiasis (CDC), also known as hepatosplenic candidiasis (HSC), is a rare invasive fungal infection typically found in patients with hematological diseases and severe neutropenia.

Methods We retrospectively reviewed electronic medical record system and collected clinical data of 49 patients diagnosed with chronic disseminated candidiasis at the Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, between January 2014 and December 2023.

Results The majority of patients had hematological malignancies (n=43, 87.8%), including acute myeloid leukemia (n=21, 42.9%), acute lymphoblastic leukemia (n=18, 36.7%), myelodysplastic syndrome (n=2, 4.1%) and invasive B-cell lymphoma (n=2, 4,1%). Severe neutropenia was a common risk factor (n=30, 61.2%) among the patient population, and 19 patients (38.8%) had persistent severe neutropenia for more than 20 days prior to CDC. Symptoms were present in 85.7% of patients (n=42), while CT scans revealed liver lesions in 44 patients, spleen lesions in 34 patients, and kidney lesions in 9 patients. Proven, probable and possible CDC was diagnosed in 5 (10.2%), 2 (4.1%) and 42 patients (85.7%), respectively. Among the confirmed diagnoses, DNA sequencing identified 2 cases of Candida tropicalis and 1 case of Candida albicans infections, while the other 2 cases showed only positive microscopic examination of yeasts without a determined species. As for the treatment, azole monotherapy (n=16, 32.7%) and azole + echinocandin combination (n=12, 24.5%) were most commonly utilized, and more patients (n=28, 57.1%) were treated with antifungal monotherapy (azole=16, caspofungin=6, amphotericin=6) compared to combination regimens (n=21, 42.9%). Abdominal CT scan was performed to evaluate response, showing complete response (CR), partial response (PR) and treatment failure rate of 10.2% (n=5), 69.4% (n=34) and 20.4% (n=10), respectively. Univariate logistic regression analysis demonstrated that proven diagnoses (OR= 25.333 (95% CI 2.405-266.803), P=0.007) and severe neutropenia > 20days (OR=5.250 (95% CI 1.155-23.856), P=0.032) were significantly associated with treatment failure at 3 months, while patients with possible diagnoses had a significantly improved antifungal response (OR=0.083 (95% CI .015-0.461), P=0.004). In addition, a strong trend toward CR/PR at 3 months was observed in patients treated

with caspofungin (OR=0.193 (95% CI 0.036-1.30), P=0.054), while such effects were not demonstrated in patients receiving azoles or amphotericin B. Multivariate cox proportional regression analysis revealed that age > 45 years old predicted dismal 1-month survival (HR=10.175 (95% CI 1.011-102.396), P=0.049) and overall survival (OS) (HR=5.756 (95% CI 1.409-23.523), P=0.017), and patients achieving CR/PR within 3 months had increased 3-month OS rate (92.3% vs. 70% in treatment failure patients, P=0.168).

Conclusion In conclusion, this retrospective study reviewed clinical data, treatment planning and clinical factors for remission and survival in 49 CDC patients diagnosed in the past 10 years, offering perspectives into the epidemiology, disease characteristics and treatment response for both researchers and physicians. Nevertheless, prospective researches and clinical trial are required to improve antifungal

磁微粒发光法检测抗 IAA 抗体的性能验证

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目的 验证磁微粒发光法检测抗 IAA 抗体的分析性能。

方法 参考美国临床实验室标准化协会 (CLSI) 系列文件，根据实验室的验证需求，对浩欧博 SMART 6500 检测 IAA 的正确度、重复性、中间精密度、线性区间、可报告范围和参考范围进行验证和评价。

结果 室内质控品 QC1 和 QC2 的重复性分别为 4.73% 和 5.56%，中间精密度分别为 5.75% 和 7.12%; 可报告范围为 0. 5-6000RU/mL; 在 0.5-400RU/mL 范围内线性良好，α 为 1.0062，线性相关系数 r2 为 0.9902；参考区间为 0.5-20.00RU/mL。

结论 浩欧博 SMART 6500 磁微粒化学发光法检测 IAA 的分析性能良好，能够满足临床检测的需求。

抗胰岛素自身抗体 (Insulin Autoantibodies, IAA) 是自身免疫抗体的一种，与谷氨酸脱羧酶（GAD）抗体，ZnT8（zinc transporter-8 autoantibodies）抗体联合检测，是诊断一型糖尿病（T1DM）最可靠的胰岛自身抗体生物标志物 [1,2]。对 IAA 进行检测有助于了解 T1DM 的自身免疫病程，并对 T1DM 患者进行诊断、鉴别诊断，以及对一般人群和患者一级亲属的风险预测有极大的价值。如在初发胰岛素依赖性糖尿病患者中查出 IAA 有助于排除二型糖尿病，有助于糖尿病的诊断分型。

磁微粒化学发光法检测 IAA 采用间接法原理，通过免疫分析两步法实现对样本的检测。根据美国临床实验室改进修正案和 ISO15189 等文件对实验室质量的管理要求和实验室认可的要求，实验室检测分析系统在临床应用前须对其进行分析性能验证 [3,4]。本研究对浩欧博 SMART 6500 检测系统检测 IAA 的正确度、重复性、中间精密度、线性范围、可报告区间和参考区间进行分析性能验证，为投入临床应用提供可靠的依据。

血液

自身抗体和补体在狼疮肾病的应用价值

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目的 分析自身抗体与补体在狼疮肾炎 (LN) 患者中的水平，探讨各个检测项目在 LN 诊断及治疗中的作用，为临床的诊断、治疗提供可靠的诊断依据。

方法 收集 80 例临床诊断为 LN 患者作为为观察组，132 例临床诊断为系统性红斑狼疮累及器官患者列为病例对照组，另选取 62 例健康体检者为健康对照组，检测抗核抗体、抗 URNP 抗体、抗 Sm 抗体、抗核小体抗体、抗组蛋白抗体、抗 dsDNA 抗体及补体 C3，C4 并对结果进行统计分析。采用卡方检验、方差分析、t 检验、非参数检验及 Spearman 相关分析等统计方法分析。

结果 观察组和病例对照组抗核抗体、抗 URNP 抗体、抗 Sm 抗体、抗核小体抗体、抗组蛋白抗体阳性率均高于于健康对照组，差异有统计学意义 ($p<0.05$)，观察组和病例对照组抗 dsDNA 抗体、补体 C3、C4 水平明显高于健康对照组（$P<0.05$），差异有统计学意义。LN 活动组抗 dsDNA 抗体、补体 C3、C4 水平高于非活动组，差异有统计学意义，LN 活动组抗核小体抗体阳性率高于 LN 非活动组，差异有统计学意义。

结论 抗核抗体、抗 URNP 抗体、抗 Sm 抗体、抗核小体抗体、抗组蛋白抗体、抗 dsDNA 抗体及补体 C3，C4 联合检测可提高对 LN 的检出，对 LN 诊断、判断病情变化具有重要价值。

血小板参数联合 CRP 在类风湿关节炎活动度中的相关性研究

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目的 分析类风湿性关节炎 (rheumatoid arthritis，RA) 患者的血小板参数中的血小板计数 (PLT)、血小板压积 (PCT)、血小板分布参数 (PDW)、平均血小板体积 (MPV) 及 C 反应蛋白 (CRP) 与疾病活动度的相关性，探讨血小板参数与 CRP 在 RA 病情活动度中评估的价值。

方法 回顾性分析 2022 年 1 月 -2023 年 3 月期间收集到在广东省人民医院诊治的 201 例 RA 患者资料，根据 28 个关节疾病活动指数 (DAS28) 评分进行分组，分为缓解组和活动组，活动组再进行分成低活动组、中活动组和高活动组。分析各组间血小板参数和 CRP 等指标水平以及这些指标与 RA 患者病情活动度的关系和诊断价值。

结果 1. 活动组 PLT、PCT 和 CRP 水平明显高于缓解组，差异具有统计学意义，而 PDW 和 MPV 水平在活动组和缓解组差异不具有统计学意义；2.PLT、PCT 和 CRP 水平在不同组别中有差异；经事后两两比较，PLT、PCT 的高度活动度组高于中度活动度组、低度活动度组和缓解组，中度活动度组高于缓解组，其余两两组别比较无统计学差异；CRP 中高度活动度组高于中度活动度组、低度活动度组、缓解组，中度活动度组高于低度活动度组和缓解组，低度活动度组和缓解组差异没有统计学意义；3. PLT、PCT 和 CRP 与 DAS28 评分呈正相关关系，PDW 和 MPV 与 DAS28 评分呈负相关；4. 单独检测中 CRP 的诊断 RA 病情活动度的效能最高，联合检测指标血小板参数四者联合 CRP 的诊断效能最高。

结论 PLT、PCT 和 CRP 水平与 RA 患者病情活动度相关，可以作为评估 RA 患者病情活动度以及进行病情监测以及疗效观察的指标。

母亲抗核抗体阳性对新生儿的影响

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目的 探讨母亲抗核抗体阳性对新生儿造成不良影响的相关性研究。

方法 选取广东省某医院妇产科 2019 年 9 月至 2022 年 1 月生产的抗核抗体阴性产妇的新生儿 39 例作为对照组；抗核抗体阳性产妇的新生儿 39 例作为对研究组 1，研究组 1 中分选出 ANA 特异靶抗原 SSA（Ro-52）、SSA（Ro-60）和或 SSB 阳性的新生儿 15 例作为研究组 2，分别对研究组和对照组新生儿的血细胞计数（WBC、RBC、PLT）、体液免疫指标（IgG、IgM、C3、C4）、新生儿出生的状态及其他不良反应进行对比分析，研究新生儿不良预后的异同。

结果 研究组 1 和对照组比较，新生儿血细胞（WBC、RBC、PLT）差异无统计学意义（P>0.05）；体液免疫指标的除 IgG 外差异无统计学意义（P>0.05），IgG 轻度升高（P<0.05）。研究组 2 和对照组比较，结果显示 WBC 和 RBC 差异无统计学意义（P>0.05），而 PLT 显著降低（P=0.01）。研究组 2 中有 9 例（60%）为早产低体重儿或高危儿，其中有 1 例诊断为Ⅲ度房室阻滞。

结论 母亲特异性抗核抗体 SSA（Ro-52）、SSA（Ro-60）和或 SSB 百分百通过胎盘传递给胎儿，导致新生儿血小板减少，1 例（6.7%）的新生儿出现Ⅲ度房室阻滞，但病例数较少，需要更多的病例佐证。

儿童造血干细胞移植骨髓空巢期使用康替唑胺联合抗结核治疗案例报告

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目的 首次报告在造血干细胞移植（HSCT）患儿中使用康替唑胺联合抗结核以避免潜在的利奈唑胺相关不良反应的案例。

方法 回顾性分析我院一例 HSCT 骨髓空巢期使用康替唑胺联合异烟肼、左氧氟沙星治疗结核分枝杆菌患儿的临床资料。

结果 患儿反复咳嗽、发热伴腹泻 1 年余，确诊重症联合免疫缺陷病 1 月余，为行 HSCT 入院。入院前 1 月余肺泡灌洗液 NGS 结果回报结核分枝杆菌复合群等多种细菌、病毒感染，针对结核分支杆菌感染予异烟肼、乙胺丁醇、左氧氟沙星、利奈唑胺联合静脉营养支持治疗，体温正常，呼吸道症状好转。入院后考虑利奈唑胺骨髓抑制不良反应，改为异烟肼、左氧氟沙星联合康替唑胺 16mg/kg q12h 方案。预处理采用白消安 1.275 mg/kg q6h×3d 和氟达拉滨 30mg/m^2/d×5d，移植物抗宿主病预防方案为环孢素联合甲氨蝶呤。预处理前患儿白细胞 4.56×10^9/L，血小板 379×10^9/L。-4d 起患儿出现低热 37.4℃，后自行降至正常，偶有咳嗽，可吸出少许白色黏痰，-2d 体温正常未再发生低热。回输当天患儿白细胞 0.64×10^9/L，血小板 146×10^9/L，回输同胞全相合供者外周血干细胞，CD34+ 细胞计数为 10.45×10^6/kg。+6d 起患儿出现腹泻症状，稀水便 15 次，予对症治疗后缓解，血小板 +10 天植入，粒细胞 +17 天植入，未出现分枝杆菌感染加重及与药物相关不良事件。

结论 HSCT 骨髓空巢期使用康替唑胺联合治疗结核分枝杆菌未影响粒细胞及血小板植入，未出现分枝杆菌感染加重及药物相关不良事件。

来特莫韦治疗及二级预防异基因造血干细胞移植后巨细胞病毒感染的临床研究

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目的 探究来特莫韦治疗及二级预防异基因造血干细胞移植后巨细胞病毒感染的疗效及安全性。

方法 搜集 2022 年 3 月至 2023 年 3 月苏州弘慈血液病医院使用来特莫韦治疗 CMV 病毒感染的 17 例患者的临床资料，回顾性分析了这些患者 CMV-DNA 转阴时间及后续 CMV-DNA 再阳性的情况及药物使用过程中的副反应

结果 所有 17 例患者，仅 1 例患者使用单药来特莫韦抗 CMV 病毒，余患者均联合一线抗病毒药物（更昔洛韦或磷甲酸钠）。单药患者 CMV-DNA 转阴时间为 30 天。剩余 16 例患者中，仅 1 例在使用来特莫韦期间未转阴，余均获得完全缓解（CR），其中包括视网膜炎受累患者。使用来特莫韦后外周血 CMV-DNA 拷贝数首次转阴时间中位数为 7（3-30）天。CMV 视网膜炎患者在外周血 CMV-DNA 转阴后，继续玻璃体内注射更昔洛韦联合来特莫韦治疗，在使用来特莫韦第 48 天获得 CR。所有患者在获得 CR 后继续口服来特莫韦，做为二级预防。随访至今，除 1 例女性 MDS 患者因颅内感染于移植后 +4 月死亡，余均存活至今，且 CMV 病毒未再激活。来特莫韦治疗及后期预防的患者表现出良好的耐受性，仅 1 例在治疗过程中出现恶心、呕吐，余患者未观察到与药物明显相关的副作用。

结论 来特莫韦治疗及二级预防异基因造血干细胞移植后巨细胞病毒感染安全、有效，仍需大样本数据进一步证实。

Increased Epstein-Barr virus reactivation but comparable post-transplant lymphoproliferative disorders incidence following allogeneic hematopoietic cell transplantation in letermovir era for cytomegalovirus prophylaxis

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Abstract Content The prophylactic use of letermovir (LTV) has significantly reduced the incidence of cytomegalovirus (CMV) infection. Although LTV itself does not have intrinsic activity against Epstein-Barr virus (EBV), it may impact the in vivo immune reconstitution due to the reduction in CMV antigenic stimulation. The impact on EBV reactivation and the incidence of post-transplantation lymphoproliferative disorders (PTLD) is yet to be determined.

Methods This retrospective cohort study was conducted and included patients aged 14 and older who underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) from January 2022 to May 2023. The primary outcomes were EBV related complications. The secondary outcomes included CMV related complications and overall survival. We compared the cumulative incidence of EBV and CMV related complications among patients between LTV and non-LTV group, treating death and subsequent HSCT as competing risks. To account for baseline differences between LTV and non-LTV group, adjusted cox competing models were constructed for each outcome.

Results A total of 359 patients, 187 in the non-LTV group and 172 in the LTV group were enrolled. Among these cases, 249 (69.4%) were diagnosed with acute leukemia. With identical EBV surveillance protocols in both groups, the cumulative incidences of EBV viremia (35/172, 20.3% vs 22/187, 11.8%, P=0.028) and csEBV infection (32/172, 18.6% vs 14/187, 7.5%, P=0.003) were significantly higher in patients belonging to the LTV group. However, the incidence of probably and proven PTLD was not significantly different between the two groups of patients (20/172, 11.6% vs 12/187, 6.4%, P=0.100). The lack of significance may be attributed to the fact that clinicians applied rituximab (CD20 monoclonal antibody) preemptive therapy timely (11/172, 6.4% vs 2/187, 1.1%, P=0.018). The cumulative incidences of CMV viremia (40/172, 23.3% vs 136/187, 72.7%, P <0.001), CMV disease (1/172, 0.6% vs 10/187, 5.4%, P=0.033), and csCMV infection (40/172, 23.3% vs 135/187, 72.2%, P <0.001) were significantly reduced among patients in the LTV group. Upon controlling for baseline differences, notable disparities in csEBV

infection persisted (P=0.041; HR, 2.014; 95%CI, 1.028~3.947). Multivariable cox competing analysis revealed LTV usage was associated with an elevated risk of csEBV infection. Sensitivity and subgroup analyses yielded results consistent with the principle analyses.

Conclusion While LTV prophylaxis reduced CMV reactivation, there was a simultaneous increase in EBV reactivation. Whether it led to an uptick in PTLD incidence remains to be ascertained through further exploration.

一例误诊为播散性感染的间变大细胞淋巴瘤

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目的 报道 1 例误诊为播散性感染的间变大细胞淋巴瘤，并探讨其诊治过程，为临床发热原因待查诊治提供思路。

方法 患者男性，21 岁，因左髋部疼痛伴发热 6 个月于 2024 年 5 月 4 日入院。4 个月前出现黑便，行胃镜检查示胃溃疡出血。2 个月前髋关节 CT 平扫及 MRI 均提示两侧髂骨及坐骨、左髋臼，左侧坐骨感染，行左侧髂骨穿刺活检术，培养为表皮葡萄球菌，经抗感染治疗未见明显好转。入院后查体发现右侧胸壁红肿，有压痛。化验 PCT、CRP、ESR、IL-6 等炎症指标明显升高，LDH、HBDH 升高。PET-CT 考虑淋巴瘤可能性大。行骨髓穿刺活检术，骨髓象可见噬血细胞，骨髓病理未见明显异常。胸部肿物穿刺活检病理示小细胞未分化肉瘤，培养示鲍曼不动杆菌。抗感染治疗效果欠佳，且患者诉胃痛明显，行胃镜检查及组织活检，考虑间变大细胞淋巴瘤可能。再次行胸部肿物切开活检，病理示非霍奇金淋巴瘤，考虑间变大细胞淋巴瘤，ALK 阳性。

结果 患者转血液科行化疗治疗后，体温降至正常，髋关节疼痛减轻，胸部肿物缩小，胃痛减轻，目前继续治疗中。

结论 对于表现为播散性感染的患者，即使有病原学证据，但当抗感染治疗效果欠佳时，应考虑血液系统肿瘤，如淋巴瘤等，设法拿到病理证据以确诊指导治疗。



真菌

泊沙康唑与伏立康唑经验治疗或诊断驱动治疗免疫功能低下患者侵袭性霉菌病的成本 – 效果分析

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目的 从中国卫生体系角度评估泊沙康唑对比伏立康唑经验治疗或诊断驱动治疗免疫功能低下患者侵袭性霉菌病 (IMD) 的经济性。

方法 基于一项 III 期临床试验和其他公开可用的数据建立决策树模型，评价泊沙康唑相对于伏立康唑所产生的增量成本 – 效果比 (ICER)，并对结果进行单因素敏感性分析、概率敏感性分析以及情境分析。

结果 基础分析结果显示，在 3 倍我国人均 GDP 的意愿支付值 (WTP) 下，泊沙康唑比伏立康唑多获得 0.04 个 QALYs 且少花费 1711.24 元，具有绝对优势。敏感性分析结果显示，伏立康唑、泊沙康唑治疗侵袭性曲霉感染的全因死亡率以及伏立康唑片的费用对 ICER 影响较大；在不同的 WTP 下，泊沙康唑经济性优势的概率始终大于伏立康唑。情境分析显示，毛霉的感染率并未影响结果；但伏立康唑降价后，将显示出成本 – 效果优势。

结论 相比伏立康唑，使用泊沙康唑经验治疗或诊断驱动治疗免疫功能低下患者 IMD 是一种有经济效益的选择。

毛霉菌感染患者艾沙康唑治疗药物监测的价值

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目的 探讨艾沙康唑治疗药物监测在真实世界中的应用及治疗药物监测的价值。

方法 连续纳入我院 2022 年 6 月至 2023 年 6 月使用艾沙康唑并进行治疗药物监测的患者，分析血药浓度与患者基础情况、合并用药、临床转归之间的关系。

结果 共纳入 12 例患者，7 例为移植术后，5 例患者入住 ICU；死亡的 2 例患者均不归因于侵袭性毛霉菌病。所有患者均有明确病原学（培养或高通量测序）检出。所有患者均使用统一标准给药方案，一半患者使用口服制剂，其中 2 例为打开胶囊鼻饲给药。所有艾沙康唑血药浓度均＞2ug/ml，4 名患者＞ 5ug/ml，其中 1 名极低体重患者＞ 10ug/ml。艾沙康唑带来的药物相互作用不显著。

结论 在侵袭性毛霉菌病患者中，艾沙康唑可达到有效的药物暴露量，可能无需特殊监测。对于极端体重的患者，建议加强监测并调整剂量。

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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Abstract Content 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 pulmonary infection patients admitted to Beijing You An 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 microbiota (via 16S rRNA gene sequencing) and host immune (via RNA-sequencing) on bronchoalveolar lavage fluid samples. The datasets were analyzed individually using bioinformatics approaches. Then we constructed a diagnostic model using differential genes with LASSO regression. The immune infiltration analysis was performed to explore the landscape of lung immune in patients with PCP. Additionally, we performed spearman correlation analysis to assess the correlation between the OUT abundance of differential species and the expression levels of the differentially expressed genes (DEGs) related to the MAPK signaling pathway.

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 transcriptomic marker MAPK10, TGFB1, and EFNA3 indicated a potential to predict the onset of PCP (AUC = 0.86, 0.73-0.99). The lung immune landscape of patients with PCP showed

the lower levels of naïve CD4 T cells and activated dendritic cells compared to non-PCP individuals. 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. 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.

马尔尼菲篮状菌感染淋巴结引起的上腹部肿块：病例报告

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目的 无压痛的上腹部肿块一旦排除肝脏或脾脏增生，则通常表明发生了肿瘤，而马尔尼菲篮状菌（Talaromyces Marneffei，TM）感染引起的淋巴结病性肿块非常罕见，本研究通过个案报道的形式探讨一例由 TM 感染引起上腹部肿块的病例。

方法 患者男，29 岁，腹胀 10 余天，体格检查发现上腹部有一个直径约为 10 厘米的肿块，颈部有多个肿大的淋巴结。实验室检查显示：HIV 抗体检测为阳性，CD4+ T 细胞计数仅为 8/μL，HIV 载量超过 1×106 copies/mL，红细胞沉降率、C- 反应蛋白和降钙素原升高，血红蛋白和白细胞减少；腹部 CT 扫描显示：上腹部有一个巨大的肿块。结合临床和影像学检查结果，对该患者的初步诊断为淋巴瘤。随后进行了颈部淋巴结活检，结果显示淋巴结组织大面积坏死，周围有大量泡沫细胞反应，细胞质中含有大量酵母样细胞，提示存在真菌感染。最终，通过对腹膜后淋巴结组织进行下一代测序技术（Next Generation Sequencing,NGS）分析，结果显示 TM 是主要病原体，序列数为 39182 个，相对丰度最高，为 96.42%，确定诊断为 TM 感染。血液和组织培养分别在 11 天和 5 天后培养出 TM，进一步证实了 TM 感染的诊断。

结果 在颈部淋巴结活检确诊为真菌感染后，患者开始接受两性霉素 B 治疗。当 NGS 确认了 TM 的诊断后，继续进行当前的治疗。经过一个月的治疗，该患者的临床症状减轻，腹部肿块显著缩小，病情得到稳定控制，患者已出院。

结论 在临床实践中，应当考虑潜在的真菌感染，对于非典型真菌感染的情况，NGS 相比传统的活检或培养诊断方法更为迅速，能够快速确定诊断并开始治疗，这对于免疫功能低下的患者尤为重要。

初始抗真菌治疗策略对重症侵袭性肺曲霉菌病患者的临床预后影响：一项单中心、回顾性研究

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目的 探究不同初始抗真菌治疗策略对重症 IPA 患者的临床预后影响。

方法 在本项回顾性队列研究中，我们纳入入住重症医学科时间为 2018 年 1 月 1 日至 2022 年 12 月 31 日的临床诊断或确诊 IPA 患者，根据初始治疗启动依据情况分为经验性治疗组、抢先治疗组，以及根据初始用药情况分为伏立康唑组、卡泊芬净组。我们比较两组患者的临床资料和治疗预后，并以院内死亡率作为主要结局指标。本研究采取单因素 / 多因素 logistic 回归分析方法校正混杂因素。本研究 IPA 的诊断标准以 2021 年 EORTC/MSGERC 侵袭性真菌感染定义标准作为参考。

结果 我们共检索出 362 例 IPA 患者。经过筛选后，根据初始治疗启动依据情况，共 159 例患者被纳入分析，其中经验性治疗组 82 例、抢先治疗组 77 例；根据初始用药情况，共 136 例患者被纳入分析，其中伏立康唑组 70 例，卡泊芬净组 66 例。

经验性治疗组患者的院内死亡率为 23.2%，抢先治疗组患者的院内死亡率为 19.5%，两组差异无统计学意义（$p > 0.05$）。经验性治疗组患者的中位 ICU 住院时间、中位住院时间分别为 14.5 天、22.5 天，抢先治疗组患者的中位 ICU 住院时间、中位住院时间分别为 19.0 天、33.0 天，两组差异亦无统计学意义（$p > 0.05$；$p > 0.05$）。

伏立康唑组患者的院内死亡率为 21.4%，卡泊芬净组患者的院内死亡率为 18.2%，两组差异无统计学意义（$p > 0.05$）。伏立康唑组患者的中位 ICU 住院时间、中位住院时间分别为 16.0 天、27.5 天，卡泊芬净组患者的中位 ICU 住院时间、中位住院时间分别为 15.0 天、27.0 天，两组差异亦无统计学意义（$p > 0.05$；$p > 0.05$）。

结论 对于重症 IPA 患者，相比于抢先治疗，经验性治疗不降低患者的院内死亡率；对于初始抗真菌治疗，采用伏立康唑或卡泊芬净的患者的院内死亡率无显著差异。

伏立康唑分散片致骨髓抑制不良反应分析

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目的 伏立康唑引起骨髓抑制少见报道，本文对伏立康唑分散片致骨髓抑制不良反应进行分析，旨在临床抗真菌应用时引起重视。

方法 分析患者用药过程，并查阅相关文献报道，进行伏立康唑分散片致骨髓抑制的原因分析。

结果 患者减量应用后未见发生骨髓抑制相关不良反应。

结论 伏立康唑的不良反应与其血药浓度有明显相关性。可以通过对患者的血药浓度进行监测，必要时开展基因分析，将其血药浓度控制在安全范围内，既能保证临床疗效又可以降低不良反应的发生率。

Successful management of chronic pulmonary mucormycosis with multi-facet diagnosis and non-surgical therapy: a case series

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Abstract Content Pulmonary mucormycosis is considered challenging to diagnose and treat. Here we presented a case series of successful management of chronic pulmonary mucormycosis with multi-facet diagnosis and non-surgical therapy.

Methods 15 cases diagnosed with pulmonary mucormycosis with follow-up were enrolled. All the patients took pulmonary computed tomography on admission in order to assess the radiological features of the lesions.All the patients underwent either pulmonary needle biopsy (PNB) or bronchoscopy or both, in order to achieve diagnostic evidences.

Results The average age was 54.1±15.3 years. 86.7% of the patients (13/15) were immune compromised. Patients were admitted with illness course for a median of 8 weeks. Radiological imaging suggested that mass or consolidation was the most common finding observed in this series (14/14, 100%). Patients underwent either pulmonary needle biopsy or bronchoscopy to achieve diagnostic evidence. Histopathological findings indicated fungal infection in 12 cases (80%, 12/15). Culture of lung tissue or BALF show positive results in only two cases, leading to an overall positivity rate of 20% (2/10). Microbiological next generation sequencing (mNGS) showed positive results in all nine cases that took the test (100%, 14/14). Two patient died, after six months' treatment due to multi-organ failure and during in-hospital treatment due to hemoptysis. Patients were treated with a median course of six months. Ten patients claimed a significantly relieved symptom or improved radiological manifestation. None of the patients underwent surgical debridement.

Conclusion This report presented the clinical characteristics and successful management of a series of chronic pulmonary mucormycosis, utilizing a workflow including diagnostic procedures (PNB and bronchoscopy), multi-facet diagnostic tools (culture, histomorphology and mNGS), and non-surgical medical treatment.

重度肝硬化患者合并侵袭性肺曲霉菌病的临床特征和短期预后

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目的 研究重度肝硬化合并侵袭性肺曲霉菌病 (IPA) 患者的临床特征和短期预后的危险因素。

方法 本研究采用随机抽样的方法连续性收集 2011 年 12 月 1 日至 2022 年 12 月 1 日，因肝硬化就诊于首都医科大学附属北京佑安医院的患者。随访患者诊断为 IPA 后 28d 的结局，记录为死亡或存活。比较死亡组和存活组患者的临床特征、治疗和预后，采用 Kaplan-Meier 生存曲线评估使用伏立康唑和非使用伏立康唑治疗的患者预后，采用 Cox 回归分析患者的预后危险因素。

结果 本研究共纳入 74 例重度肝硬化合并 IPA 的患者，随访 28d，死亡 36 例，病死率为 48.6% (36/74)。死亡组患者的年龄 (57.4 ± 11.7) 岁大于存活组 (49.4 ± 14.7) 岁，差异有统计学意义 (t=2.58,P<0.05)。2 组患者的性别、吸烟、重度肝硬化的病因、临床表现、合并症、影像学表现，差异均无统计学意义 (均 P>0.05)。死亡组患者的白细胞计数、降钙素原、血肌酐和国际标准化比值，呼吸衰竭的比例，住院期间接受侵入性操作≥ 5 次的比例，以及因病情加重入住重症监护室的比例，均高于存活组患者 (均 P< 0.05)。Kaplan-Meier 生存分析提示，与使用非伏立康唑治疗 IPA 的重度肝硬化患者相比，使用伏立康唑者 28d 病死率更低 [40.0% (20/50) 比 66.7% (16/24)，χ^2 =4.54，P=0.033]。Cox 多因素回归分析显示 PCT ≥ 0.5 μg/L (RR:3.743，95%CI:1.435~9.763，P<0.05) 和呼吸衰竭 (RR:2.586，95%CI:1.291~5.177，P<0.05) 是重度肝硬化合并 IPA 患者短期预后的独立危险因素。

结论 重度肝硬化合并 IPA 患者的短期病死率高。PCT ≥ 0.5 μg/L 和呼吸衰竭是这类患者短期预后的独立危险因素。使用伏立康唑治疗重度肝硬化患者的 IPA，病死率相对较低。

真菌感染与肿瘤免疫治疗之纽：基于 C 型凝集素受体调控的抗真菌免疫预测黑色素瘤免疫治疗效果

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目的 皮肤富含微生物群落。然而，微生物群落是否参与黑色素瘤的发生发展以及这一感染过程如何影响免疫检查点抑制剂（ICB）的疗效仍然不明确。本研究旨在探索黑色素瘤中的真菌模式识别受体 C 型凝集素受体（CLRs）的表达模式，及其与黑色素瘤患者 ICB 疗效之间的相关性。

方法 我们获取了黑色素瘤单细胞转录组谱面的原始数据，提取了顶级可变基因进行主成分分析 (PCA)。保留了顶级主成分进行 UMAP 可视化和聚类。进一步使用 Seurat R 软件包中实施的 FindClusters 函数进行了细胞聚类。随后，分析了肿瘤微环境中浸润细胞中 CLR 的表达以及不同细胞类型之间的差别。为了分析 CLRs 的表达模式与黑色素瘤患者的 ICB 疗效之间的关联，获取了基因表达数据集 GSE100797、GSE106128、GSE78200、GSE91061、GSE93157 和 PRJEB23709。还使用 KM 生存分析和 log-rank 检验来比较 CLR 高表达组和 CLR 低表达组黑色素瘤患者的生存差异。此外，还使用 Wilcoxon 检验方法比较了 ICB 应答者和非应答者之间的 CLR 表达差异。

结果 我们发现 CLR 主要在单核细胞 / 巨噬细胞群中一致地表达，其中 Dectin-1 表达突出。在反应患者中，单核细胞 / 巨噬细胞群上 CLR 的整体表达水平比非反应者患者高。此外，我们发现 CLR 更多与巨噬细胞和 CD8+ T 细胞有关，这表明 CLR 可能参与了黑色素瘤的先天免疫和适应性免疫过程。基于多个临床试验结果，我们发现接受 ICB 免疫治疗的反应者患者的 CLR 表达水平明显高于非反应者患者。CLR 高表达的黑色素瘤患者的整体生存期明显长于 CLR 低表达的黑色素瘤患者。

结论 黑色素瘤肿瘤微环境中 CLR 的高表达代表着更高的有效 ICB 治疗反应可能性和更好的预后。CLRs 主要表达在单核细胞 / 巨噬细胞上，可能主要通过调节天然免疫增强黑色素瘤中 ICB 效果。

Research trends and hotspots of invasive pulmonary aspergillosis: bibliometric and visual analysis

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Abstract Content Background Invasive pulmonary aspergillosis (IPA) predominantly occurs in patients with severely and persistently reduced neutrophil counts, malignant hematological diseases, and those who have undergone solid organ transplants, all conditions associated with compromised immune function. Although previous studies have investigated the pathophysiology, epidemiology, and risk factors of IPA, research trends and hotspots on this topic remain relatively unexplored. The aim of this study is to develop a visual knowledge map based on bibliometric analysis to identify research hotspots and predict future trends.

Methods A search was conducted in the Web of Science Core Collection (WOSCC) for materials published from January 1, 2000, to March 31, 2024. Tools such as CiteSpace and VOSviewer were utilized to evaluate annual publications, countries, institutions, journals, authors, references, and key areas to delineate current research hotspots and future research directions.

Results A total of 4,058 articles were included in this study, representing contributions from 3,409 institutions across 749 journals and 214 countries or regions. The United States published the most articles (1,321) and was the most influential country on this topic. The journal "Medical Mycology" published the most articles (206) while "Clinical Infectious Diseases" was the most cited journal (27,450 citations). The most frequently cited literature focused on expert consensus and clinical guidelines for IPA. The dominant keywords in this field primarily revolved around the diagnosis and treatment of IPA.

Conclusion By applying bibliometric methods to review research in the field of IPA, this study not only identifies key authors, countries, institutions, and journals in terms of collaboration and influence but also aims to enhance the understanding of popular areas within IPA research. It comprehensively reviews the trends in IPA studies and provides insights into potential collaborative researchers, institutions, and prospects for future research.

基于 LASSO 回归的心脏外科术后侵袭性真菌病患者短期死亡风险预测模型的建立与验证

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目的 构建心脏外科术后侵袭性真菌病患者短期死亡风险的预测模型并验证其效能。

方法 回顾性分析了 2020 年 1 月至 2023 年 12 月期间山东大学齐鲁医院心脏外科 ICU 术后诊断侵袭性真菌病患者的病历数据，共纳入 98 例，根据术后生存情况分为生存组 56 例、死亡组 42 例。获取患者一般资料及术后相关指标，采用 LASSO 回归筛选出变量后将其纳入多因素 logistic 回归分析出独立危险因素，建立列线图预测模型，并绘制列线图的 ROC、DCA、CIC 曲线评估模型的预测能力。

结果 经 LASSO logistic 回归分析，吸烟史、SOFA 评分、APACHE Ⅱ 评分、平均动脉压、快速型心律失常是预测心脏外科术后侵袭性真菌病患者短期死亡的独立危险因素（$P<0.05$）。预测模型的 AUC 为 0.886 (95% CI 0.871 ~ 0.955)。校准曲线的平均绝对误差为 0.029。DCA 分析显示阈概率范围为 0 ~ 0.85 时患者的净获益率较高。CIC 显示本预测模型判断的死亡风险与实际情况匹配程度高。

结论 吸烟、SOFA 评分、APACHE Ⅱ 评分、MAP < 70mmHg、快速型心律失常是心脏外科术后侵袭性真菌病患者短期死亡的独立危险因素，基于 LASSO logistic 回归建立的预测模型准确性较高。

1 例由迟缓曲霉感染引起的心脏瓣膜置换术后并发侵袭性肺曲霉病

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目的 侵袭性肺曲霉病 (IPA) 是一类严重的感染类型，以往较常见于免疫抑制状态的患者，但近年由于广谱抗生素和激素的广泛应用，IPA 的发病率也在逐渐上升。由于 IPA 的症状不典型且往往合并其他感染，因此难以早期诊断，从而导致较差的预后。迟缓曲霉 (Aspergillus lentulus) 于近年来首次被发现，最初被误认为是烟曲霉，但分子生物学证据显示这是一种罕见的新物种。以往的案例表明迟缓曲霉引起的 IPA 会导致更高的死亡率，因为它对多种常见的抗真菌药物表现出耐药性。我们报道了一例经体外循环通过直视下心脏瓣膜置换手术治疗先天性部分型心内膜垫缺损，术后并发迟缓曲霉肺部感染的病例。

方法 患者病情危重，术后接受了高级别生命支持治疗及抗感染治疗。起初患者生命体征逐渐平稳，但在术后第 11 天患者突发快速进展的呼吸衰竭，影像学显示双侧肺叶大片渗出影。对该患者进行了肺泡灌洗液的 NGS 检验，结果显示这是一例迟缓曲霉感染导致的 IPA，真菌培养结果随后证实了该诊断。

结果 在接受了伏立康唑联合米卡芬净的抗真菌治疗后，患者肺部症状得到显著改善，最终脱机康复成功。

结论 据我们所知，这是首次报道在非心脏移植的心外术后患者身上发现的，由迟缓曲霉导致的 IPA。

经验性抗真菌治疗对非粒缺 ICU 患者病死率的影响：一项倾向性评分匹配的回顾性队列研究

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目的 评估经验性抗真菌治疗（empirical antifungal treatment, EAFT）对未确诊侵袭性真菌感染的 ICU 患者病死率的影响。

方法 本研究是一项单中心、倾向性评分匹配的回顾性队列研究，选择存在临床感染且具有侵袭性念珠菌病（invasive candidiasis, IC）危险因素、但未确诊侵袭性真菌感染的非移植及非粒缺 ICU 患者。暴露组为接受抗真菌治疗的患者（即 EAFT 组），对照组为没有接受抗真菌治疗的 ICU 患者。主要研究终点为住院全因病死率。次要研究终点为住院感染归因病死率及出院时感染好转等。

结果 在 640 名入组的 ICU 患者中，经倾向性评分匹配后，177 名接受 EAFT 的患者和 177 名对照患者被纳入分析。与对照组相比，EAFT 并不降低 ICU 患者住院全因病死率（OR，0.911；95%CI，0.541- 1.531；P=0.724）及住院感染归因病死率的风险（OR，1. 149；95% CI，0.632-2.092；P=0.648）。EAFT 对出院时感染的改善、机械通气的持续时间和不使用抗生素的天数没有益处。然而，在疑似 IC 的这部分患者中，EAFT 启动的时机越晚，患者的住院全因病死率（OR，1.039；95%CI，1.003- 1.076； P=0.034）和住院感染归因病死率（OR，1.046；95% CI，1.009- 1.085；P = 0.015）增加的风险越高。同样地，在疑似 IC 的脓毒症患者也发现了这种效应（OR，1.042；95%CI，1.005- 1.081；P=0.027）。

结论 EAFT 不能降低非粒缺非移植且 IC 风险 ICU 患者的住院病死率。EAFT 的启动时机对于改善疑似 IC 患者的预后可能至关重要。

耶氏肺孢子菌感染与定植的临床特征分析

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目的 总结通过下一代测序 (NGS) 检测到耶氏肺孢子菌 DNA 患者感染与定植的情况，并对其进行临床特征分析，为 PJP 精确治疗与预防提供临床经验

方法 回顾性收集接受 mNGS 检查，并检测到耶氏肺孢子菌 DNA 的患者。根据标准，分为感染组和定植组。连续变量资料组间比较使用 t 检验或秩和检验，分类变量资料组间比较使用卡方检验或 Fisher 确切检验。最后行 logistic 回归分析。

结果 在 7 个月间期间收集到符合标准并经筛选的患者，共纳入 117 人，根据 EORTC/MAGERC 指南， 81 名 (69.2%) 为感染，36 名 (30.8%) 为定植。耶氏肺孢子菌感染与慢性肾功能不全（24.7% vs 8.3%，P= 0.04）、使用麦考酚酯（18.5% vs 2.8%，P =0.046）、磨玻璃表现（38.3% vs 19.4%，p=0.045）以及更高的数量的耶氏肺孢子菌相关序列数和相对丰度（两者 P 均 < 0.001) 有关。相比之下，耶氏肺孢子菌定植与 COPD（2.5% vs 13.9%，P=0.048）、胸腔积液（19.8% vs 55.6%，P<0.001）、1 年内放射治疗（0% vs 11.1%，P=0.012）密切相关。

结论 mNGS 方法检测耶氏肺孢子菌感染有重要作用，但仍需结合临床、影像学表现及实验室指标等综合分析。

曲霉 PCR、宏基因组测序及半乳甘露聚糖对血液病患者 侵袭性肺曲霉病的诊断性能研究

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目的 本研究旨在探讨不同的微生物学技术在血液病患者侵袭性肺曲霉菌病（IPA）诊断中的价值，包括抗原检测 [G 试验、半乳甘露聚糖（GM）]、曲霉抗体（IgG）检测、曲霉 PCR、宏基因组二代测序（mNGS）

方法 回顾性纳入 186 例 IPA 患者（IPA 组：确诊 1 例、临床诊断 75 例、拟诊 110 例）以及 410 名非 IPA 患者（对照组）。分析血液样本及呼吸道样本不同检测方法的敏感性、特异性、阳性预测值、阴性预测值以及不同条件下最佳检测联合方式。

结果 不同方法的检测灵敏度从高到低为：呼吸道样本曲霉 PCR(81.5%)、呼吸道样本 GM(70.4%)、呼吸道样本 mNGS(63.2%)、血液 mNGS(57.0%)、血液曲霉 PCR(51.6%)、血液 GM(44.5%)、曲霉抗体 IgG(22.6%) 和 BDG 检测 (10.4%)。对于粒缺患者，mNGS 在血液样本中灵敏度高于非粒缺患者（75.8% vs. 26.8%, $p<0.001$）。而对于呼吸道样本及血液其他检测方法粒缺与非粒缺患者并无灵敏度差异。对于粒缺患者，如只能获得血液样本，以 mNGS 为基础的联合检测灵敏度可达 80%，特异度可达 90%；而对于非粒缺患者，以 PCR 为基础的联合检测更为适宜（灵敏度 57%，特异度可达 90%）；对于呼吸道样本，粒缺与非粒缺患者均以曲霉 PCR 为基础的联合检测灵敏度更佳（灵敏度 80%-100%）。此外，唑类抗真菌药物暴露≥ 7 天降低血液 GM、曲霉 -PCR 和 mNGS 的敏感性，但对于呼吸道样本无显著差异。

结论 曲霉 PCR、GM 和 mNGS 检测在血液病患者 IPA 诊断中表现出良好的诊断性能。呼吸道样本应首选曲霉 PCR 和 GM 检测，而血液 mNGS 检测在粒缺患者中更为适用。联合检测方法可以提高 IPA 诊断效率。

尖端赛多孢菌椎体感染 1 例

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目的 报道尖端赛多孢菌椎体感染 1 例，并探讨其诊治过程，为临床少见菌感染诊治提供思路。

方法 患者男性，74 岁，主要表现为“新冠肺炎”后腰痛 8 个月，间断发热 6 个月。患者于 2023 年 11 月 15 日第一次入院时影像学检查示胸 10- 腰 1 椎体感染性病变，结核可能，化验结核干扰素释放试验阳性，PPD 阳性，ESR、CRP 升高，经四联抗结核治疗无好转，行椎体活检术，NGS 及培养均未找到病原体，抗酸染色阴性，病理示慢性炎症，先后给与哌拉西林他唑巴坦、万古霉素经验性抗感染治疗效果欠佳。患者病情持续进展，于 2024 年 2 月 19 日再次入院，复查核磁示胸 9- 腰 4 椎体、多发椎间盘及椎旁软组织改变，考虑感染性病变，由骨肿瘤科再次行椎体活检术，抽出脓液及破碎骨组织，NGS 示尖端赛多孢菌，病理示急性炎症伴坏死，并见少许肉芽组织增生，PAS 染色 (局灶 +), 六胺银 (-)，同时化验 G 试验阳性，GM 试验阴性。诊断“尖端赛多孢子菌椎体感染”，给与伏立康唑联合两性霉素 B 抗真菌治疗，同时给与胸腺法新调节免疫治疗。

结果 经伏立康唑联合两性霉素 B 抗真菌治疗，患者体温逐渐下降，腰痛逐渐减轻，复查炎症指标下降，影像学检查好转。

结论 尖端赛多孢菌感染常见于免疫功能缺陷者，或有外伤、溺水、侵入性操作后患者，肺部感染多见，骨关节感染少见。本例患者高龄，免疫功能低下，出现椎体感染，经两次椎体活检术明确诊断为尖端赛多孢子菌感染，经抗真菌治疗有效。临床工作中应重视感染患者的病原体检测，针对性的进行抗感染治疗，同时预防抗生素的不良反应。

基于动态表面增强拉曼光谱法的代谢轮廓分析用于克服白念珠菌耐药性

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目的 随着抗真菌药物耐药性的上升，现有的药敏试验方法以及抗真菌药物难以满足临床诊疗真菌的迫切需求。因此，本研究旨在开发一种新的代谢轮廓分析方法，以简单、快速、精准、动态地实现对耐药真菌的早期诊断以及发现新的临床治疗方案。

方法 本研究利用动态表面增强拉曼光谱法(Dynamic surface-enhanced Raman spectroscopy, D-SERS)检测氟康唑耐药和敏感白念珠菌表型(经金标准验证过的)，并基于这些表型的光谱特征，结合有监督学习(Supervised learning, SL)算法建立可视化的分类模型并预测未知表型。同时，利用二维相关分析(Two-dimensional correlation analysis, 2DCOS)对筛选的耐药/敏感白念珠菌表型差异代谢物进行时序分析，动态地探测白念珠菌在耐药过程中产生的代谢行为变化。

结果 经D-SERS和SL处理后，氟康唑耐药表型和敏感表型的代谢轮廓呈现出明显的区分(准确率>95%)。进行未知白念表型的预测时样本处理时间仅约20 min，从而大幅缩短获取检测报告的时间。同时，有监督学习算法筛选出耐药和敏感白念珠菌表型的差异代谢物分别为次黄嘌呤以及麦角固醇(真菌耐药标志物)。结合2DCOS分析，发现随着白念珠菌耐药水平的提高，次黄嘌呤要先于麦角固醇产生变化，即真菌受到氟康唑的胁迫后产生的代谢重编程可能导致了真菌耐药。

结论 本研究提出的代谢轮廓分析不仅能够快速预测耐药真菌表型从而及时应对临床抗真菌治疗，同时提出了一种潜在的抗真菌药物耐药机理以发现合适的小分子佐剂协同抗真菌药物来减缓真菌耐药性的进程。

一例播散性毛霉菌病合并肺马尔尼菲篮状菌的诊治

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目的 通过一例播散性毛霉菌病合并肺马尔尼菲青霉病的诊疗观察，探讨播散性毛霉菌病的诊治方法及肺马尔尼菲青霉病的病理特点及治疗方法。

方法 57 岁男性患者，既往二型糖尿病，血糖控制不佳。因“发热、咳痰 17 天，呼吸困难 7 天”到我院就诊，BAL 高通量测序：米根霉 序列数 408 、热带念珠菌 序列数 7648 ； 人冠状病毒 O C 43 序列数 38340 ，人偏肺病毒 序列数 28444 。入院后给与心包穿刺引流，多重 PCR：米根霉 5555，诊断为重症播散性毛霉菌病，ARDS，假性肠梗阻，二型糖尿病。肺部 CT 提示右肺中叶实变，右肺上叶及下叶渗出性病变。气管镜检查发现右上叶及右下叶大量白色脓性分泌物，右中叶管口黏膜充血水肿狭窄，镜身不能通过。抗真菌治疗给与两性霉素 B 脂质体 300mg/ 天，联合艾沙康唑针剂。6 天后复查肺部 CT 发现右肺中叶及下叶实变，右肺上叶部分实变。继续抗真菌治疗并在右肺各叶段两性霉素 B20mg/ 天灌洗治疗。联合抗真菌治疗 1 月余，复查肺部 CT 右肺下叶及上叶实变吸收，右肺中叶实变形成周边厚壁。继续艾沙康唑针剂抗真菌治疗。住院治疗 2 个月后口服艾沙康唑片剂回家。2024 年 1 月复查肺部 CT 右肺中叶厚壁实变无好转，1 月 29 日手术切除右肺中叶，术后病理提示间质纤维组织增生伴多量慢性炎细胞，部分肺泡腔内见出血，倾向马尔尼菲篮状菌。术后继续口服艾沙康唑，4 月 18 日复查肺部 CT 右肺中叶切除术区团片状阴影明显缩小。

结果 免疫功能低下患者，特别是糖尿病患者呼吸道病毒感染后容易合并真菌感染，特别是混合真菌感染。早期明确病原学对真菌的治疗具有重要意义。

结论 重症播散性毛霉感染，两性霉素 B 脂质体联合治疗方案可早期控制症状。药物治疗对于厚壁病变效果差，病变局限后手术治疗具有重要意义。非 HIV 阳性患者肺部马尔尼菲篮状菌病理学特点与毛霉菌病不同。病原学的完善对于患者预后具有重要意义。

成人灰色小克银汉霉侵袭性毛霉菌病 1 例

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目的 探讨灰色小克银汉霉感染导致成人毛霉菌病患者的临床特点及诊治方案。

方法 总结某院重症医学科收治的 1 例灰色小克银汉霉感染致成人侵袭性毛霉菌病患者的临床诊疗过程，并结合相关文献进行复习。

结果 患者以急性发热、黄疸为主要表现的灰小克银汉霉感染的患者，排除肿瘤、病毒性肝炎等疾病后，经经验性抗细菌治疗无效，传统方法未检测到病原体，考虑感染性所引起的发热及急性肝衰竭，遂行外周血宏基因组学二代测序检测，检测出灰小克银汉霉，给予两性霉素 B 胆固醇硫酸脂复合物小剂量爬坡方案 + 艾莎康唑联合抗真菌治疗后患者病情仍进展至死亡。

结论 灰色小克银汉霉感染所致成人毛霉菌病发病率低但病死率高，临床表现缺乏特异性，病原学诊断十分重要，mNGS 作为一种分子生物学技术，为临床诊治提供新的思路。

mNGS Combined with Traditional Microbiology Identifies the First Case of Candida auris in Southwest China

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Abstract Content Introduction The emergence of Candida auris, a multidrug-resistant yeast, poses a significant threat to global health. This study aimed to identify and characterize the first case of C. auris in Southwest China using metagenomic next-generation sequencing (mNGS) combined with traditional microbiological methods, and to investigate its molecular epidemiology, antifungal susceptibility, and clinical implications.

Methods Clinical data were collected from a hospitalized 81-year-old female patient with multiple comorbidities who presented with dyspnea and fever. Respiratory tract specimens were subjected to mNGS and traditional microbiological culturing. The mNGS workflow included sample processing, DNA extraction, library construction, sequencing, and data analysis. Antifungal susceptibility testing was performed, and whole-genome sequencing was conducted to analyze the molecular characteristics of the isolate.

Results The patient's sputum mNGS test revealed C. auris, which was subsequently confirmed by culture and MALDI-TOF identification. The isolate, SCHX0001, was resistant to fluconazole (MIC 32 mg/L) and amphotericin B (MIC 2 mg/L), belonged to the South Asian clade (clade I), and harbored resistance genes ERG11 and CDR1. The patient's clinical course was complicated by the infection, and despite treatment with caspofungin, the patient eventually succumbed to her underlying conditions.

Conclusion This study reports the first case of C. auris in Southwest China, highlighting the utility of mNGS for rapid and accurate identification of emerging pathogens. The findings underscore the importance of enhanced surveillance, infection control measures, and the development of new antifungal strategies to combat the spread of this emerging pathogen.

The Diagnostic Value of Metagenomic Next-Generation Sequencing for Mucormycosis and the Risk Factors of Poor Prognosis in Mucormycosis

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Abstract Content Introduction Mucormycosis currently lacks highly specific and sensitive detection methods. Metagenomic next-generation sequencing (mNGS), as an emerging technology, provides new possibilities for the diagnosis of mucormycosis. This study aims to systematically summarize the clinical characteristics of mucormycosis and factors related to poor prognosis in the southwestern region of China, and to evaluate the value of mNGS in the diagnosis of mucormycosis.

Methods The study used a retrospective case analysis method, collecting 67 cases from patients who visited West China Hospital of Sichuan University from November 1, 2022, to October 31, 2023, and tested positive for mucormycosis through mNGS, of which 46 cases were ultimately diagnosed with mucormycosis (16 confirmed and 30 clinically diagnosed). The performance efficacy of mNGS, measured by Ig(RPKM), was assessed using the ROC curve, and the reads were utilized to predict the diagnostic value of mucormycosis.

Results The study found that mucormycosis mainly occurs in patients with underlying diseases or impaired immune function, with the most common being diabetics, organ transplant recipients, and patients with hematological malignancies. Typical clinical symptoms include fever, cough, sputum production, dyspnea, and headache. Imaging presentations are primarily characterized by nodules, consolidation, and patchy masses, often accompanied by pleural effusion. In laboratory tests, elevated levels of procalcitonin, C-reactive protein, and interleukin-6, along with decreased lymphocyte count, hemoglobin, platelets, albumin, CD3+T-lymphocyte, CD4+T-lymphocyte, and CD8+T-lymphocyte, suggest a poor prognosis. Additionally, mucormycosis patients with fatigue symptoms, impaired immune function, imaging findings combined with pleural effusion, and concurrent COVID-19 infection have a poor prognosis. The ROC curve shows that the area under the AUC for predicting mucormycosis by mNGS reads lg(RPKM) is 0.862, and the cutoff for lg(RPKM) calculated by the Youden index is greater than 8 reads.

Conclusion Mucormycosis is more common in patients with diabetes or impaired immune function, and the clinical manifestations are non-specific. When patients with mucormycosis exhibit fatigue

symptoms, elevated inflammatory indicators, reduced lymphocyte subset counts, concurrent COVID-19 infection, impaired immune function, and pleural effusion on imaging, these may be associated with a poor prognosis. mNGS is a rapid and highly sensitive diagnostic tool, offering significant advantages in the diagnosis of mucormycosis.

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。

淮安地区公立医疗机构真菌感染检测能力调查

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目的 近年来，我国真菌感染病例不断增加，对真菌感染特别是侵袭性真菌感染的快速、准确诊断的需求日益增长。然而，目前有关医疗机构真菌感染检测能力的文章鲜有报道。

方法 于 2023 年 12 月进行在线调查，收集淮安地区医疗机构的实验室结构、人力、设备和诊断测试方法等真菌检测相关信息。采用已有的评分系统来评估整体诊断能力，并对 21 家二级甲等及三级医院的调查结果进行了分析。

结果 21 家医疗机构中，95.2% 的实验室至少配备了 1 名能独立从事真菌检测工作的员工，52.4% 的实验室有专门的真菌检测相关设备，但 80.9% 被调查的医院没有单独的真菌实验室空间。革兰染色和墨汁染色方法被广泛使用（>70%），而六胺银染色在本地区仅有 1 家实验室使用。在 17 家进行真菌鉴定的实验室中，94.1% 的机构采用全自动微生物鉴定及药敏系统，有 50% 的三级甲等医院采用 MALDI-TOFMS 进行菌种鉴定。57.1% 的实验室开展了 G 试验等真菌血清学检测项目，但是本研究纳入的医疗机构均未开展念珠菌抗原和抗体检测。66.7% 的受访医院采用全自动微生物鉴定及药敏系统进行酵母菌的体外抗真菌药物敏感性试验，暂未开展丝状真菌的药物敏感性试验。21 家医疗机构中参与室间质量评价的实验室比例为 42.9%。被调查的 11 家三级医院的平均得分为 33 ± 11.2 分，而在 6 家三级甲等医院中有 33.3% 的实验室得分 > 50 分，仅 1 家三级甲等综合医院开展了真菌相关科学研究。

结论 江苏省淮安市地区医疗机构总体上对真菌感染的临床检测能力不足。需要在薄弱的方面进行更多的关注和培训，以此促进获得高质量的诊断服务。

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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目的 黑曲霉复合群是多个种属的黑曲霉构成的复杂种群，由于无法通过外观鉴定到种，所以被称为复合群。黑曲霉复合群包含至少 27 个种，除了黑曲霉外，该复合群包含其他与人类和动植物感染有关的种包括巴西曲霉、图宾根曲霉、百岁兰曲霉等，不同的种对抗真菌药物的敏感性有所不同。黑曲霉复合群中以黑曲霉最常见，但关于图宾根曲霉对人体的病理（临床）意义及抗真菌药物活性尚不明确。因此，分析 23 株呼吸道标本中分离到图宾根曲霉患者的临床特征及分离株在体外对抗真菌药物的敏感性。

方法 对 2019 年 7 月至 2023 年 6 月呼吸道标本分离到的黑曲霉菌株进行分子鉴定，回顾性收集图宾根曲霉分离患者的临床特征。采用 Yeast OneTM 肉汤微量稀释法，测定伊曲康唑、伏立康唑、泊沙康唑、艾沙康唑、两性霉素 B 对黑曲霉复合群的 MIC。

结果 45 株黑曲霉复合群中包括图宾根曲霉 23 株、黑曲霉 19 株、泡盛曲霉 2 株及百岁兰曲霉 1 株。23 株图宾根曲霉中 1 株分离自 BALF，其余均分离自痰标本。23 例患者中，男性 16 例，患者的平均年龄为 63.9±7.4 岁。所在的科室依次为：重症监护室（7 例）、呼吸科（6 例）、感染科（5 例）、急诊科（1 例）、肾内科（1 例）、全科（1 例）。12 例患者有不同程度的呼吸道疾病：4 例患有 CPA（2 例合并非 NTM），1 例患有 ABPA，3 例患有支气管哮喘，3 例患有 COPD，4 例患有肺恶性肿瘤。其余 10 患者患有系统性疾病：4 例患有恶性肿瘤（3 例肝脏、1 例弥漫大 B 细胞淋巴瘤）；2 例类风关、1 例肾移植术后，均长期服用激素及免疫抑制剂治疗；4 例患有糖尿病。5 例患者在分离出图宾根曲霉时合并 COVID-19 感染。45 株黑曲霉复合群中有 7 株对伏立康唑耐药，均为图宾根曲霉，其对艾沙康唑的药物敏感性与伏立康唑相一致。

结论 图宾根曲霉是呼吸道分离出的黑曲霉复合群中最常见的亚种，大部分患者合并有肺部基础疾病。与黑曲霉相比，图宾根曲霉对伏立康唑的耐药性较高。

耳念珠菌持续血流感染及血管移植物感染一例

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目的 报告一例特殊的非创伤性脾破裂后耳念珠菌持续性血流感染且伴有血管移植物感染的病例，丰富对耳念珠菌感染临床表现及复杂性的认识。

方法 对该例 52 岁男性患者的病史（包括 A 型主动脉夹层手术史、非创伤性脾破裂及脾切除术等）进行详细描述。记录患者血培养及药敏的结果以及抗真菌治疗的过程和反应。对相关检查（如心脏超声）结果进行呈现和分析。

结果 报道了一名 52 岁免疫功能正常、有 A 型主动脉夹层手术史的男性患者，在非创伤性脾破裂行脾切除术后出现耳念珠菌持续性血流感染。尽管应用了多种抗真菌药物治疗，患者仍发热且血培养持续检出耳念珠菌，相关药物的 MIC 升高。

心脏超声发现降主动脉支架有弱回声团块，提示该病例为首次报道的耳念珠菌血管移植物感染病例。

结论 该病例展示了耳念珠菌在非创伤性脾破裂患者中引发持续性血流感染的情况，且对多种抗真菌药物耐药，治疗效果不佳。首次发现耳念珠菌可能导致血管移植物感染，提示临床需重视这种新兴多药耐药真菌可能带来的特殊且复杂的感染表现。强调了耳念珠菌感染的严重性和复杂性，以及进一步研究其特性和治疗方法的必要性。

一例急性 B 淋巴细胞白血病 CART 治疗后播散性镰刀菌感染的诊治

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目的 总结一例 Ph 阳性急性 B 淋巴细胞白血病患者 CD19-CART 治疗后播散性镰刀菌感染的临床特点。

方法 总结分析 2024 年 1 月在解放军总医院第一医学中心血液科住院治疗的 1 例复发难治 Ph 阳性急性 B 淋巴细胞白血病患者，接受 CD19-CART 治疗后发生播散性镰刀菌感染的病例资料。

结果 患者男性，36 岁，2020-6-4 因 Ph 阳性急性淋巴细胞白血病行同胞全合异基因造血干细胞移植。移植后 1 年出现中枢神经系统白血病，予达沙替尼口服、鞘注化疗药物及全脑全脊髓放疗后达到完全缓解。2023 年 9 月患者出现疾病血液学复发，予减低剂量 VDCP+ 达沙替尼治疗未缓解。患者于我院接受供者来源的 CD19-CART 细胞治疗。2023-11-21 回输供者来源 CD19-CART 细胞 1×106/kg。回输第 2 天出现发热，体温 38.4℃，血常规示粒细胞缺乏，怀疑为 1 级 CRS 反应，予托珠单抗治疗后体温正常。回输后第 13 天 (2023.12.08) 患者四肢皮肤出现圆形或类圆形红色皮疹，不排除为药诊，给与氯雷他定口服。2023.12.10 四肢皮疹增多，伴有疼痛，皮肤科会诊考虑感染性皮疹，给与美罗培南、利奈唑胺、伏立康唑联合抗感染。患者皮疹疼痛逐渐加重，逐渐扩散至躯干部皮肤，部分皮疹出现中央破溃、结痂，GM 试验波动在 4.335-5.394。2023.12.11 外周血宏基因测序回报轮状镰刀菌，便培养结果回报增生镰刀菌，治疗方案调整为脂质体两性霉素 B 联合伏立康唑。023.12.15 后背皮疹破溃处拭子培养为镰刀菌阳性，2023.12.18 痰培养镰刀菌，继续脂质体两性霉素 B 联合伏立康唑治疗。患者持续粒细胞缺乏状态，皮疹逐渐扩散至四肢、躯干、面部皮肤，咳嗽加重伴咳痰，2023.12.30 患者出现呼吸功能衰竭，2023.12.31 患者因呼吸功能衰竭死亡。

结论 CART 治疗后出现发热、痛性皮疹需警惕播散性镰刀菌感染，死亡率高。



重症

头孢他啶阿维巴坦双组分在重症感染患者中的药代动力学

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目的 研究探讨酶抑制剂复合制剂的双组分是否在重症患者中均能达到有效的治疗目标。

方法 连续纳入 2022 年 7 月 -2023 年 11 月我院呼吸中心 MICU 使用头孢他啶阿维巴坦的成人患者，建立方法学，并使用 UPLC-MS/MS 方法同时测定头孢他啶和阿维巴坦的谷浓度。

结果 建立了使用 UPLC-MS/MS 同时测定头孢他啶和阿维巴坦的血药浓度方法并进行了方法学验证。能够同时、快速、使用微量血液标本对头孢他啶和阿维巴坦两药进行测定。本研究发现 27.78% 的患者阿维巴坦浓度小于 4mg/mL（EUCAST 推荐的阿维巴坦折点）；11.11% 的患者头孢他啶 / 阿维巴坦血药浓度比值小于 4，50% 的患者的头孢他啶 / 阿维巴坦血药浓度比值在 4-6 之间，38.89% 的患者头孢他啶 / 阿维巴坦血药浓度比值大于 6。

结论 本研究中 50% 的患者头孢他啶与阿维巴坦的比例不适宜，可能带来头孢他啶的毒性反应，同时由于阿维巴坦不足量而导致未能产生足够的酶抑制效果。因此对头孢他啶和阿维巴坦同时进行血药浓度监测，并根据患者情况实时进行剂量调整，是正确评估 PK/PD 目标实现与微生物学或临床结果之间关系的唯一有效方法。

血清 CA125 检测与心力衰竭疾病的相关性

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目的 分析血清 CA125（糖类抗原 125；Carbohydrate antigen 125）检测与心力衰竭疾病的相关性。

方法 选取 2023 年 1 月 -6 月送检至本单位的心力衰竭患者血清样本 120 例，作为实验组，按血清 NT-proBNP（氨基末端脑钠肽前体）水平将其分为 B（正常水平）、C（异常水平）两组，各组 60 例；随机选取与实验组相近年龄段健康体检者血清样本 60 例，作为对照 A 组，分别测定各组血清 NT-proBNP、CA125 水平；通过测定数据分析血清 CA125 水平与心力衰竭、NT-proBNP 水平的相关性。

结果 B、A 两组相比较，血清 NT-proBNP、CA125 水平差异无统计学意义（P>0.05）；C、A 两组相比，血清 CA125、NT-proBNP 水平差异有统计学意义（P<0.05）；C、B 两组相比，C 组血清 NT-proBNP、CA125 水平升高明显，且 C 组 CA125、NT-ProBNP 水平远高于 B 组，差异有统计学意义（P<0.05）。

结论 从本次样本数据分析，血清 CA125 水平与心力衰竭疾病有一定相关性。以 35U/mL 为界限，心力衰竭患者血清 CA125 水平会有不同程度的升高，且与其 NT-proBNP 水平有一定相关性。血清 NT-proBNP 水平正常心力衰竭患者 CA125 水平基本 <35U/mL。血清 NT-proBNP 水平异常心力衰竭患者 CA125 水平异常，且升高明显。血清 CA125 和血清 NT-proBNP 联合检测对心力衰竭的诊断分级、治疗效果以及预后风险预估有一定潜力及价值。

重症

血清 25- 羟基维生素 D 与成人脓毒症患者死亡风险的荟萃分析

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目的 维生素 D 在人体健康中具有重要作用，而其缺乏与脓毒症（Sepsis）的风险增加有关。然而，关于血清 25- 羟基维生素 D（25（OH）D）与 Sepsis 患者死亡风险之间关联的前瞻性研究结果存在不一致。本研究旨在通过系统评价和荟萃分析评估血清 25（OH）D 水平与 Sepsis 患者死亡风险的关系。

方法 本研究为系统评价和荟萃分析，通过 PubMed、Cochrane Library、EMBASE、中国知网、万方、维普数据库检索关于 Sepsis 患者血清 25（OH）D 与死亡风险关系的随访研究。使用随机效应模型合并分析结果。

结果 共有 10 项研究纳入荟萃分析，共有 2239 例患者。总体荟萃分析结果显示，血清 25(OH)D 水平较低的患者死亡风险增加（RR：1.68，$P < 0.001$；I^2=2%）。进一步的分析显示，维生素 D 不足和缺乏与死亡风险显著相关（RR 分别为 1.56 和 2.11，$P < 0.001$）。低血清 25（OH）D 与高死亡风险之间的关联在不同 Sepsis 诊断标准、不同国家以及在前瞻性和回顾性研究中均保持一致。

结论 本研究表明维生素 D 不足和缺乏可能与 Sepsis 患者的死亡风险增加独立相关。为了进一步验证我们的发现，需要大规模前瞻性研究进行验证。

糖尿病与脓毒症患者死亡风险的一项荟萃分析

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目的 糖尿病是一种可能增加患者感染并发症发生风险的严重医疗问题，甚至可能导致脓毒症，但其对脓毒症患者预后影响的研究结果存在争议。因此，我们进行本次荟萃分析，以探究糖尿病是否会恶化脓毒症患者的预后，增加该类患者死亡率。

方法 我们检索了自2008年至2023年的PubMed、Embase、Cochrane Library、中国知网、万方、维普数据库中的相关研究。我们选择的主要研究结果是28天、30天和住院期间的总体死亡率。我们采用严格的研究筛选、数据提取和评估偏倚的方法，对收集到的数据进行了分析。

结果 我们的荟萃分析包括了2008年至2023年间发表的12项研究，涉及糖尿病合并脓毒症患者和非糖尿病的脓毒症患者。就28天、30天死亡率（RR为0.99，95%CI为0.85至1.16）和住院期间死亡率（RR为1.14，95%CI为0.98至1.31）而言，糖尿病组和非糖尿病组的死亡率统计上无显著差异。并且进一步分析糖尿病与高死亡风险之间的关联在不同研究类型、不同国家、不同脓毒症诊断标准研究中均保持一致。

结论 尽管存在一定的局限性，荟萃分析结果显示，糖尿病对脓毒症患者的预后并无明显影响。这类发现仍需要更多设计良好的试验来进一步验证和明确。我们呼吁未来的研究在设计时考虑到各种可能的混杂因素和偏倚，以提高研究的准确性和可靠性。

维生素 D 水平在脓毒症患者中与营养状况和炎症反应之间的关系

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目的 脓毒症 (Sepsis) 存在营养不良、炎症反应和维生素 D（VD）缺乏的情况，而这些症状之间的关系尚不明确。VD 是免疫系统的调节剂，与 Sepsis 的发病有关。本研究旨在评估 VD 与营养状况、炎症反应之间的关系，并确定更准确的 VD 阈值。

方法 本研究纳入了 2021 年 10 月至 2022 年 10 月期间确诊的 97 名 Sepsis 患者和 95 名健康志愿者。进行了血清 25（OH）D 水平、营养指标、炎症指标以及其他生化评估。

结果 Sepsis 患者和健康参与者在其 25（OH）D 水平以及营养和炎症指标水平上存在显著差异。出现 Sepsis 的最佳 VD 临界值为 22.55nmol/L。25（OH）D 水平与营养状况和炎症均相关。

结论 VD 水平很可能是评估 Sepsis 患者病情进展的一个有用的额外工具。VD 水平可能与 Sepsis 患者的营养状况和炎症水平以及疾病进展有关。

2022 年某院神经外科 ICU 多重耐药菌分布及耐药性分析

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目的 探讨神经外科重症监护病房 (NICU) 多重耐药菌的分布特点、耐药情况，以及多重耐药菌感染的危险因素，以采取有效措施控制多重耐药菌医院感染的发生。

方法 采用回顾性调查方法，对 2022 年 1 月 – 12 月在我院神经外科重症监护室出院病人 1592 人，患者住院总日数 9432 日，对 NICU 患者的各类标本鉴定到的常见多重耐药菌的发生率、病原菌分布特征进行分析。

结果 分离出的 605 株病原菌中，分别为肺炎克雷伯菌 (216 株 ,35.7%) 、鲍曼不动杆菌 (229 株 ,37.8%)、铜绿假单胞菌 (81 株 ,13.4%) 、金黄色葡萄球菌 (33 株 ,5.5%) 和大肠埃希菌 (46 株 ,7.6%) 为主。多重耐药情况：肺炎克雷伯菌的超广谱 β – 内酰胺酶阳性率为 42.4%、耐碳青霉烯肺炎克雷伯菌 (CRE) 阳性率为 42.4%；耐碳青霉烯鲍曼不动杆菌 (CR-AB) 阳性率为 84%；大肠埃希菌的超广谱 β – 内酰胺酶阳性率为 79.2%、耐碳青霉烯大肠埃希菌 (CRE) 阳性率为 5.26%; 金黄色葡萄球菌中 MRSA 阳性率为 34.6%；多重耐药铜绿假单胞菌 (PDR-Pa) 17.7%%。未检出耐万古霉素肠球菌 (VRE) 。

结论 NICU 多重耐药菌感染发生率高 , 特别是鲍曼不动杆菌、肺炎克雷伯菌检出率及耐药率较高。需从治疗、用药、护理等方面采取有效措施进行监督和指导，以预防和控制 NICU 病房中多重耐药菌带来的医院感染。

重症

揭秘！发热合并低氧血症背后的单一真相究竟为何？ ——1 例脓毒症休克合并 ARDS 患者的救治心得体会

郑宏、叶飞翔、周怡彤、庞城锴、富学林
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目的 探讨一名发热合并低氧血症患者致病原因及治疗过程，为该类患者及时的诊断及救治提供经验及教训。

方法 莫 XX，女，85 岁，退休职工。主诉“发热伴全身乏力 4 小时”入院。予查头颅、胸部 CT：脑白质变性；老年性脑萎缩；两肺炎症；右侧胸膜增厚；甲状腺右叶病变，请结合超声检查；左侧第 3 前肋陈旧性骨折；胆囊结石，不除外合并胆囊炎，请结合临床。急诊科抢救室拟 1. 发热查因 2. 低氧血症收治急诊内科监护室。入院患者持续性发热、低血压，患者逐渐出现意识障碍，呈嗜睡状，体温 39.9° C，血压维持在 75/34mmHg 左右，心率 115 次 / 分，呼吸频率 31 次 / 分，指脉氧下降至 82% 左右。立即改面罩给氧为无创呼吸机辅助呼吸。急查床旁肺部、心脏彩超提示患者存在 ARDS 及感染性休克表现。患者病情危重，改气管插管有创呼吸机辅助呼吸，并予以美罗培南抗感染、低分子肝素钠抗凝、氢化可的松抗炎、西维来司他纳改善 ARDS、去氧肾上腺素维持血压及输注血浆、保护脏器、维持水电解质平衡等强化对症支持治疗。待患者病情平稳后进一步送放射科完善腹部、盆腔 CT：1 右侧输尿管上段结石并以上右肾、输尿管轻度积水，伴周围及右腹腔渗出性改变，右肾筋膜增厚；2 双肾囊肿；3 胆囊结石；4 两肺炎症：两侧膜腔积液并肺组织膨胀不全；5. 盆腔少量积液。6. 腰 5 推体前滑脱。至此患者诊断考虑 1. 脓毒症 2 脓毒症休克 3. 急性呼吸窘迫综合征 4. 右侧输尿管上段结石伴右肾轻度积水 5. 泌尿系感染 6. 弥散性血管内凝血 7. 多器官功能衰竭（循环、凝血、肾、呼吸）。

结果 在住院治疗第 11 日患者成功脱机拔管。在住院第 23 日患者病情平稳顺利出院。

结论 结合以上病程，考虑患者因存在有输尿管结石合并肾周感染，在做家务时伸腰促使细菌入血，导致脓毒症及炎症风暴，出现 ARDS 及多器官功能衰竭。通过此次病例了解到病情变化是动态的，辅助检查也应该是动态的，床旁超声可留下动态依据，更利于诊断。

短效 β 受体阻滞剂在治疗 1 例脓毒症合并持续交感应激反应患者中的应用体会

郑宏、秦佳、周怡彤、富学林、庞城锴
桂林医学院附属医院

目的 探讨短效 β 受体阻滞剂在救治一例脓毒症合并持续交感应激反应患者中的价值。

方法 张某，男，52 岁，主因发热半天入院。入院查体 T38.6℃，P152 次 /min，R37 次 / min，BP101/61mmHg，骶尾部多处压疮，两臀部有 20*15cm 深部组织损伤，有波动感，左臀部有一处 1.5cm*1.5cm 破口，破口处有黄色脓液流出。治疗 3 日后患者仍持续发热伴有心率增快，体温在 38.5 至 39.6℃左右波动，心率基本维持在 141 次 / 分左右，持续发热考虑感染控制不佳，而心率持续增快考虑脓毒症引起的持续交感应激反应导致，于是改用万古霉素 + 美罗培南加强抗感染治疗。在继续治疗 2 日后患者体温能下降至 37.8℃以下，复查炎症指标轻微下降，但心率仍持续较快，仍然有 130 次 / 分左右，予以加用短效 β 受体阻滞剂艾司洛尔 0.05-0.2mg/kg/min 持续泵入加强控制心率治疗。在继续治疗 3 日后患者已无发热，心率维持在 90 次 / 分，予以改用哌拉西林抗感染及美托洛尔口服控制心室率继续巩固治疗。

结果 在总住院第 14 日。查体 T36.7℃，P85 次 /min，R21 次 /min，BP127/74mmHg，骶尾部压疮伤口愈合可，未见明显黄色脓液流出。病人病情好转明显，生命征平稳，予以安排出院。

结论 短效 β 受体阻滞剂具有以下作用：1. 阻断肾上腺素作用：能对抗应激反应时交感神经过度兴奋，对抗心律失常；阻断儿茶酚胺对心脏毒性，避免心肌损伤。2. 改善血流动力学：降低心率，减少心肌氧耗；延长心脏舒张期，增加冠脉充盈；改善灌注缓解心肌缺血。3. 炎症代谢方面：下调炎症介质表达；改善代谢；恢复血管瀑布改善微循环。结合短效 β 受体阻滞剂以上作用，其能有效控制脓毒症患者持续交感应激反应，从而起到控制心室率及降低心肌耗氧量的作用，降低了急危重症心血管事件发生率和患者死亡率，值得在临床推广应用。

Plasma and blood-cell co-metagenomic sequencing in precise diagnosis and severity evaluation of sepsis, a prospective cohort study

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Abstract Content Introduction The usefulness of plasma metagenomic next-generation sequencing (mNGS) and blood cell mNGS in precise diagnosis and prognosis prediction of sepsis is uncertain.

Objectives 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.

新生儿重症监护室规范化护理干预对红臀发生率的影响分析

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目的 探究新生儿重症监护室规范化护理干预对红臀发生率的影响。

方法 选我院 2022 年 1 月至 2023 年 12 月期间 18334 例新生儿重症监护室患儿，以不同护理干预方式分为 A 组（10000 例）、B 组（8334 例），分别实施常规护理、规范化护理，比较两组患儿红臀发生率、生长发育情况。

结果 B 组患儿红臀发生率为 0.15%，较 A 组 0.58% 低，差异有统计学意义（P<0.05）；B 组患儿家长护理满意度较 A 组高（98.84%vs98.48%%），差异有统计学意义（P<0.05）。

结论 在新生儿重症监护室中实施规范化护理干预，可降低患儿红臀发生率，提升患儿家长护理满意度。

The value of ursodeoxycholic acid and mesenchymal stem cells in the treatment of critical COVID-19

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Abstract Content Abstract

Objective The objective of this study was to evaluate the therapeutic efficacy of ursodeoxycholic acid (UDCA) and mesenchymal stem cells (MSCs) in patients with critical COVID-19.

Methods We included critical COVID-19 patients hospitalized at Shulan (Hangzhou) Hospital between December 2022 and June 2023. We used a Logistic regression model to compare the use of UDCA and MSCs in the two distinct groups of improved and poor outcomes. It is noteworthy that the deterioration group encompassed instances of both death and abandonment of treatment. The receiver operating characteristic (ROC) curve was plotted to assess the performance of the model. The aim was to assess the therapeutic effect of UDCA and MSCs on the outcome of critical COVID-19 patients.

Results A total of 168 patients with critical COVID-19 were included in this study, 37 (22%) improved and were discharged after treatment(= healing group), and 131 (78%) progressed to a poor outcome (= deterioration group). There were no differences in gender, comorbidities, hormones, antibiotics, or antifungal use between the two groups. The healing group was younger than the deterioration group ($p = 0.001$) and had higher utilization of UDCA and MSCs ($p < 0.05$).

Conclusions UDCA and MSCs positively reduce the risk of adverse outcomes in critical COVID-19 patients.

Keywords: UDCA; MSCs; COVID-19; Prognosis

Effectiveness of polymyxin B-immobilized hemoperfusion in adult patients with sepsis and septic shock: a systematic review and meta-analysis

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Abstract Content Polymyxin B-immobilized hemoperfusion (PMX-HP) is a therapeutic strategy for removing circulating endotoxins from patients with sepsis/septic shock. However, the survival advantage from PMX-HP treatment remains controversial for patients with sepsis/septic shock. As a result, this study collected all the clinical trials to assess the effect and the safety of PMX-HP treatment.

Methods PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials were searched for eligible trials from commencement through June 30, 2023. All clinical trials that investigated the effect of polymyxin B hemoperfusion on 28-day mortality in patients with sepsis/septic shock were eligible. The Cochrane risk of bias assessment instrument and the ROBINS-I tool were used to assess the risk of bias.

Results A total of 30 trials, including 25680 adult patients, were included. PMX-HP decreased 28-day mortality (OR 0.75, 95% CI 0.65–0.88; $p < 0.00001$). Subgroup analysis revealed that 28-day mortality was significantly reduced after PMX-HP treatment in the mixed infection site group and in the age under 70 years old group. PMX-HP might also lower endotoxin levels (MD -1.22, 95% CI -1.62 – 0.81, $p < 0.00001$) and improve SOFA scores (MD -2.11, 95% CI -3.80- 0.43, $p = 0.01$). PMX-HP was not linked to the development of significant adverse events (p=0. 05).

Conclusion Our findings suggest that PMX-HP therapy can reduce 28-day mortality in individuals with sepsis/septic shock. The therapy effect may be due to PMX-HP's ability to lower endotoxin levels and enhance hemodynamics. However, there are required to further assess the clinical effects of PMX-HP on sepsis/septic shock.

血清唾液酸检测的临床价值

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目的 唾液酸存在于人体的各种组织细胞，是细胞膜的重要组成成分，当细胞代谢异常时，唾液酸脱落进入人体液，导致血清唾液酸含量升高，血清唾液酸（SA）水平的升高与一些肿瘤特别是肺癌之间的关系密切。近年来又有报道，在一些炎症、发热等情况下 SA 也会升高，临床上可作为一种特异性炎症指标之一。随着检测 SA 的快速一步法的问世，使其在临床的应用更为方便。为探讨 SA 的临床价值．下文从肿瘤和肾功能衰竭两个比较典型的方向予以综述。

方法 阅读国内外多篇学术论文，总结成果

结果 临床上 SA 水平监测对疾病诊断和预防意义重大，它能有效反映人体细胞结构与功能的变化。

结论 SA 为细胞表面糖链末端的氨基酸残基，是糖蛋白与糖脂的一个主要成分，参与细胞的多种生理功能，当细胞发生突变成为癌细胞时，细胞表面成分发生改变，使 SA 升高。一般认为其增高的机制是，细胞癌变过程中伴有细胞膜上糖蛋白的唾液酸化和含 SA 的神经节苷酯的改变，使癌变后细胞表面 SA 升高，癌变过程和 SA 升高量呈正相关的增加。另一方面，肿瘤细胞的浸润、转移等恶性变化 SA 均可升高，但 SA 不能确定病因，也无器官特异性。在这方面，相信以后会得到越来越多的研究和关注

临床药师参与 1 例暴发型流行性脑脊髓膜炎（休克型）重症感染患者的药学监护与治疗体会

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目的 临床药师参与 1 例暴发型流行性脑脊髓膜炎（休克型）患者的诊疗经过，为该类患者的临床诊疗提供治疗参考。

方法 患者 2023 年 3 月 16 日病发后送至黄石市中心医院重症医学科救治，其间神经内科会诊考虑颅内感染，转至该科重症监护室，患者脑脊液标本的高通量测序检查结果和血培养结果均提示脑膜炎奈瑟菌，请临床药师会诊，临床药师基于 PK/PD 理论给出诊疗方案。

结果 该患者从重症医学科到神经内科重症监护室再到神经内科最后到整形外科处理四肢及臀骶尾创面，在临床医师与药师共同监护下，情况明显好转出院，共住院治疗 33 天。

结论 暴发型流行性脑脊髓膜炎（休克型）起病急骤、病情凶险，在临床医师与药师共同监护下，能显著提升临床反应能力，最终提高患者的救治成功率。

脓毒血症治疗和防护的纳米药物

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目的 脓毒血症是一种严重的全身性感染，需要及时、有效的治疗。治疗的主要目标是控制感染源，消除感染，防止感染的进一步扩散，以及维持患者的生命体征稳定。其中两个重要的环节包括高效的感染治疗和感染源控制以及对于形成免疫抑制患者有效调控免疫和防护继发感染。

方法 基于具有抗生素佐剂效应纳米载体制备的纳米抗生素，我们提供了从制剂上全新开发的“可细菌靶向变形”的纳米载体，从高效、广谱对抗多重耐药菌上全新提出的”细菌膜曲率快速改变“导致的高效抗生素协同治疗机制，从免疫调控和免疫抑制方面，提供了纳米抗生素快速杀菌后的”原位疫苗“新理念，有望为后续的重症脓毒血症感染提供面向临床的解决方案。

结果 智能的纳米抗生素具有特异性的细菌靶向特性，可以在细菌膜表面从纳米颗粒变形成纳米纤维，从微观上破坏细菌细胞膜，促进抗生素高量、原位释放，将抗生素的药物利用率提高 4 倍，与抗生素的协同抗菌将 MIC 降低 10~30 倍，将抗菌速率 MDK99 降低 1-2 个数量级；从宏观上将血液或者原发感染灶的细菌网罗到机体，类似中性粒细胞的 NETosis 过程，快速清除血液细菌，形成原位疫苗。

结论 智能纳米抗生素具备高效、快速清除脓毒血症细菌感染，相比传统的抗生素治疗，可将重症感染小鼠的生存率提高到 92%，二次感染（包括复杂性耐药感染）的生存率保护达到 100%。这种新剂型具备未来作为新抗生素制剂开发的潜力，目前已与华北制药集团签署联合开发项目，推进转化。

特重度烧伤患者术后反复难治性铜绿假单胞菌血流感染治疗 1 例及文献复习

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目的 探讨产丝氨酸 β－内酰胺酶 (SBL) 和金属 β－内酰胺酶（MBL）铜绿假单胞菌血流感染的药物治疗方案

方法 以临床药师全程参与 1 例特重度烧伤患者多次植皮术后继发产（SBL+MBL）铜绿假单胞菌血流感染的抗感染方案为例，综合分析，发现多黏菌素以及头孢他啶阿维巴坦 + 氨曲南分开输注方案疗效均不佳，结合最新临床研究，探讨（头孢他啶阿维巴坦 2.5g + 氨曲南 2.5g），q8h，双通道同时给药输注 2 小时在产（SBL+MBL）-PA 血流感染中的应用，同时复习国内外相关文献，总结产 MBL ± SBL 铜绿假单胞菌感染的治疗方案

结果 本患者最终使用（头孢他啶阿维巴坦 2.5g + 氨曲南 2.5g），q8h，双通道同时给药输注 2 小时的方案获得满意的治疗效果

结论 仅有 3 篇国外文献报道了头孢他啶阿维巴坦联合氨曲南有效治疗耐氨曲南的产 MBL 铜绿假单胞菌感染，暂无治疗同时产（SBL+MBL）铜绿假单胞菌感染的报道，本研究可为该方案治疗该耐药菌感染提供临床数据

Serum Exosome Proteomics Reveals Molecular Characteristics Severe Sepsis

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Abstract Content Background The high heterogeneity of sepsis poses a great challenge for diagnosis and treatment. Our objective was to identify molecular targets for high-risk populations to mitigate mortality risks.

Methods Exosome proteomics analysis of 279 serum samples, including four sepsis cohorts and one healthy cohort, was conducted. Transmission electron microscopy, nanoparticle tracking analysis, and Western blot were utilized for exosome identification. Mass spectrometry and bioinformatics were employed for sepsis classification based on exosomal markers.

Results Molecular typing of 96 sepsis-only samples revealed a severe sepsis subtype (Sep-severe) marked by elevated procalcitonin (PCT) levels and shock incidence. Screening identified 47 proteins distinguishing sepsis severity, primarily associated with tissue repair. In further analysis, we found that Sep-severe, sepsis with AKI, and sepsis with ARDS and AKI were characterized by a high incidence of shock and high PCT, but the mortality rate of sepsis with ARDS and AKI group was significantly higher than that of Sep-severe group and sepsis with AKI group. Downregulated metabolic characteristics and six protein biomarkers panel were identified in deceased patients. Validation with 24 samples confirmed consistency.

Conclusion Serum exosome proteomics reveals novel sepsis classifications, differentiates severity, and identifies a subgroup with high PCT and high shock rates , informing personalized treatment strategies.

Dynamic expression analysis of peripheral blood derived exosome miRNAs in sepsis progression

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Abstract Content Immune disorders caused by sepsis have recently drawn much attention. We sought to dynamically monitor the expression of exosome miRNAs in peripheral blood during sepsis to explore these miRNAs as potential biomarkers for monitoring immune function in sepsis patients.

Methods This study included patients with sepsis. Blood samples were obtained from 10 patients on the first through 10th days, the 12th day, and the 14th day since sepsis onset, resulting in 120 collected samples. Serum exosomes were extracted from peripheral venous blood, and levels of MIR497HG, miR-195, miR-497, and PD-L1 in serum exosomes were detected by qPCR, and clinical information was recorded.

Results Our study revealed that the levels of MIR497HG, miR-195, miR-497, and PD-L1 in serum exosomes showed periodic changes; the time from peak to trough was approximately 4-5 days. The levels of exosome MIR497HG and miR-195 had a positive linear relationship with SOFA score (r values were -0.181 and -0.189; P values were 0.048 and 0.039, respectively). The recorded quantities of exosome MIR497HG, miR-195, and PD-L1 showed a substantial correlation with ARDS. ROC curve analysis revealed that exosome MIR497HG, miR-195, and miR-497 could predict the 28-day mortality of sepsis patients with an AUC of 0.66, 0.68, and 0.72, respectively.

Conclusion Levels of exosomes MIR497HG, miR-195, miR-497, and PD-L1 showed periodic changes with the immune status of sepsis, which provides a new exploration direction for immune function biomarkers and immunotherapy timing in sepsis patients.

Effect of one dose of ceftriaxone during endotracheal intubation on the incidence of aspiration pneumonia in cerebral hemorrhage patients

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Abstract Content Introduction Due to the use of analgesic and sedative drugs during endotracheal intubation and the opening of the glottis may easily cause aspiration pneumonia. Ceftriaxone is a semi-synthetic third-generation cephalosporin with strong antimicrobial activity against most gram-positive and gram-negative bacteria. It can effectively prevent and treat aspiration pneumonia.

Methods This is a prospective, randomized, controlled, double-blind clinical study. Patients with intracerebral hemorrhage (ICH) undergoing endotracheal intubation in Dong E Hospital of Shandong Province from January 2023 to December 2023 will be enrolled and randomly assigned to the intervention group or control group. The intervention group will be treated using 100mL 0.9% sodium chloride with 2g ceftriaxone intravenously over the course of one hour beginning within two hours after endotracheal intubation. The control group will be given 100mL 0.9% sodium chloride injection intravenously of the course of one hour beginning within two hours after endotracheal intubation.

Results The primary outcome is the incidence of aspiration pneumonia within 48 hours after endotracheal intubation. Secondary outcomes include: intensity of antimicrobial use, length of hospital stay, duration without mechanical ventilation, and 28-day mortality.

Conclusion The primary objective of this study is to explore whether a single dose of ceftriaxone administered during endotracheal intubation in patients with ICH reduced the incidence of pneumonia within 48 hours and provide evidence for the prevention of aspiration pneumonia in patients with ICH with endotracheal intubation.

液滴数字 PCR 在脓毒症患者队列中快速、敏感地鉴定病原体：一项前瞻性诊断研究

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目的 脓毒症患者急需一种快速、灵敏的病原体检测方法。本研究旨在探讨数字液滴聚合酶链反应 (ddPCR) 对疑似脓毒症患者病原菌的诊断效果。

方法 我们进行了一项前瞻性诊断研究，来临床验证 ddPCR 诊断疑似脓毒症患者病原体的效能。总共纳入了 89 例患者共发生了 100 次脓毒症。

结果 与血培养相比，ddPCR 整体敏感性为 75.0%，特异性为 69.7%，对脓毒症的总体额外检出率为 17.0%，周期为 2.5 h。经验抗生素治疗组和非经验抗生素治疗组 ddPCR 敏感性分别为 78.6% 和 80.0% ($p > 0.05$)。在 13 份样品中鉴定出耐药基因。每当 ddPCR 检测到 β – 内酰胺酶 – 肺炎克雷伯菌碳青霉烯酶 (blaKPC) 或 β – 内酰胺酶 – 新德里金属 (blaNDM) 基因时，这些结果与碳青霉烯耐药革兰氏阴性菌的培养相对应。动态 ddPCR 监测显示定量 ddPCR 结果与 c 反应蛋白和降钙素原水平观察到的趋势一致。

结论 与血培养相比，ddPCR 对疑似脓毒症患者的病原体诊断具有更高的敏感性，可在更短的时间内提供病原体和耐药信息。ddPCR 的定量结果与 c 反应蛋白和降钙素原水平的趋势基本一致，表明 ddPCR 可以作为脓毒症患者病原体负荷的动态监测工具。

脓毒症相关肺损伤中 JAK/STAT 通路介导巨噬细胞极化的机制及潜在治疗靶点

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目的 脓毒症是因机体对感染的免疫反应失衡引起的一种威胁生命的多器官功能障碍综合征，其病情复杂多 变，是导致 ICU 患者死亡的主要原因之一。急性肺损伤是脓毒症患者最早发生、也是最常见的器官损伤。巨噬细胞 是先天性免疫和适应性免疫的重要组成部分，可通过不同的极化类型主导机体免疫状态，在脓毒症的早期常呈现促炎 的 M1 型极化并导致免疫亢进，而在脓毒症后期又往往转化为抑炎的 M2 型造成免疫抑制。Janus 激酶（JAK）/ 信号 转导及转录激活蛋白（STAT）通路对炎症信号的调节具有重要作用，该通路的激活贯穿了整个脓毒症发展及巨噬细 胞极化的全过程。本文分析了 JAK/STAT 通路通过影响巨噬细胞极化进而介导脓毒症相关肺损伤的作用机制，并总结 了潜在的治疗靶点，以期为脓毒症的治疗提供新的思路。

方法 无

结果 无

结论 无

The value of the proportion of perfused vessels change rate in the evaluation of early organ function deterioration in septic shock and ARDS

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Abstract Content This study explores the relationship between the proportion of perfused vessels change rate (ΔPPV), the shedding of the glycocalyx marker syndecan-1 (SDC-1), and the utility of ΔPPV in assessing early organ function deterioration in septic shock and acute respiratory distress syndrome (ARDS) patients.

Methods Patients were categorized into two groups based on the change in their Sequential Organ Failure Assessment (SOFA) score over 24 hours: the organ function deterioration group (SOFA24h-0h score $\geqslant$ 1) and the non-deterioration group (SOFA24h-0h score < 1). Sublingual microcirculation, lactic acid levels, and SDC-1 were evaluated at 0 and 6 hours. The primary endpoint was the area under the curve (AUC) for ΔPPV and its combination with lactate clearance rate (LCR). Secondary endpoints included the correlation between ΔPPV and SDC-1, hospital mortality, and survival analysis.

Results The study included 67 patients. The AUC for ΔPPV was 0.813 (95% CI: 0.707-0.919), and when combined with LCR, it was 0.871 (95% CI: 0.785- 0.957). Additionally, a negative correlation between ΔPPV and SDC-1 was observed. Patients who met the criteria of ΔPPV ≥ 7.6% and LCR ≥ 14.6% demonstrated a higher survival rate compared to other groups (Log-rank test: $\chi^2 = 6.489$, $P < 0.011$).

Conclusion Microcirculatory disorders are closely linked to glycocalyx shedding. ΔPPV, particularly when combined with LCR, can effectively predict early organ function deterioration and has significant prognostic value for hospital mortality.

重症

Trex1 介导 Irf3 入核促进单核 / 巨噬细胞免疫耐受的机制研究

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目的 探讨 TREX1 在脓毒症免疫耐受中的作用及机制。

方法 公用数据集探讨脓毒症免疫耐受时 TREX1 在单核细胞的转录本表达水平，及通路富集。用 LPS 诱导细胞的内毒素免疫耐受。构建内毒素免疫耐受模型，采用 Western blot 检测 Trex1 和 cGAS-STING 通路蛋白表达。免疫荧光和核浆分离实验，观测炎症期和免疫抑制期蛋白 Irf3 和 Trex1 在胞内的定位。琼脂糖凝胶电泳观测基因组 DNA 断裂情况。彗星实验验证基因组 DNA 单链和双链的断裂程度。免疫荧光等方法检测 Trex1 和 Parp1 的内源性相互作用。分别构建原核和真核载体，观测二者液液相分离情况，以 Trex1 作为诱饵蛋白，检测 Trex1 的 ADP- 核糖化修饰水平。使用 Parp1 特异性抑制剂 AG14361 等，检测 TREX1 对 DNA 降解和结合 DNA 能力。

结果 TREX1 主要在脓毒症免疫抑制状态的患者单核细胞中表达，且与 STING-IRF3-IFN 通路相关。在内毒素免疫耐受的巨噬细胞中，Trex1、Tbk1 的蛋白表达水平明显增高，而 p-Irf3 的蛋白表达水平显著下降。同时，内毒素耐受时 Irf3 和 Trex1 主要聚集于细胞核，基因组 DNA 片段减少，彗星尾部较短。免疫荧光染色及免疫共沉淀显示耐受组中 Parp1 和 Trex1 在细胞核内共定位，其相互作用区在 Trex1 的关键结构域是 NTF 区。体内和体外液滴形成实验表明，Trex1 和 Parp1 可以形成相分离，其存在形式可被相分离抑制剂 1,6-Hex 所抑制。且基因组 DNA 片段增多，基因组的稳定性降低。且 Trex1 的 ADP- 核糖化修饰较非耐受组明显增多。EMSA 实验结果显示，Parp1 特异性抑制剂处理后，Trex1 与 dsDNA 结合能力显著增加。

结论 内毒素免疫耐受时 Trex1 与 Irf3 互作入核，诱导 Trex1 的 ADP- 核糖化修饰及发生液液相分离，促进基因组 DNA 的稳定性。

Global research trends and focus of Sepsis bundle research from 2000-2024: A bibliometric and visualized study

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Abstract Content To improve and standardize practices, the Surviving Sepsis Campaign (SSC) was initiated to increase bedside clinician and nurser's awareness, develop consensus definition of sepsis and evidence-based guidelines stressing a 'bundle' approach to sepsis management, reinforcing the importance of sepsis early care. Compliance to the Surviving Sepsis Campaign (SSC) guidelines is limited, which is known to be associated with increased mortality. The Sepsis Bundle includes antibiotic administration, fluid bolus, blood cultures, lactate measurement, vasopressors for fluid-refractory hypotension, and a reevaluation of volume status. This study mainly describes the hotspots of Sepsis Bundle research and its evolution in the past two decades, evaluates the scientific cooperation network, and finally predicts the field's future development trend using bibliometric analysis and a visualized study.

Methods The Science Citation Index Expanded (SCI-Expanded 1999- present) of Clarivate Analytics'S Web of Science Core Collection (WoSCC) is one of the most comprehensive and influential databases in interdisciplinary fields, containing extensive academic journals and literature, which is wildly used as the data source for bibliometric study. In this study, all the publications we obtained were retrieved and downloaded from WoSCC database on March 12, 2024. The literature searching was performed by two independent researchers to ensure the reliability and authenticity of results.

The Bibliometrix R packages 3.1.4, VOSviewer 1.6.16, and CiteSpace 5.8.R6 were mainly used to perform and visualize co-authorship, co-citation, and co-occurrence analysis of countries, institutions, authors, reference and keyword in this field. Bibliometric outcomes included citation counts, co-citations and co-occurrences. Citation count are the number of citations to a publication, and co-citation count is defined as the frequency with which two published articles are cited together by subsequently published articles. A co-citation network is particularly suitable for systematic reviews because co-citation linkages may reveal how groupings continuously evolve independently from original publications. Co-occurrence networks are a graphical representation of how frequently variables appear together. Systematic mapping outcomes were networks and co-citations(or co-occurrence) clusters.The interpretation of these clusters is augmented by CiteSpace's automatic

Results Global trends in publication outputs and citations

The number of research papers published in different periods demonstrates the popularity and development tendency of research in a particular field. A total of 2038 articles related to Sepsis Bundle between January 1, 2000 and March 12, 2024 from WoSCC based on inclusion criteria.

Distribution of Countries/regions

A total of 503 countries/regions had contributed in the field of Sepsis bundle. United States ranked first with 889 (43.62%) publications, followed by England (171, 8.39%) and China (167, 8.19%).

Contributions of top institutions

More than 8213 institutions participated in publishing research papers on sepsis bundle. It was evident that all the institutions in the top 10 were from North America, of which 6 were from the United States and 3 were from Australia. Specifically, University of Pittsburgh ranked first with 75 papers, followed by the University of Washington and Monash University.

Analysis of top journals and co-cited journal

At present, the research papers related to Sepsis bundle had been published in 541 scholarly journals. the journal Critical Care Medicine had the highest number of publications, with a total number articles of 131, followed by Critical Care (98) and Shock (67). Fig. 8 was a dual-map, which was used to represent the discipline distribution of journals involved in sepsis bundle research, and through this method, we could clearly understand the knowledge flows among different disciplines and the frontier or hotspot of each discipline. it could be found that the literature published in Molecular/Biology/Immunology or Medicine/Medical/Clinical journals often cited the literature from Microbiology/Rehabilitation/Health/Nursing/Pharmacology/Psychology education journals.

Analysis of the active authors and co-cited authors

A total of 10,942 authors participated in the publication of papers in the field of Sepsis Bundle. Table 4 summarized the top 10 most productive authors and the top 10 co-cited authors.

Analysis of references and co-cited references

A total of 2038 papers were included in this study, of which 159 publications were cited more than 100 times. Analyzing Enriched cited references can help researcher understand citation purposes and discover impactful related article. Table 4 listed the top 10 enriched cited papers and the most cited article

Keywords co-occurrence analysis

A total of 2850 author keywords were included in this study. Figure 12 summarized the top 40 keywords with the highest frequency. The top four most common keywords were “Sepsis”、“Sepsis shock”、“Mortality”、 “Severe Sepsis”，which was consistent with our study topic. In addition, “Resuscitation” 、“Antibiotics” and “Early goal-directed therapy” were currently the most studied topics in this field.

Conclusion Sepsis bundle is in the stage of vigorous development and has a bright prospect. International transboundary cooperation among countries and institutions should be strengthened in the future. It is foreseeable that more research foci will be lied in the interpretability of Sepsis bundle quality improvement.

重症

机械通气患者抗菌药物雾化吸入的临床实施

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目的 规范机械通气患者抗菌药物雾化吸入的临床护理，为制订合适的抗菌药物雾化管理方案提供借鉴。

方法 本文综述了机械通气患者抗菌药物雾化吸入的临床实施，包括抗菌药物剂型的选择、药物配置与使用、雾化装置的选择与连接、机械通气参数设置，阐述相关不良事件的预防和处理

结果 通过选择具有雾化剂型的抗菌药物、关注药物间的协同及配伍作用，保证联合用药的相容性、稳定性，以及选择合适的溶媒溶剂，无菌条件下现配现用等是保证抗菌药物浓度的有效措施。根据不同雾化装置的特点、治疗需求、成本效益等角度选择合适的雾化装置，推荐对实施抗菌药物雾化治疗的机械通气病人选择呼吸机同步雾化或振动筛孔雾化，提高抗菌药物的肺部沉降率。机械通气雾化抗菌药物治疗效果除了受到药物特性、雾化装置的影响，还受到呼吸机的设置、雾化装置的连接、人工气道、病人等因素影响。针对机械通气病人行抗菌药物雾化治疗时，呼吸机设置不应该把增加抗菌药物的肺部沉降率作为调整的唯一条件。推荐将呼吸机同步的喷射雾化器放在靠近Y型管的吸气段，雾化前需做好人工气道的准备工作以提高抗菌药物的肺部沉降率，雾化过程中关注病人是否出现人机不同步，必要时予镇静治疗以提高人机同步性。

结论 在机械通气期间，向感染的肺区域输送高浓度抗生素是实现高效雾化抗生素治疗的关键。需要考虑以下实际因素并予以优化，包括：药物、雾化器、人工气道、呼吸机设置、病人管理。同时，雾化抗菌药物也可能会产生一些并发症，临床医护人员需要临床实践中关注。目前尚缺乏机械通气病人雾化抗菌药物的规范操作流程，需要在扩大其临床用途之前，迫切需要雾化技术的优化和雾化程序的标准化。

Dynamic Decline of Lymphocytes Predicts Extracorporeal Membrane Oxygenation-related Infections: A Retrospective Observational Study

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Abstract Content Background Limited data are available regarding the current microbiological characteristics of extracorporeal membrane oxygenation (ECMO)-related infections in intensive care units (ICUs) in China. This retrospective study aimed to determine the epidemiology, risk factors and impact on the outcome of ECMO-related infections.

Methods A retrospective observational study from January 2014 to December 2019 was performed, and adult patients receiving ECMO support for more than 48 hours were included in this study. The primary outcome was the incidence rate of ECMO-related infection. Clinical data were recorded, and risk factors associated with an increased risk of ECMO-related infection were analyzed.

Results A total of 174 adult patients who received ECMO and underwent ECMO for 1670 days were included in this study. Forty-six patients (26.4%) developed ECMO-related infections, corresponding to 27.5 first episodes/1,000 ECMO days. The most common ECMO-related infection observed was ventilator-associated pneumonia (VAP). Infected patients had longer durations of mechanical ventilation (20.2 (interquartile range (IQR) 12.6, 30.7) vs. 9.0 (IQR 5.8, 14.7) days, P<0.001), ECMO support (11.6 (IQR 8.1, 17.3) vs. 7.6 (IQR 5.6, 9.7) days, P<0.001) and hospital stays (28.2 (20.7) vs. 22.0 (15.6) days, P<0.001). The factors independently associated with ECMO-related infection were a dynamic decrease in lymphocyte count (adjusted odds ratio (OR) 3.578, 95% confidence interval (CI) 2.175-4.906, P<0.001) and ECMO duration (adjusted OR 1.207, 95% CI 1.096-1.330, P<0.001). Compared to patients without infection, infected patients had greater hospital mortality (39.1% vs. 78.3%, P<0.001) and 90-day mortality (40.6% vs. 87.0%, P<0.001). ECMO-related infections were associated with worse outcomes (adjusted Kaplan–Meier curve, log rank test P<0.001).

Conclusion Patients supported by ECMO had a high risk of developing ECMO-related infection. The most common ECMO-related infection observed was VAP. A dynamic decrease in lymphocyte counts was significantly associated with an increased risk of ECMO-related infection.

Efficacy and Safety of Prone Position Ventilation in Severe Acute Respiratory Distress Syndrome Patients Undergoing Extracorporeal Membrane Oxygenation: A Prospective Multicenter Randomized Controlled Study

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Abstract Content This study aims to investigate the efficacy and safety of prone position ventilation (PPV) in severe acute respiratory distress syndrome (ARDS) patients under extracorporeal membrane oxygenation (ECMO). PPV has shown benefits in ARDS without ECMO, but its effectiveness with ECMO lacks evidence. This prospective multicenter randomized controlled trial evaluates PPV's value in ECMO to provide evidence-based guidelines.

Methods Patients with severe ARDS requiring ECMO from multiple Chinese ICUs will be randomly assigned within 48 hours of ECMO initiation to a control group (standard treatment) or an intervention group (16 hours of daily PPV for the first four days).

Results The primary outcome is successful ECMO weaning within 60 days, defined as survival without lung transplantation or re-ECMO within 30 days post-ECMO removal. Secondary outcomes include mortality, duration of ECMO support, ICU and hospital stay, mechanical ventilation duration, and oxygenation improvement. Safety outcomes will record complications related to PPV and ECMO. The study aims to demonstrate PPV's effectiveness in improving oxygenation, reducing mortality, and shortening ICU stay and ECMO duration, as well as its safety.

Conclusion This study seeks to clarify PPV's role in ECMO treatment, offering new methods for severe ARDS management. Combining PPV and ECMO is expected to improve outcomes, optimize resources, and enhance ICU efficiency, advancing critical care medicine.

SepsisSCA: a comprehensive database integrating single-cell transcriptome atlas of sepsis

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Abstract Content Sepsis is a leading cause of mortality in the intensive care unit. To date, treatment of sepsis is limited by heterogeneity of immune response and incomplete description of cellular atlas. Prior bulk-sequencing have identified the host-gene expression profiling of sepsis, but have not resolved signatures in transcriptional states of specific cell types. Recent advances in single-cell RNA sequencing (scRNA-seq) technology provides an unprecedented opportunity to comprehensively characterize the heterogeneity of immune system in sepsis, but poses computational challenges on integrating and utilizing the massive published datasets to inform treatment. Thus, there is an urgent need to build a dedicated resource to decode the various function of immune cells and parenchymal cells in sepsis. We developed SepsisSCA (Sepsis Single Cell Atlas), the dedicated database that aims to comprehensively explore the cellular signatures of sepsis at single-cell level.

Methods We systematically collected sepsis-related scRNA-seq datasets in human and mouse from Sequence Read Archive (SRA), Gene Expression Omnibus (GEO). For each dataset, we carefully read the original paper, if available, and extracted the metadata, including the tissue types and potential pathogens, sites of infection. For each dataset, we performed several basic analysis of high-quality cancer single-cell expression, including PCA and t-SNE analysis.

Results We developed SepsisSCA, a large-scale curated database that aims to comprehensively explore distinct functional cellular states of sepsis at single-cell level. SepsisSCA integrates single-cell transcriptomic profiles of nearly 500 thousand cells from 12 high-quality sepsis datasets across 6 tissue types. All the data were uniformly processed with a standardized workflow, including quality control, batch effect removal, clustering, cell-type annotation, differential expression analysis and functional enrichment analysis. SepsisSCA provides interactive gene expression visualization across multiple datasets at the single-cell level or cluster level, allowing systematic comparison between different cell-types, patients, tissue origins.

Conclusion In summary, SepsisSCA provides a user-friendly interface for systematically visualizing, searching and downloading gene expression atlas in the sepsis from multiple tissues, enabling fast, flexible and comprehensive exploration of sepsis.

Effect of individualized positive end-expiratory pressure titrated by electrical impedance tomography on ventilation-perfusion distribution in patients with acute respiratory distress syndrome

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Abstract Content Objectives The effects of PEEP titrated by EIT on ventilation/perfusion (V/Q) distribution remain unclear. Therefore, this study aimed to describe the effects of individual PEEP titrated by EIT on regional ventilation and perfusion distribution in patients with acute respiratory distress syndrome (ARDS).

Methods This is a prospective, cross-over randomized study in a single medical ICU. 69 patients with moderate to severe ARDS undergoing mechanical ventilation. Patients were randomized to three different PEEP strategies which were set according to (1) crossing points method using EIT (PEEPEIT), (2) low PEEP-FIO2 table (PEEPlow), or (3) high PEEP-FIO2 table (PEEPhigh). Each PEEP level was maintained for 15 minutes, and subsequently, gas exchange, lung mechanics, and EIT data were collected. Patients were defined as high recruiters (R/I > 0.5) or low recruiters (R/I < 0.5).

Results PEEPEIT was higher compared with PEEPlow, but lower compared with PEEPhigh (11.6 ± 2.6 cmH2O vs. 8.7 ± 1.9 cm H2O and 15.8 ± 2.0 cm H2O, respectively; P < 0.001 each). V/Q matching was higher with PEEPEIT compared to PEEPlow (76.4 ± 8.7 % vs. 70.9 ± 12.4 %, P = 0.007). PEEPEIT and PEEPhigh reduced total shunt compared to PEEPlow. Dead space at global and ventral regions did not differ among different PEEP strategies.For high recruiters, V/Q matching was higher using PEEPEIT compared to PEEPlow and PEEPhigh. For low recruiters, there was no difference among three PEEP strategies.

Conclusions Individual PEEP titrated by EIT improves V/Q matching by reducing shunt without altering dead space in patients with moderate to severe ARDS.

脓毒症发病机制及潜在治疗靶点

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目的 脓毒症是机体对感染的免疫反应失调引起的，危及生命的器官功能障碍。虽然，以“液体复苏、早期抗生素、血管活性药物”为主的治疗策略能够改善患者的预后，但该策略仅仅停留在对症支持水平，脓毒症的死亡率仍高达 30-41%，临床上急需针对性的治疗手段。近年来，随着脓毒症机制研究的不断深入，认识到免疫介导的损伤是脓毒症发病的核心，而对器官损伤的机制研究也深入到细胞、细胞器层面。针对新的发病机制，脓毒症药物研发策略主要包括调控免疫稳态、加速病原体清除、保护脏器功能。本文综述了目前脓毒症治疗领域具有临床转化潜力的治疗靶点，总结其发挥疗效的分子机制，以期为后续的脓毒症药物开发提供参考。

方法 无

结果 无

结论 无

重症

Endothelial cell-derived extracellular vesicles modulate the therapeutic efficacy of mesenchymal stem cells through IDH2/TET pathway in ARDS

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Abstract Content Acute respiratory distress syndrome (ARDS) is a severe and fatal disease. Although mesenchymal stem cell (MSC)-based therapy has shown remarkable efficacy in treating ARDS in animal experiments, clinical outcomes have been unsatisfactory, which may be attributed to the influence of the lung microenvironment during MSC administration. Extracellular vesicles (EVs) derived from endothelial cells (EC-EVs) are important components of the lung microenvironment and play a crucial role in ARDS. However, the effect of EC-EVs on MSC therapy is still unclear. In this study, we established lipopolysaccharide (LPS) - induced acute lung injury model to evaluate the impact of EC-EVs on the reparative effects of bone marrow-derived MSC (BM-MSC) transplantation on lung injury and to unravel the underlying mechanisms.

Methods EVs were isolated from bronchoalveolar lavage fluid of mice with LPS - induced acute lung injury and patients with ARDS using ultracentrifugation. and the changes of EC-EVs were analysed using nanoflow cytometry analysis. In vitro assays were performed to establish the impact of EC-EVs on MSC functions, including cell viability and migration, while in vivo studies were performed to validate the therapeutic effect of EC-EVs on MSCs. RNA_x0002_Seq analysis, small interfering RNA (siRNA), and a recombinant lentivirus were used to investigate the underlying mechanisms.

Results Compared with that in non-ARDS patients, the quantity of EC-EVs in the lung microenvironment was significantly greater in patients with ARDS. EVs derived from lipopolysaccharide-stimulated endothelial cells (LPS_x0002_EVs) significantly decreased the viability and migration of BM-MSCs. Furthermore, engrafting BM-MSCs pretreated with LPS-EVs promoted the release of inflammatory cytokines and increased pulmonary microvascular permeability, aggravating lung injury. Mechanistically, LPS-EVs reduced the expression level of isocitrate dehydrogenase 2 (IDH2), which catalyses the formation of α-ketoglutarate (α-KG), an intermediate product of the tricarboxylic acid (TCA) cycle,in BM-MSCs. α-KG is a cofactor for ten-eleven translocation (TET) enzymes, which catalyse DNA hydroxymethylation

in BM-MSCs.

Conclusion This study revealed that EC-EVs in the lung microenvironment during ARDS can affect the therapeutic efficacy of BM-MSCs through the IDH2/TET pathway, providing potential strategies for improving the therapeutic efficacy of MSC-based therapy in the clinic.

重症

CD39-A2aR 通路介导肺驻留 NK 细胞功能障碍在脓毒症肺损伤中的作用研究

唐颖
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目的 脓毒症是机体对感染反应失调引起的危及生命的器官功能障碍，申请人所在课题组的一项横断面研究显示，我国 ICU 住院者中 20.6% 为脓毒症患者，其 90 天病死率高达 35.5%。脓毒症期间肺是最易累及的器官，合并肺损伤显著提高其病死率，但脓毒症尤其是肺外源性脓毒症如何引起肺损伤机制不明。因此，本研究旨在深入研究脓毒症肺损伤的发生发展机制从而寻找有效的药物靶点。

方法 单细胞测序等多组学 / 流式细胞术 / 差速超速离心 / 磁珠分选 / 免疫荧光等。

结果 ①筛选得到脓毒症免疫状态相关标志物皆主要表达于 NK 细胞，提示 NK 细胞在脓毒症中起关键作用。②单中心回顾性观察性研究，结果显示脓毒症合并 ARDS 患者 NK 细胞计数低于脓毒症不合并 ARDS 的患者，说明 NK 细胞可能影响脓毒症肺损伤发生发展。③观察到脓毒症小鼠血中 NK 细胞活性略升高，而肺部 NK 细胞活性显著降低，说明肺中 NK 与循环 NK 功能不同。④去除肺部 NK 细胞加重肺损伤，去除血中 NK 细胞无显著影响，推测肺驻留 NK 细胞（trNKs）在脓毒症中起肺保护作用。⑤分别通过单细胞测序及流式细胞术证实，脓毒症中肺 trNKs 活性显著降低。⑥肺 trNKs 活性降低很可能是由于受疾病微环境影响，通过分析脓毒症中各种细胞与肺 trNKs 间的通讯作用，发现内皮细胞到肺 trNKs 间的 CD39-A2aR 通讯显著增强，且 CD39、A2aR 表达具有细胞特异性。⑦进一步分析显示，内皮释放 CD39+ sEVs，作用于肺 trNKs 表面 A2aR，抑制其清除有害细胞的能力。

结论 肺外脓毒症中，内皮细胞释放 CD39+ sEVs，远隔作用于肺 trNKs 表面 A2aR，使肺 trNKs 表面活化型受体 NKG2D 减少，肺 trNKs 细胞活性降低，其清除功能被抑制，肺损伤加重。

Clinical performance and impact of hybridization Probe Capture Next-generation sequencing for sepsis diagnosis and therapeutic adjustment: a multicenter and prospective study

Qin Sun,Ling Liu
Zhongda Hospital, Southeast University

Abstract Content Objective To evaluate the clinical performance of a Probe-capture-based next-generation sequencing (NGS) technology for sepsis diagnosis and its impact on therapeutic adjustment and prognosis.

Methods We performed a multicenter and prospective study and included sepsis patients suspected of bloodstream infection (BSI) from four centers. All blood samples were sent for culture and Probe-Capture NGS before antibiotic use. When pathogens identified through Probe-Capture NGS were not detected by conventional blood cultures, the blood samples were verified using Real-time PCR (RT-PCR). The positive rate and diagnostic performance were compared between Probe-Capture NGS, blood culture and RT-PCR. Pathogen-oriented antibiotic adjustments were also recorded, and clinical impact was assessed by antibiotics adjustments combined with changes in SOFA score on day 0, day 3, and day 7.

Results 184 septic patients suspected of BSI were included in from April 2022 to November 2022. The mean age of included patients was 66 (56, 74) and 124 were male (67.4%). Probe-Capture NGS results confirmed by RT-PCR showed a significantly higher positive rate than blood culture (51.6% vs 17.4%, P<0.001). Probe-Capture NGS and culture revealed consistent results in 41.3% (76/184) samples. After combining the results of culture and RT-PCR, an overall consistent rate of 91.8% (169/184) was achieved by Probe-Capture NGS. In terms of clinical impact, Probe-Capture NGS led to antibiotic adjustments in 64 patients (34.8%) and confirmed antibiotic therapy in 43 patients (23.4%). 42 patients (65.6%) benefited from Probe-Capture NGS directed antibiotic adjustments, which was defined as a more than 2 decreased SOFA score.

Conclusion Probe-Capture NGS showed a significantly improved detection rate for pathogens in sepsis patients than blood culture. Further analysis of antibiotic treatment and delta SOFA also proved the beneficial effects of Probe-Capture NGS on patients' prognoses. Our study presents a comprehensive, semi-quantitative analysis of Probe-Capture NGS's diagnostic performance and clinical impact in sepsis.

Trial registration This study has been registered in clinical trials (clinicaltrials.gov) in November 30, 2018 and the registered number is NCT03760315.

Left ventricular global longitudinal strain is independently associated with mortality in hyperdynamic patients with sepsis

Jin Zhang, Feng-Mei Guo
Zhongda Hospital, Southeast University

Abstract Content The association between left ventricular systolic dysfunction (LVSD) and mortality of septic patients remains unclear. The object of this study is to investigated the prognostic value of left ventricular global longitudinal strain (GLS) for sepsis.

Methods We recruited 125 septic patients without cardiac dysfunction in this prospective study. Transthoracic echocardiography was performed and speckle tracking echocardiography were analyzed within 24 hours of enrollment. Full clinical data of patients were collected.

Results The age of all septic patients was 62.7 years old, and the 28-day and 90-day mortality were 24.8% (n=31) and 31.2% (n=39), respectively. The non-survivors with 28 days had higher Arterial blood lactates (3.1 pg/ml vs 2.1 mmol/L, $p<0.05$), Troponin I (0.03 ng/mll vs 0.01 pg/ml, $p<0.05$), NT-proBNP (2980 pg/ml vs 1590 pg/ml, $p<0.05$) than survivors. Non-survivors had lower absolute GLS than that of survivor group (-17.2% vs -19.3%, $p=0.045$), however, GLS was not an independent risk factor for mortality of sepsis after adjusting for clinical variables. Patients were categorized into three groups based on left ventricular ejection fraction (LVEF). GLS has good accuracy in predicting both 28-day and 90-day mortality in hyperdynamic patients (area under the receiver operating characteristic curve were 0.865 and 0.851, respectively). Cox regression analyses showed that less negative GLS was an independent predictor of mortality for septic patients with hyperdynamic LVEF.

Conclusion GLS is independently associated with mortality in hyperdynamic patients with sepsis.

Left ventricular global longitudinal strain is associated with mortality in hyperdynamic patients with sepsis

Jin Zhang, Feng-Mei Guo

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Abstract Content The association between left ventricular systolic dysfunction (LVSD) and mortality of septic patients remains unclear. The object of this study is to investigated the prognostic value of left ventricular global longitudinal strain (GLS) for sepsis.

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Conclusion GLS is independently associated with mortality in hyperdynamic patients with sepsis.

重症

染色体外环状 DNA 相关基因作为脓毒症脑病的生物标志物研究

梁云鹏、王皓飞、胡文瀚、蔡阳、黄蔚、吴晓菁、姚红红、黄英姿
东南大学

目的 本研究旨在筛选并验证 SAE 患者血浆显著差异性表达染色体外环状 DNA 相关基因（eccDNA-related differentially expressed genes，eccDEGs）表达水平差异，探讨其在 SAE 中的诊断价值。

方法 纳入东南大学附属中大医院重症医学科（intensive care unit，ICU）脓毒症患者，根据是否合并脑病将患者分为 SAE 和脓毒症非脑病（Non-SAE）两组，对两组患者进行 Circle-seq 测序，筛选 eccDEGs，同时纳入后续验证队列。通过绘制受试者特征曲线（Receiver Operating Characteristic curve，ROC）评估筛选基因诊断 SAE 的效能

结果 共纳入年龄、性别、BMI 匹配的 SAE 组 3 例，Non-SAE 组 3 例进行 Circle-seq 测序。选择差异倍数 2 倍以上基因构建蛋白互作网络筛选出 10 个备选基因：GRIN2A，DLG2，GRM5，DLGAP2，BUB1B，CENPE，DLGAP3，DLGAP4，EXO1，RACGAP1。 后续验证队列共纳入 82 例脓毒症患者，其中 SAE 患者 17 例，Non-SAE 患者 65 例， Q-PCR 验证结果发现 EXO1，CENPE 的表达在 SAE 和 Non-SAE 患者中存在显著差异（$P<0.001$）。EXO1，CENPE 诊断脑病的 ROC 分析曲线下面积分别为 86.68%，82.69%。

结论 EXO1，CENPE 可能是诊断 SAE 的潜在生物标志物

超声图像相位分析在重症患者膈肌连续厚度超声测量应用中的可靠性研究

孙晨靓[1]、周思平[3]、袁恺豪[2]、李听听[2]、赵宏胜[2]、周光泉[3]、郭凤梅[1]

1. 东南大学附属中大医院

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3. 东南大学

目的 脓毒症患者极易发生膈肌萎缩，精准评估膈肌厚度对早期发现膈肌萎缩至关重要，但传统测量方法的精准性受到挑战。本研究拟利用超声图像相位分析技术提出一种针对膈肌的连续性厚度测量法，并评价其测量可靠性，为膈肌形态的精准评估提供依据。

方法 选择 2022 年 5 月至 2023 年 3 月入住东南大学附属中大医院和南通大学附属医院重症医学科的机械通气患者为研究对象。由经超声资质培训的检查者对患者的对位区膈肌进行超声下厚度测量并记录超声图像，通过评价检查者一致性以及与 CT 膈肌厚度测量法间的可重复性，分析膈肌连续厚度测量法较传统膈肌厚度测量法的可靠性优势。

结果 研究共纳入并测量了 80 名患者的呼气末膈肌厚度，膈肌连续厚度测量法测量的检查者内部一致性和外部一致性分别为 0.972 和 0.960(均 $P < 0.01$)，传统的膈肌局部厚度测量法的检查者内部一致性和外部一致性的 ICC 值分别为 0.885 和 0.833(均 $P < 0.01$)，两种方法的可靠性等级分别为优秀和良好。与 CT 膈肌厚度测量法比较，传统膈肌厚度测量法的测值最大变异率为 18.1%，连续性测量法的测值最大变异率为 4.5%。以膈肌萎缩标准 10% 作为临床最大可接受测量误差，传统测量法有 21.3%(17/80) 的测值在最大可接受测量误差范围之外，连续性测量法的测值均在 10% 误差范围之内。

结论 超声相位分析技术可实现对膈肌图像的膈肌边缘进行精准识别。与传统测量法比较，膈肌连续厚度测量法具有更好的测量一致性和稳定性，利用该方法可更精准地发现膈肌萎缩并提升膈肌厚度评估的精度。

Ultrasound echo characteristics of respiratory muscles and weaning outcomes in mechanically ventilated patients with sepsis: a prospective observational study

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1. Zhongda Hospital Southeast University

2. Affiliated Hospital of Nantong University

Abstract Content Septic patients undergoing mechanical ventilation are at high risk of respiratory muscle injury, which can be indicated by an increase in ultrasound echo intensity. This study aims to observe the relationship between characteristic changes in ultrasound echo intensity of respiratory muscles and the outcomes of weaning from mechanical ventilation in septic patients.

Methods From July 2022 to December 2023, a prospective observational study was conducted at the Department of Critical Care Medicine of Zhongda Hospital Southeast University and the Affiliated Hospital of Nantong University, involving septic patients undergoing mechanical ventilation. Based on the weaning outcomes, patients were categorized into the successful weaning group (n=75) and the failed weaning group (n=35). Baseline respiratory muscle echo intensity and its trend were observed in both groups, evaluating the relationship between respiratory muscle ultrasound echo characteristics and weaning outcomes.

Results Patients in the failed weaning group exhibited significantly higher baseline respiratory muscle echo intensity compared to those in the successful weaning group (diaphragm: 74.26±15.94 vs 61.50±14.36, $P < 0.001$; intercostal muscles: 72.51±12.11 vs 65.96±13.63, P=0.017). Additionally, during mechanical ventilation, the incidence of increased respiratory muscle echo intensity was significantly higher in the failed weaning group compared to the successful weaning group (diaphragm: 47.3% vs 34.7%, $P < 0.001$; intercostal muscles: 33.6% vs 26.7%, P=0.024). Compared to respiratory muscle atrophy, increased respiratory muscle echo intensity was more readily detected early in patients experiencing weaning failure. Moreover, increased respiratory muscle echo intensity was associated with a decrease in the cumulative incidence of weaning when compared to decreased respiratory muscle echo intensity (diaphragm: HR=0.284, $P < 0.001$; intercostal muscles: HR=0.471, P=0.005).

Conclusion In septic mechanically ventilated patients, increased respiratory muscle echo intensity is common. This characteristics can early indicate potential respiratory muscle injury or fatigue, serving as an early warning indicator for predicting weaning outcomes or guiding assessments in periweaning period.

右美托咪定与脓毒症所致急性肺损伤患者的死亡率降低相关

张玉[1]、张建国[1]、贾昭远[1]、陶志敏[2]
1. 江苏大学附属医院
2. 江苏大学

目的 尽管研究表明使用右美托咪定（Dexmedetomidine, DEX）通过提高生存率来治疗急性肺损伤（Acute lung injury, ALI）的啮齿动物模型的益处，但关于 DEX 对 ALI 患者影响的临床研究仍然很少。通过这项研究，我们旨在更多地了解脓毒症诱导的 ALI 的潜在机制以及 DEX 对患者标准治疗的影响。

方法 208 例入住 ICU 的脓毒症 ALI 患者分为两组；即对照组（n=102）和 DEX 组（n=106）。两组患者都接受了机械通气及常规抗生素和镇静剂的治疗，但只有 DEX 组患者通过输液泵接受了 DEX 的治疗。比较两组脓毒症 ALI 患者的人口统计学信息、基线特征、实验室参数、动脉血气分析和炎症指标，以评估不同治疗途径下患者的治疗效果。

结果 年龄和男性是 ALI 发生率高的危险因素，高血压居于患者合并症中的首位。虽然基线特征（包括主要诊断和 ALI 病因）以及 APACHE Ⅱ评分和预测死亡率等预后值在两组患者之间具有可比性，但 DEX 组的多器官功能障碍综合征 MODS 的发生率和实际死亡率远低于对照组。此外值得注意的是，DEX 组血气分析有更好的表现，以 PH 值和氧合为代表，以及更好的炎症和感染反应。

结论 通过改善动脉血气和炎症反应，静脉注射 DEX 与降低住院死亡率至少部分相关。

重症

基于贝叶斯预测的万古霉素个体化给药在重症患者中的应用研究

白嘎力、文睿婷、赵慧颖、吕杰、周刚、张晓红、安友仲
北京大学人民医院

目的 AUC/MIC 为万古霉素的主要 PK/PD 靶标，国内外相关指南均推荐基于贝叶斯预测的个体化给药软件为可靠的万古霉素 AUC 预测工具，然而这些软件在重症患者中尚未进行充分评价。本研究旨在评估贝叶斯软件应用于重症患者万古霉素个体化给药的有效性和安全性，为其临床应用提供数据参考。

方法 本研究分为回顾性评价和前瞻性队列研究两部分。第一部分纳入 2020 年 1 月至 2022 年 8 月北京大学人民医院重病监护病区静脉使用万古霉素患者的相关信息，使用三种目前广泛使用或经研究认可推荐的软件进行血药浓度预测，评价软件预测能力的准确度与精密度。第二部分选择其中预测性能较好的软件于 2023 年 1-12 月应用于重症患者万古霉素个体化给药方案的制定，根据医生是否接纳软件计算方案分为采纳组和未采纳组，分析两组患者血药浓度、AUC 达标率及用药安全性的差异。

结果 回顾性研究中纳入的三种软件预测偏差在临床可接受范围，但精密度欠佳，其中 Pharmado 更接近评价标准，用于前瞻性队列研究。采纳组患者万古霉素稳态谷浓度达标率（68.8%vs34.8%）、初始方案谷浓度达标率（66.0%vs32.5%）和初始方案达标患者占比（63.3%vs29.6%）均显著高于未采纳组。AUC 达标率呈相似结果。肾毒性发生率及用药疗程上，两组患者无明显差异。

结论 贝叶斯个体化给药软件预测重症患者万古霉素血药浓度的精密度欠佳，但前瞻性应用可显著提高稳态谷浓度及 AUC 达标率和达标患者占比，是具有前景的重症患者万古霉素个体化给药工具。



专家课件

专家课件

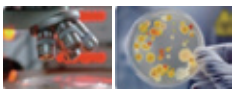
血流感染病原分子诊断靶向 NGS 初露锋芒

蔡思诗
复旦大学附属中山医院





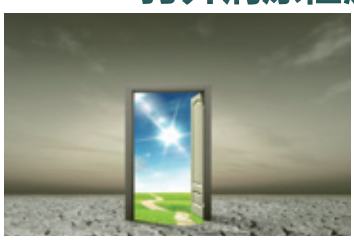
BSI临床如何选择合适的诊断工具?

	血培养检测技术	质谱技术检测	分子诊断方法	
			PCR（单重/多重）	NGS（mNGS/tNGS/探针捕获）
				
优势	血培养 • 特异性高，可进行后续体外药敏检测 血培养快速诊断技术 • 无需进行血培养后转种,缩短 TAT	• 灵敏度和特异度较高，成本低，血培养报阳后TAT短（20-30 min）,同时对病原菌耐药性也有帮助	• 敏感性, 特异性高 • 快速（2-3小时） • 可以实现定量	• 无需培养, 无需预设, 无偏好性, 靶标范围广泛 • 阳性率高, 受抗生素影响相对低, 周期适中（16-32小时） • 可用于新发或罕见病原体检测与药物敏感性预测
缺点	血培养 • 报告结果周期时间长,不能诊断难培养的病原体; 血培养快速诊断技术 • 无法进行后续的体外药物敏感试验，FilmArray 测平台可检测部分耐药基因	• 仪器要求高，基于血液培养阳性培养物 • 对某些特殊种类的细菌、分枝杆菌和丝状真菌的鉴定效果仍需提升	• 需要预设, 靶标单一 • 基于核酸, 难辨别死菌和活菌	• 需要生信分析人员 • 流程复杂，报告解读具有挑战性

[1] 上海市微生物学会临床微生物学专业委员会,上海市医学会检验医学专科分会,上海市医学会危重病专科分会,等.血流感染临床检验路径专家共识[J].中华传染病杂志,2022,40(8):457-475.
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专家课件

mNGS 打开病原检测的潘多拉星球，临床应用已经 7 年



基本概念

mNGS： Metagenomics Next-Generation Sequencing 宏基因组学二代测序。

➢ **宏基因组学（Metagenomics）：广义宏基因组是指特定环境下所有生物遗传物质的总和，它决定了生物群体的生命现象。**

➢ **广覆盖（2万多种病原），无偏倚，无需培养可直接对临床标本进行检测**

临床应用场景：
- 疑难危重感染;
- 新发罕见病原;
- 混合感染;
- 免疫缺陷患者感染;

临床适用范围：
- 呼吸道感染;
- 血流感染;
- 中枢神经系统感染;
- 局灶性感染



超广谱覆盖



➢ **探索微生物未知领域，使临床感染诊断从“预判、验证”到“无需预判”**

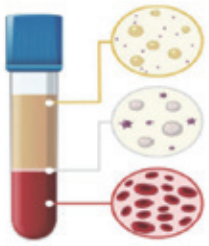
改变了临床感染病原诊断模式

专家课件

传统 mNGS 对血液标

- 血液样本通常只检测血浆层
- 也可以既检测血浆层也检测淋巴细胞层（为双流程），但是成本翻倍，患者经济负担显著增加

血液标本特点



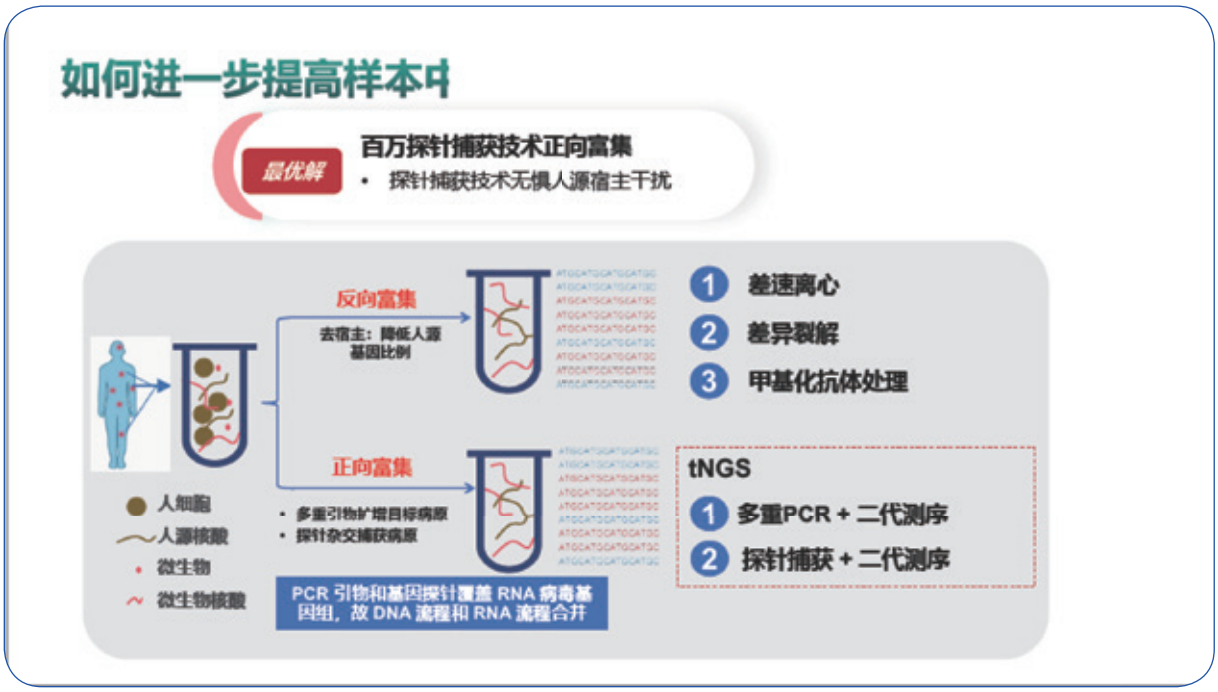
血浆层
- cfDNA占比高，相对载量低（死亡后游离核酸）
- cfDNA半衰期短、采样窗口敏感

淋巴细胞层
- 胞内病原，人源占比高，需破壁（胞内菌、厚壁菌cfDNA难释放入血，有漏检风险）

红细胞层
- 通常不检测

[1] Gu W，Deng X，Lee M，et al. Rapid pathogen detection by metagenomic next-generation sequencing of infected body fluids[J]. Nat Med. 2021 Jan; 27(1):115-124
[2] 中国宏基因组学第二代测序技术检测感染病原体的临床应用专家共识：中华传染病杂志2020年11月.




如何进一步提高样本中
最优解
百万探针捕获技术正向富集
• 探针捕获技术无惧人源宿主干扰
反向富集
去宿主：降低人源基因比例
正向富集
• 多重引物扩增目标病原
• 探针杂交捕获病原
人细胞
人源核酸
微生物
微生物核酸
PCR 引物和基因探针覆盖 RNA 病毒基因组，故 DNA 流程和 RNA 流程合并
1 差速离心
2 差异裂解
3 甲基化抗体处理
tNGS
1 多重PCR + 二代测序
2 探针捕获 + 二代测序

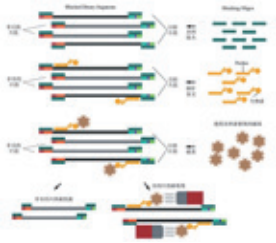

02
探针捕获法NGS病原测序技术
—MetaCAP™

专家课件

探针捕获技术临床应用的主要方向

探针捕获技术临床应用方向：

- 全外显子测序
- 活检样本中 BRCA1 和 BRCA2 基因检测
- ctDNA 中肿瘤相关标志物的筛选
- 癌症相关基因中的单核苷酸变异（SNV）和拷贝数变异（CNV）
- ……



全外显子探针捕获杂交示意图

探针捕获技术在微生物检测中应用可拓展方向：

病原体检测
- 检测低拷贝数的病原体
- 多种病原体检测

病原体鉴定分型
- 菌株分型、变异体鉴定
- 系统发育分析

基因组特征
- 基因组重排(基因获得、基因丢失)，可移动遗传元件

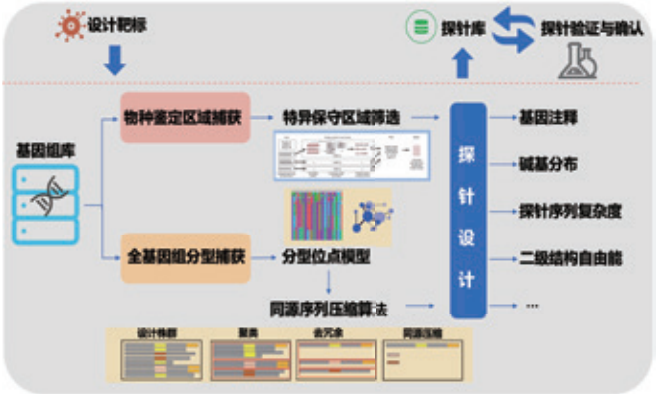
抗药性毒力基因
- 抗生素耐药或毒力基因的鉴定

[1] Singh, Rajesh R. 《Target Enrichment Approaches for Next-Generation Sequencing Applications in Oncology》. Diagnostics 12, 期 7 (2022年6月24日): 1539.
[2] Gaudin, Maxime, 和Christelle Desnues. 《Hybrid Capture-Based Next Generation Sequencing and Its Application to Human Infectious Diseases》. Frontiers in Microbiology 9 (2018年11月27日): 2924.

探针捕获mNGS——MetaCAP™（Metagenomics Capture）-

病原鉴定与全基因组探针设计

- 设计属、复合群、种、亚种等多个层级探针；
- 设计保守核苷酸多态性位点（SNP）探针，区分高度同源物种；如：肺炎链球菌等
- 构建实验筛选探针库，获得高性能探针；





基于探针捕获的靶向二代测序在血流感染中的病原学诊断性能

——上海复旦大学附属中山医院感染科胡必杰/蔡思诗团队前瞻性研究

探针捕获的靶向二代测序——tNGS
宏基因组二代测序——mNGS

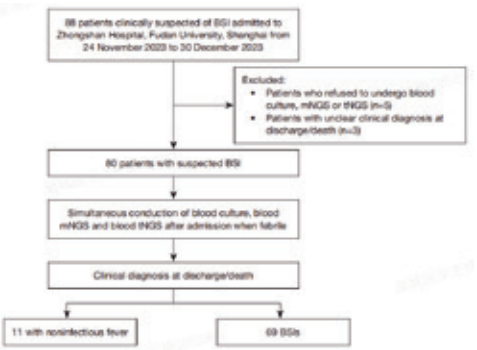
在2023年11月24日至12月30日期间，上海复旦大学附属中山医院感染科前瞻性纳入了80名疑似BSI患者。

研究方法： **方法学比较：血培养、血mNGS和血探针捕获检测；**
部分患者还进行了脓液、胸腔积液、腹腔积液、胆汁、脑脊液、尿液和痰样本的培养和mNGS检测

入院发热患者标准：88名患者入组，80名患者纳入研究，有11例患者被临床诊断为非感染性发热，而69例患者确诊为BSI

纳入标准如下： (I) 年龄≥14岁；(II) 符合全身炎症反应综合征(SIRS)的诊断标准；(III) 发热，体温≥38.5 °C；(IV) 白细胞计数(WBC)、C-反应蛋白(CRP)、红细胞沉降率(ESR)和降钙素原(PCT)，至少有一种生物标志物升高；(V) 临床上怀疑BSI的严重感染不能用局灶性感染解释。所有入院患者均年满14岁。

排除标准如下： （I）入院时发热的初始诊断为非感染性疾病，例如肿瘤和自身免疫性疾病 （II）出院/死亡时临床诊断不明确; 和（III）拒绝进行血培养、mNGS或探针捕获测序。



[1] Cai, Sishi, Jianying Yuan, Yingzhen Li, Fengming Guo, Zengshun Lin, Hongyi Li, 等. 《Etiological Diagnostic Performance of Probe Capture-Based Targeted next-Generation Sequencing in Bloodstream Infection》. Journal of Thoracic Disease, 2024年.

专家课件

谢 谢！



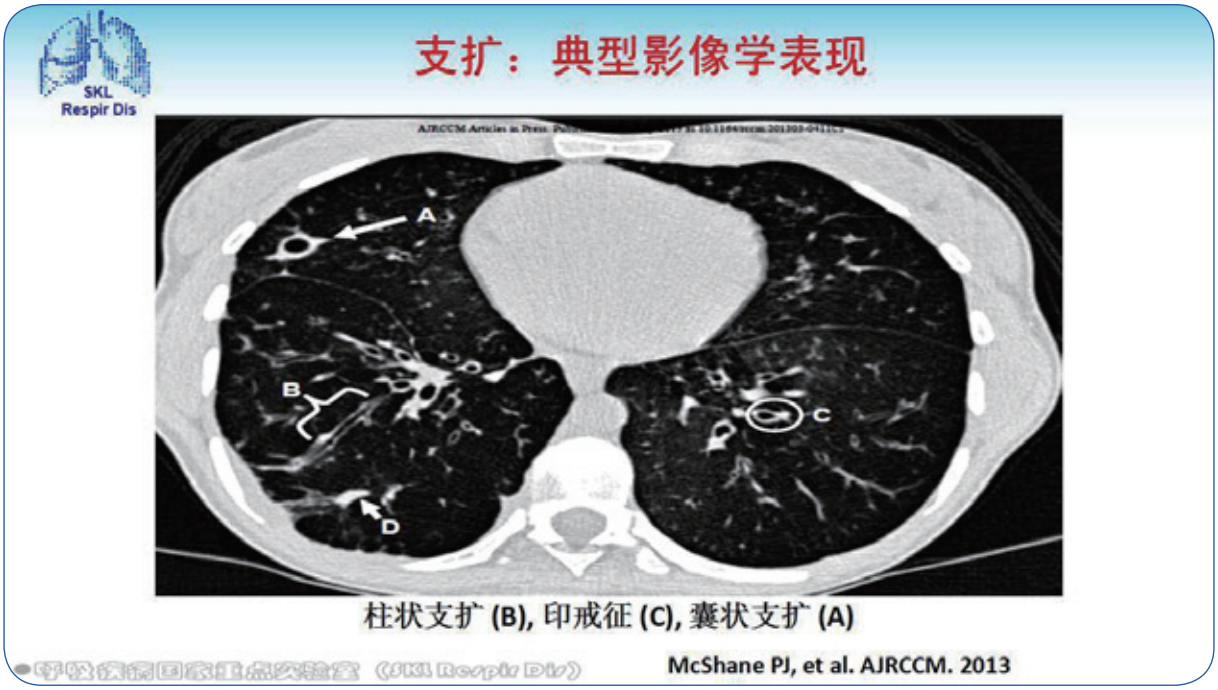
欢迎关注：SIFIC感染官微

上海中山感染探案系列

病毒感染在支气管扩张中的作用

关伟杰
呼吸疾病国家重点实验室　广州医科大学第一附属医院





专家课件

SKL Respir Dis

流行病学

⑩ 支扩：并非罕见病（患病率>5/10,000）

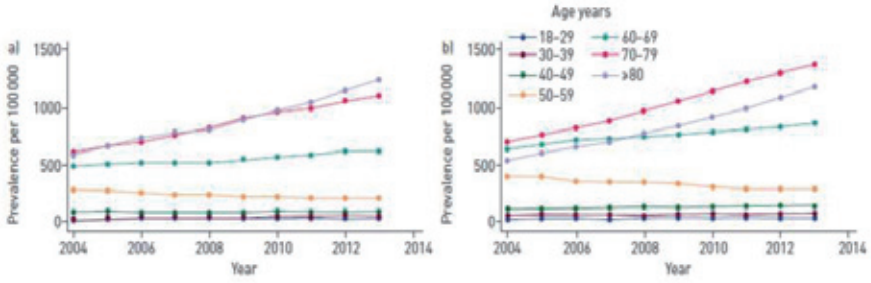


FIGURE 2 Prevalence of bronchiectasis in the UK from 2004 to 2013 stratified by age in a) men and b) women.

⑩ 我国：1.0%（问卷调查）——支扩大国

Weycker D, Clin Pulm Med. 2005
Ringshausen FC, Eur Respir J. 2015
Quint JK, Eur Respir J. 2015
周玉民，中华内科杂志. 2013

中国医科大学附属第一医院 呼吸疾病国家临床医学研究中心 (SKL Respir Dis)

SKL Respir Dis

支扩是呼吸系统常见且高负担的疾病

TABLE 1 A summary of the current evidence regarding the global economic burden of bronchiectasis

Direct expenditure
- 31.0% higher than matched controls [mean EUR 18 634.97 versus EUR 14 236.99] [16]
- USD 2319 and USD 1607 increase of overall and respiratory costs compared with matched controls [14]

Burden or expenditure for hospitalisation
- 56% higher hospital costs compared with matched controls [mean EUR 6504.37 in bronchiectasis] [16]
- 16.5 hospitalisations per 100 000 inhabitants [higher in females] [13]
- 16.52–16.99 hospitalisations per 100 000 inhabitants from 2006 to 2013 in Spain [12]
- 9.4 hospitalisations per 100 000 inhabitants in the USA [11]
- Mean USD 7 respiratory-related incremental inpatient cost compared with matched controls [14]
- Mean cost of complementary explorations: EUR 147.1 for emergency room visits and EUR 331.8 for ward management [15]
- Mean global costs: EUR 432.1 for emergency room visits and EUR 4665.9 for hospital ward stay [15]

Expenditure for treatment prescription
- Mucoactive therapies: ~5 times higher than matched controls [EUR 70.11 versus EUR 14.15] [16]
- Inhalation and home ventilation devices: ~3 times higher than matched controls [16]
- Antibiotics: significantly higher compared with matched controls [mean EUR 87 728 versus EUR 56 219] [16]
- Mean annual cost per patient: EUR 2993, EUR 4732 and EUR 9999 for mild, moderate and severe bronchiectasis [17]
- Mean annual cost per patient: EUR 2041.9 and EUR 151.2 for inhaled and oral antibiotics, and EUR 759.9 for other inhaled therapy for clinically stable and exacerbation treatment [17]

Miscellaneous
- Similar sick leave [mean 40.5 versus 45.7 days] to matched controls [16]
- Mean sick leave: 13.4 [range 3–420] days in bronchiectasis patients [15]
- Similar productivity loss [mean EUR 4230.49 versus EUR 4776.58] to matched controls [16]
- Greater length of hospital stay [mean 19.6 versus 14.8 days] compared with matched controls [16]
- 5.8% higher annualised mortality compared to matched controls [16]



Guan WJ, Eur Respir J. 2019

中国医科大学附属第一医院 呼吸疾病国家临床医学研究中心 (SKL Respir Dis)

恶性循环学说

在原发/继发病因的作用下，触发了细菌感染、气道炎症、粘液高分泌或者气道结构破坏的其中一环，导致恶性循环。最终的结果是持续的气道炎症、感染和结构破坏。



McShane PJ, et al. AJRCCM. 2013

呼吸疾病国家重点实验室 (SKL Respir Dis)

支扩细菌谱（广州地区）

INT J TUBERC LUNG DIS 19(5):610–619
© 2015 The Union
http://dx.doi.org/10.5588/ijtld.14.0613

Sputum bacteriology in steady-state bronchiectasis in Guangzhou, China

W-J. Guan,* Y-H. Gao,† G. Xu,‡ Z-Y. Lin,* Y. Tang,* H-M. Li,* Z-M. Lin,* J-P. Zheng,* R-C. Chen,* N-S. Zhong*

*State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, †Department of Respiratory and Critical Care Medicine, First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan, ‡Guangzhou First People's Hospital, Guangzhou, Guangdong, China

SUMMARY

BACKGROUND: The impact of potentially pathogenic micro-organisms (PPMs) on Chinese patients with steady-state bronchiectasis is unknown.

METHODS: Peripheral blood and sputum were sampled to determine inflammatory markers and sputum bacterial density. Spirometry and diffusing capacity were measured. Quality of life was assessed using the St George's Respiratory Questionnaire.

RESULTS: Of 144 patients with steady-state bronchiectasis, *Pseudomonas aeruginosa* was isolated in 44 cases (30.6%). Compared with other PPMs, *P. aeruginosa* had a more pronounced influence on airway inflammation and spirometry, but not on systemic inflammation or quality of life. The impact of PPMs other than *P. aeruginosa* on clinical indices was similar. Bacterial density was not correlated with most clinical parameters. Factors associated with PPM isolation included bronchiectasis symptoms for ⩾10 years (OR 2.13) and ⩾4 bronchiectatic lobes (OR 2.82). Having ⩾4 exacerbations within 2 years (OR 2.18) and cystic bronchiectasis (OR 2.23) was associated with the colonisation of PPMs, i.e., isolating an identical PPM on at least two occasions within 1 year.

CONCLUSION: In patients with steady-state bronchiectasis in Guangzhou, *P. aeruginosa* is the most common organism causing heightened airway inflammation and poor lung function. PPM isolation or colonisation should be suspected in case of longer duration of symptoms, multilobar bronchiectasis, frequent exacerbation and cystic bronchiectasis.

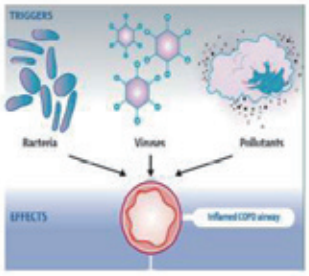
KEY WORDS: bronchiectasis; *Pseudomonas aeruginosa*; bacterial density; airway inflammation; systemic inflammation; lung function

Guan WJ, et al. *Int J Tubercul Lung Dis*. 2015

呼吸疾病国家重点实验室 (SKL Respir Dis)

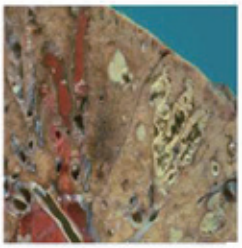
专家课件

病毒感染究竟与支扩加重是否有关？？



感染是慢阻肺急性加重最重要的因素

Jadwiga AW. Lancet 2007; 370: 786-96



支扩气道环境：
高温、低氧、营养丰富

↓

微环境改变 →



支扩急性加重

?

急性加重定义

- 目前鲜有针对支扩急性加重的研究，其定义也缺乏明确标准：



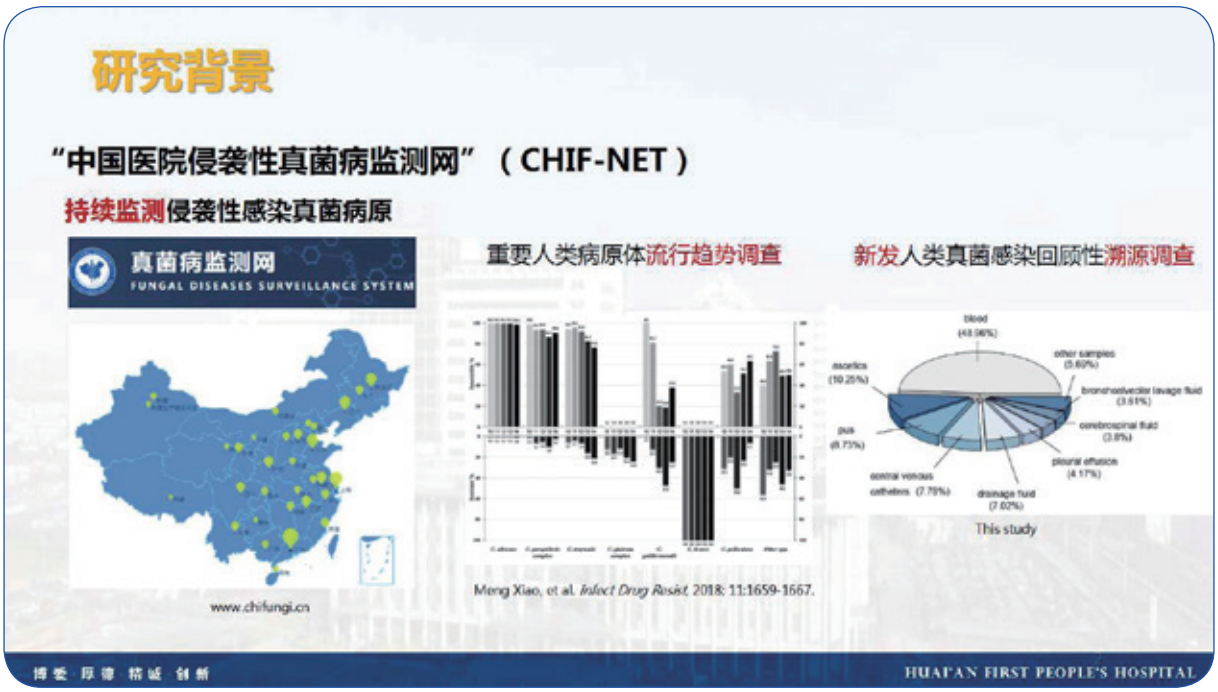
对于稳定期即有大量脓痰的支气管扩张患者，急性加重期痰量的增加及脓性并没有明显的改变，这类患者如何准确判断急性加重尚需更多研究。

Pasteur MC et al. Thorax. 2010 Jul;65 Suppl 1:i1-58.

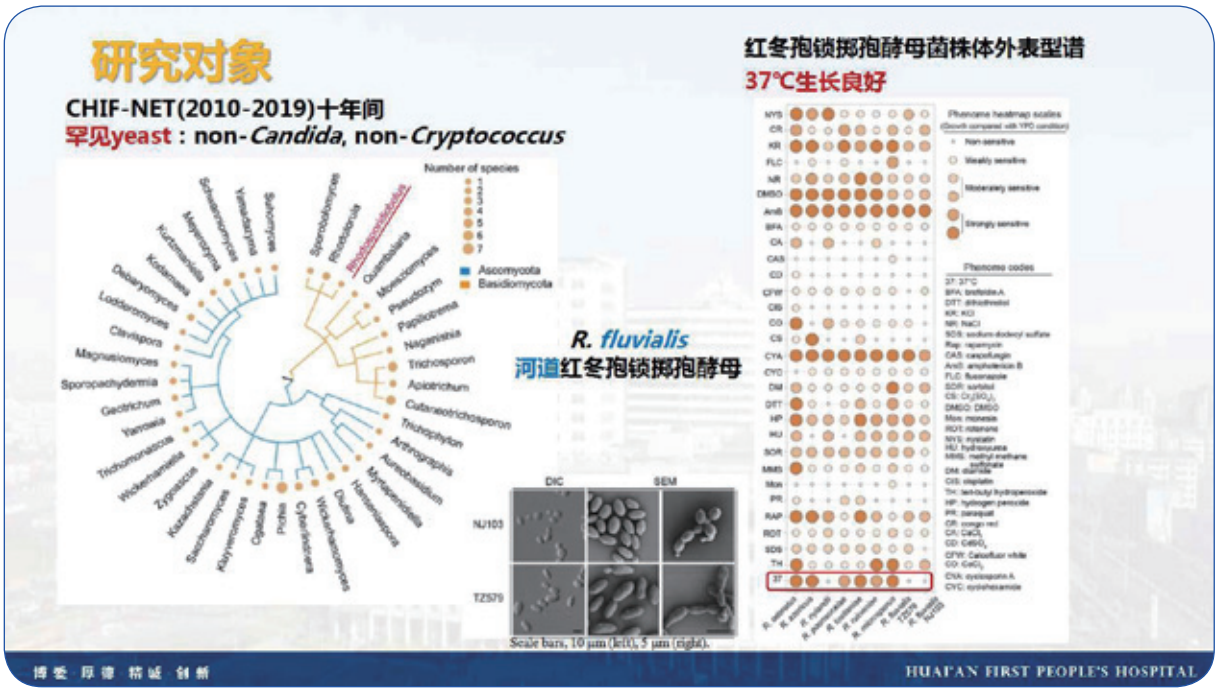
引起人类感染的环境病原真菌特征研究——Nat Microbiol 工作分享

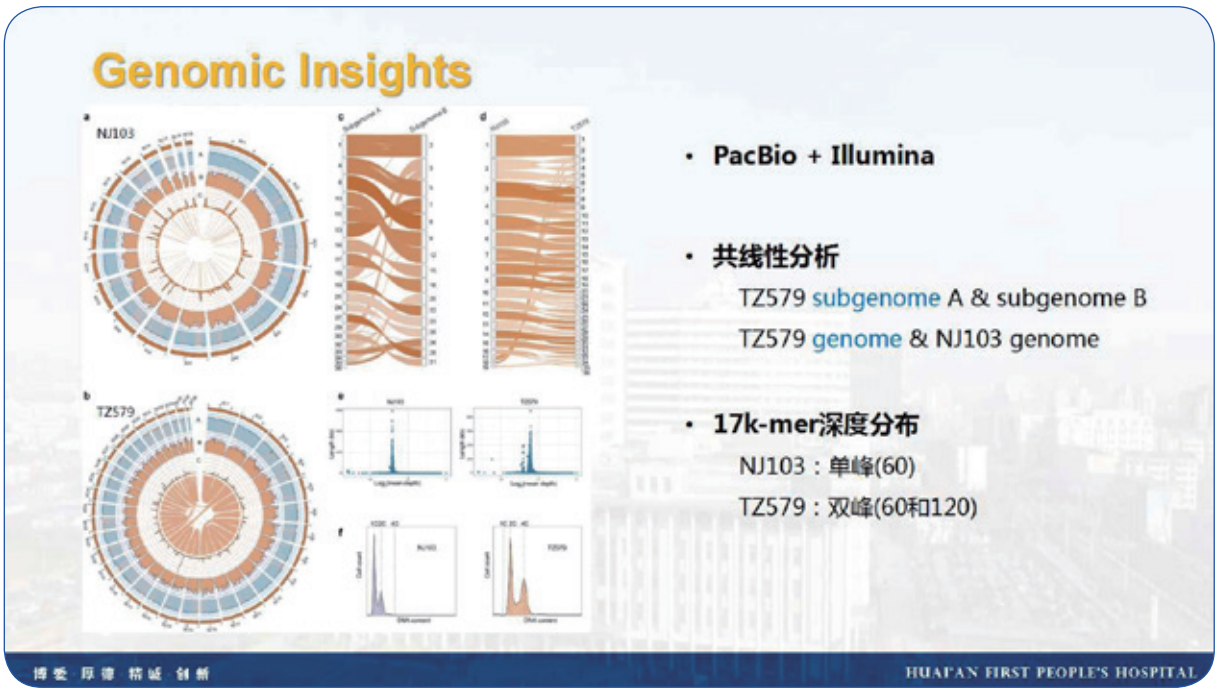
黄晶晶 胡鹏杰 叶磊鑫 徐英春 王琳淇
南京医科大学附属淮安第一医院



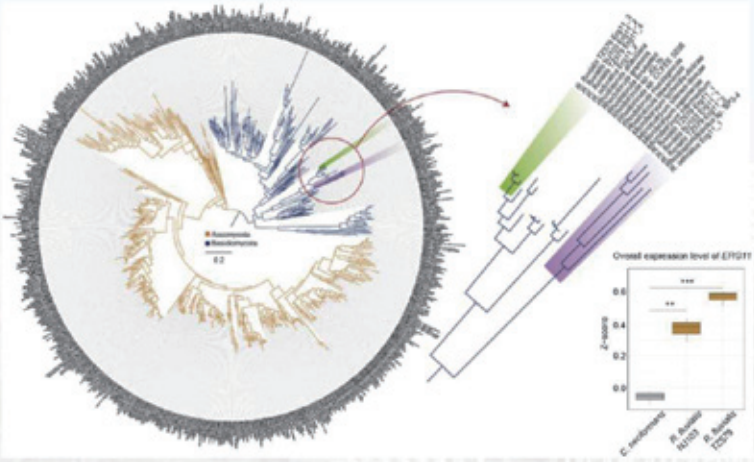


专家课件

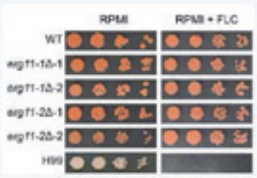

研究对象
CHIF-NET(2010-2019)十年间
罕见yeast：non-Candida, non-Cryptococcus
Number of species
Ascomycota
Basidiomycota
R. fluvialis
河道红冬孢锁掷孢酵母
红冬孢锁掷孢酵母菌株体外表型谱
37℃生长良好
DIC
SEM
NJ103
TZ579
Scale bars, 10 μm (left), 5 μm (right).
博爱 厚德 精诚 创新
HUAI'AN FIRST PEOPLE'S HOSPITAL


Genomic Insights
NJ103
TZ579
• PacBio + Illumina
• 共线性分析
TZ579 subgenome A & subgenome B
TZ579 genome & NJ103 genome
• 17k-mer深度分布
NJ103：单峰(60)
TZ579：双峰(60和120)
博爱 厚德 精诚 创新
HUAI'AN FIRST PEOPLE'S HOSPITAL

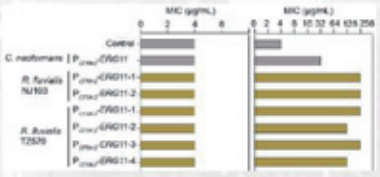
Erg11变异→氟康唑高度耐药



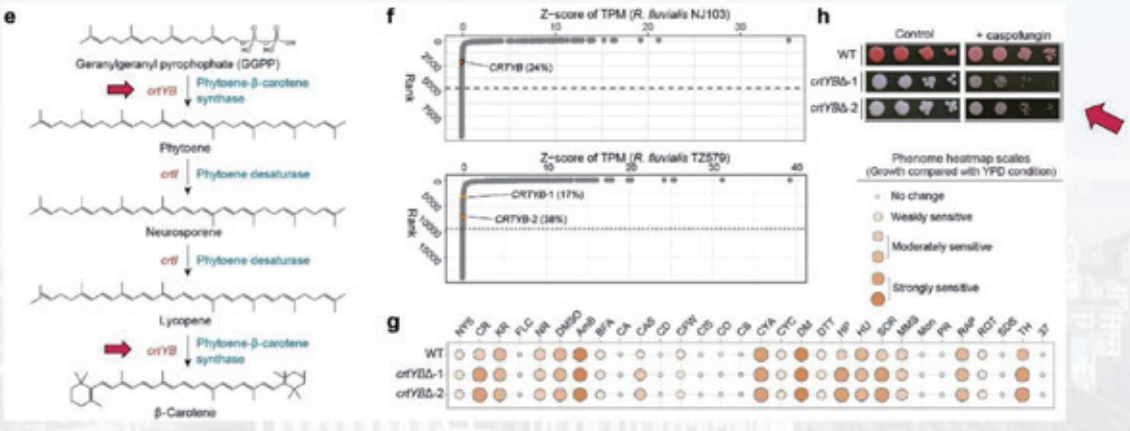
- *ERG11* 基因敲除



- Erg11异源表达

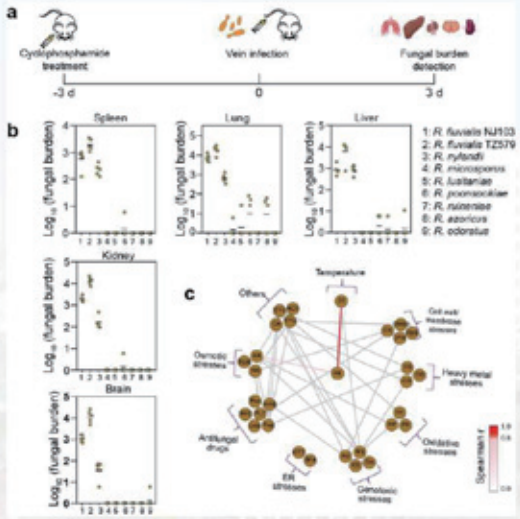


类胡萝卜素→棘白菌素耐药的基础



专家课件

37℃耐受性→在宿主内生存力



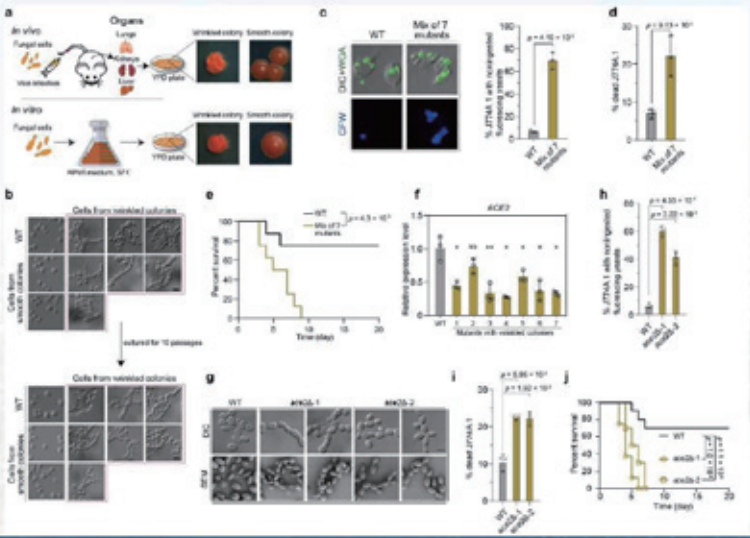
- 引发小鼠多器官侵袭性感染

  R. fluvialis > *R. nylandii* > > 其他种

- 体外+体内表型相关性分析

  37℃耐受性强→宿主内生存力强

37℃诱导假菌丝生成 增强毒力



- 褶皱菌落：假菌丝菌体细胞
- 假菌丝突变体Mix：
  - ✓ 巨噬细胞吞噬试验
  - ✓ 小鼠生存力评估
- 转录因子Ace2
  - ✓ 表达下调
  - ✓ 缺失→假菌丝生成
  - ✓ 缺失→毒力增强

感染性休克中 β 受体阻滞剂可以使用吗?

李金秀
中南大学湘雅二医院重症医学科





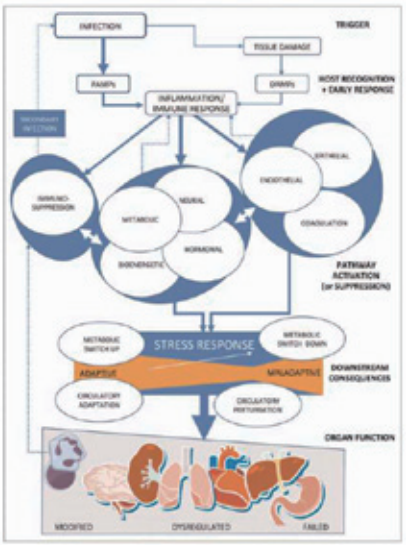
专家课件


01 脓毒症
流行病学特点
基于中国人群的脓毒症流行病学调查显示，住院患者脓毒症患病率和发病率分别为8.1%和20.6%。
基于中国ICU的脓毒症流行病学调查显示，外科ICU及综合ICU的严重脓毒症患病率分别为8.7%和37.3%，与来自欧洲的数据相近。
脓毒症是重症监护病房患者并发症和死亡率高的主要原因，脓毒症的死亡率为30%左右，脓毒性休克的死亡率为60%左右。
2004
2008
2012
2016
2021
Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012
Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016
Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021


01 脓毒症
定义
脓毒症被定义为宿主对感染的反应失调而致的危及生命的器官功能障碍
感染
SOFA>2
脓毒症
液体复苏
MAP<65
乳酸
>2mmol/L
感染性休克
脓毒症诊断标准
感染性休克诊断标准
厚仁博雅 德術求是

专家课件

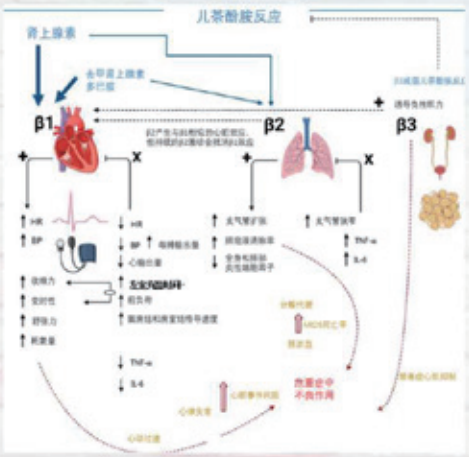
01 脓毒症 机制



免疫和内皮细胞功能障碍、神经机制受损、细胞和代谢失调、微血管功能障碍、氧输送或利用受损、内分泌病、线粒体功能障碍和跨细胞信号转导异常都与脓毒症诱导的器官损伤和功能障碍的病理生物学有关

厚仁博雅 德術求是

01 脓毒症 “过度应激反应”

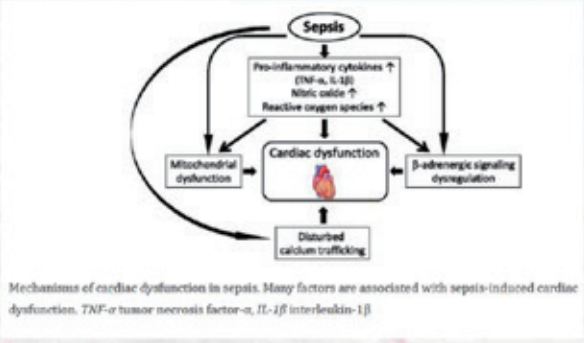


- ✓ “过度应激反应”是指应激激素一旦分泌过度，可对患者心血管、免疫及代谢系统等产生不利影响，造成自身组织器官功能损害。
- ✓ 主要表现为**儿茶酚胺**（E、NE）浓度升高。
- ✓ 脓毒性休克的早期阶段（前24小时内），其强度（反映肾上腺素能交感神经过度激活）与更高的临床严重程度和死亡率相关

厚仁博雅 德術求是

专家课件

01 脓毒症 脓毒症心功能不全



Mechanisms of cardiac dysfunction in sepsis. Many factors are associated with sepsis-induced cardiac dysfunction. *TNF-α* tumor necrosis factor-α, *IL-1β* interleukin-1β

脓毒症诱发心功能不全

- ✓ **一氧化氮和活性氧** TNF-α 和 IL-1β 是导致脓毒症心肌功能障碍的主要介质。
- ✓ **线粒体功能障碍** 在脓毒症诱导的心功能不全的发病机制中起关键作用，导致所谓的细胞病变性缺氧，可能导致多器官损伤。
- ✓ **β肾上腺素能信号失调** 在脓毒症患者中，肾上腺素能信号失调与脓毒症诱发的心功能障碍有关

厚仁博雅 德術求是

02 β受体阻滞剂 概念与作用

■ **概念：**

➢ β受体阻滞剂：是能选择性地与β肾上腺素受体结合、从而拮抗神经递质和儿茶酚胺对β受体的激动作用的一种药物类型

■ **作用：**

➢ 肾上腺素受体分布于大部分交感神经节后纤维所支配的效应器细胞膜上，其受体分为3种类型，可激动引起心率和心肌收缩力增加、支气管扩张、血管舒张、内脏平滑肌松弛等和脂肪分解

➢ 这些效应均可被β受体阻滞剂所阻断和拮抗

厚仁博雅 德術求是

Viral Pneumonia in Immunocompromised Patients

Ren Lin, Qifa Liu

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南方醫院 NAN FANG HOSPITAL

Viral Pneumonia in Immunocompromised Patients

Ren Lin Qifa Liu

Department of Hematology

Nanfang Hospital, Southern Medical University

2024.07

Outlines

- Overview
- Epidemiology
- Diagnostic strategy
- Treatment & Prevention
- Herpesviruses Pneumonia
- Community Acquired Respiratory Viruses (CARVs) Pneumonia
- COVID-19

专家课件

Overview

Overview

- **Primary infection**
  - Epidemiology & Seasonality
  - Respiratory tract infection/intestinal infection
  - Mainly RNA viruses
- **Reactivation**
  - Latent infection
  - Immunocompromised population
  - Tumorigenicity
  - Mainly DNA viruses

Epidemiology

Incidences of Viral Infections in HSCT

- **Varied in different primary diseases**
- **Herpes viruses**
  - CMV: up to 75% in HSCT
  - EBV: up to 65% in HSCT
  - HHV-6B :30-70%
  - HSV : approximately 15% with antiviral prophylaxis
  - VZV: very low with antiviral prophylaxis
- **CARVs**
  - Up to 22.3% in HSCT

Xiao J,t al. PLoS ONE 2013, 8(10): e75915. 5
Liu. et al. Journal of Hematology & Oncology 2013, 6:94
Sepkowitz ,.Clinical Infectious Diseases 2002; 34:1098–107
Sa´nchez ,et al, J Pediatr Hematol Oncol 2006;28:154–159

Diagnostic strategy

Specimens Choice

- **Blood :**
  - Viremia
  - Disseminated Diseases
- **Body fluid/Secretion**
  - BALF/CSF/Stool
  - Viral load cut-off levels have not yet been defined
- **Tissue**
  - tissue homogenate

Shimizu H, et al. Int J Hematol 2011, 94(5):495–498.
Hirsch HH, et al. Clin Infect Dis 2013, 56(2):258–266.
Styczynski J, et al. Bone Marrow Transplant 2009, 43(10):757-770
Liu Qifa, et al,Transpl Infect Dis. 2013

Prevention and Treatment: Herpesviruses

Prophylaxis

- Before HSCT: Decreasing virus loads in virus-seropositive donors and recipients
- After HSCT:
  - Routine antiviral prophylaxis
  - Pre-emptive therapy

Treatment

- Antiviral agents
- Symptomatic and supportive treatment
- Adoptive immunotherapy:
  - CMV-IgG
  - DLI

专家课件

Prevention and Treatment: CARVs

TABLE 1: Principles of Prevention and Treatment Recommendations for Hematopoietic Cell Transplant Recipients[a]

VIRUS	Prophylaxis	Asymptomatic Shedding	URTI	LRTI
RSV	• Infection control procedures • Palivizumab for children ≤2 years (during season)	• Isolation	• Isolation • Ribavirin for high-risk situations[a,b]	• Isolation • Low-risk situations: oral ribavirin[a] • High-risk situations: aerosolized ribavirin initially followed by oral[a] • Supportive care
Influenza Virus	• Infection control procedures • Vaccination of contacts • Vaccination 2-3 weeks prior to transplant in non-immunodeficiency recipients of non-myeloablative conditioning • Vaccination of HCT recipients as early as possible, depending on timing of flu season	• Isolation • Oseltamivir or Zanamivir	• Isolation • Oseltamivir or zanamivir	• Isolation • Oseltamivir or zanamivir • Consider combination therapy with rimantadine (only Influenza A) and/or ribavirin • Consider IV peramivir if mechanically ventilated • Supportive care
Parainfluenza Virus	• Infection control procedures	• Isolation	• Isolation • Consider reduction of steroid dose	• Isolation • Supportive care • Consider ribavirin if
Metapneumovirus	• Infection control procedures	• Isolation	• Isolation	• Isolation • Supportive care • Consider ribavirin if mechanically ventilated[c]
Rhinovirus	• Infection control procedures	• Isolation	• Isolation	• Isolation • Supportive care
Coronavirus	• Infection control procedures	• Isolation	• Isolation	• Isolation • Supportive care
Bocavirus	• Infection control procedures	• Isolation	• Isolation	• Isolation • Supportive care

Waghmare, et al. Blood. 2016 Mar 11

免疫功能低下肺炎使用糖皮质激素推荐

- ECIL6指南及综述：HIV患者PJP肺炎推荐使用激素(II类证据)，血液系统疾病患者的PJP肺炎不推荐使用激素。

J Antimicrob Chemother. 2016;71(9):2405-13.

Semin Respir Crit Care Med. 2020;41(1):141-157.

- ECIL7指南及综述：CMV肺炎未推荐使用激素治疗。

Lancet Infect Dis. 2019;19(8): e260-e272.

J Intensive Care Med. 2014;29(4):200-12.

- 急性及亚急性特发性间质性肺炎推荐激素治疗。

Respirology. 2016;21(5):810-20.

- 非特异性间质性肺炎也推荐使用激素治疗，但用量和疗程未确定。

Semin Respir Crit Care Med. 2016;37(3):378-94.

Viral Pneumonia and BO

Strong Association between Respiratory Viral Infection Early after Hematopoietic Stem Cell Transplantation and the Development of Life-Threatening Acute and Chronic Alloimmune Lung Syndromes

A. Birgitta Versluys,[1] John W. A. Rossen,[2,3] Bart van Ewijk,[4] Rob Schuurman,[2] Marc B. Bierings,[1] Jaap J. Boelens[1]

Alloimmune lung syndromes (allo-LS), including idiopathic pneumonia syndrome, bronchiolitis obliterans syndrome, and bronchiolitis obliterans organizing pneumonia, are severe complications after hematopoietic stem cell transplantation (HSCT). In our cohort of 110 pediatric patients, 30 had allo-LS (27.3%), 18 with ideopathic pneumonia syndrome and 12 with bronchiolitis obliterans syndrome. Multivariate analysis showed that respiratory viral infection early after HSCT is an important predictor for the development of allo-LS ($P < .0001$). This was true for all viruses tested. In multivariate analysis, allo-LS was the only predictor for higher mortality ($P = .04$). Paradoxically, prolonged administration of immunosuppressive agents because of acute graft-versus-host disease had a protective effect on the development of allo-LS ($P = .004$). We hypothesize that early infection of the respiratory tract with a common cold virus makes the lungs a target for alloimmunity.

Biol Blood Marrow Transplant 16: 782-791 (2010) © 2010 Published by Elsevier Inc.

Summary

- Viruses are most important pathogens of pulmonary complication after HSCT
- In CARVs infection, Nasopharyngeal swabs are alternative to BAL as specimen for diagnosis

专家课件

呼吸道病毒疫苗的选择

潘红星
江苏省疾病预防控制中心

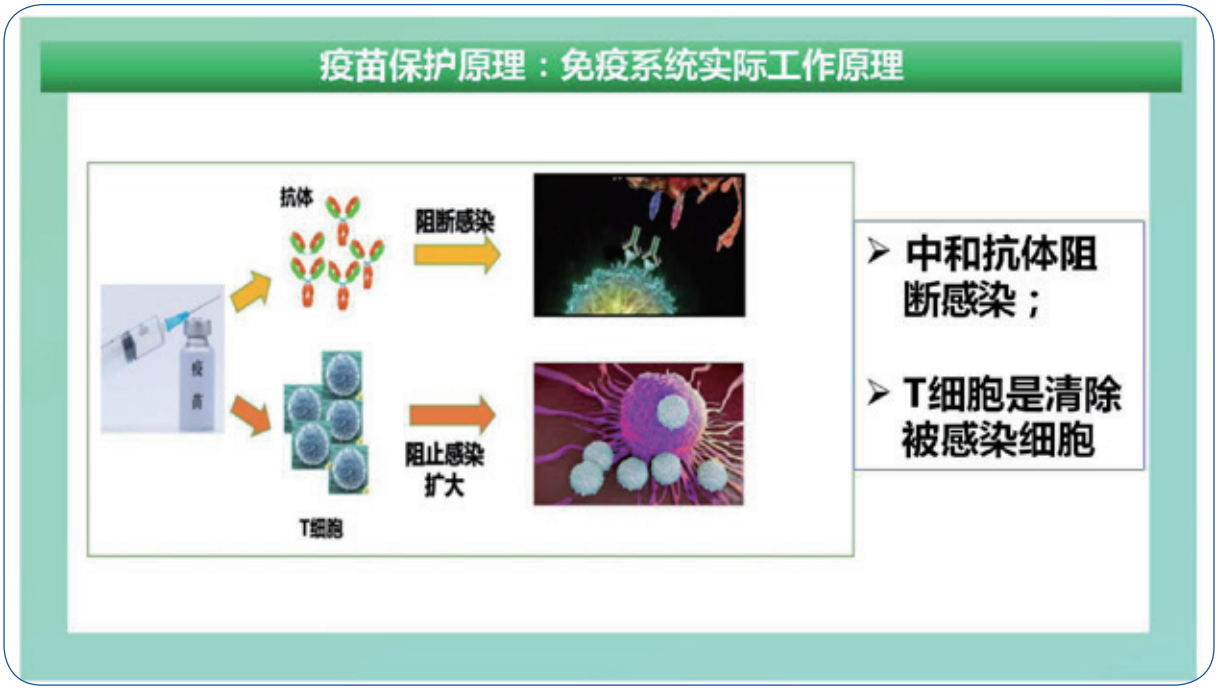


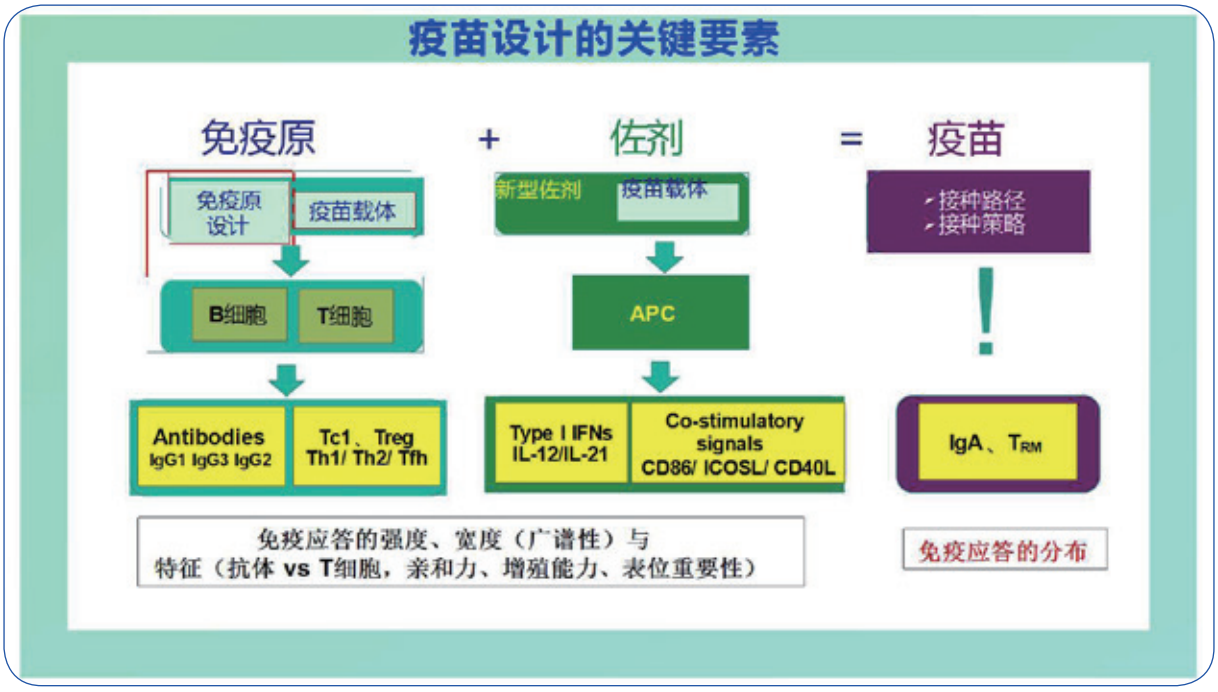



疫苗在全生命周期中均能发挥作用
特定年龄段应当接种的疫苗
百日咳疫苗
乙肝疫苗
肠炎疫苗
流脑疫苗
水痘疫苗
HPV疫苗
CMV疫苗（在研）
RSV疫苗（在研）
带状疱疹疫苗
肺炎疫苗
流感疫苗（在研）
RSV疫苗（在研）
特定人群应当接种的疫苗
治疗性疫苗（如狼卡、癌症疫苗）
癌症疫苗、自免疾病疫苗、阿尔茨海默病疫苗、代谢疾病疫苗？
应急疫苗
狂犬病疫苗、大流行疫苗（如新冠疫苗）、旅行疫苗（如黄热病疫苗）
每年都应当接种的疫苗
流感疫苗

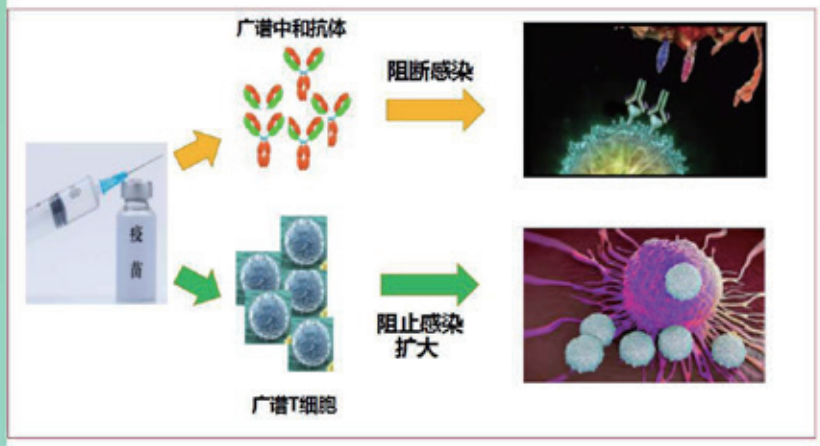

现有挑战：诸多疫苗有待升级，诸多传染病有待攻克
现有疫苗保护效果不足
卡介苗
仅能预防60%-90%的儿童重症结核病
免疫应答能力于10-20年后下降、重复接种无效
百日咳
4价次无细胞百日咳疫苗诱导的保护力仅可维持5-6年
狂犬病
现有3针，保护力不能长年维持
疫苗覆盖型别有待升级
流感疫苗
每年采用当年预测流行毒株
通用型?
HPV疫苗
2价→4价→9价→?
通用型?
肺炎疫苗
7价→13价→20价→?
通用型?
冠状病毒
SARS、MERS、SARS-2、?
通用型?
更多联苗可减少接种剂次
许多引起严重后果的病原体仍无疫苗可防
排名
疾病
主要病原体
伤残调整寿命年（万年）
占所有死亡比重
1
下呼吸道感染
肺炎球菌、b型流感嗜血杆菌、呼吸道合胞体病毒等
10565
4.2%
2
腹泻
大肠杆菌、诺如病毒、轮状病毒
7901
3.1%
3
结核病
结核杆菌
6602
2.6%
4
寄生虫病及媒介传播病
蛔虫、狂犬病、登革热、血吸虫、淋巴丝虫
4654
1.8%
5
HIV/AIDS
HIV
4015
1.6%
6
儿童聚集性疾病
麻疹、百日咳、破伤风、白喉
2820
1.1%
7
脑膜炎
肺炎链球菌、脑膜炎球菌、b型流感嗜血杆菌、肺炎球菌、结核杆菌等
1601
0.6%
8
上呼吸道感染
流感病毒、呼吸道合胞体病毒、腺病毒等
838
0.3%
9
HIV以外的性传播疾病
梅毒、衣原体、淋球菌等
525
0.2%
10
肝炎
甲肝、乙肝、丙肝等
451
0.2%
某些病原体难以研发出有效的原因
1 致病机制复杂
2 具有较大的变异性
3 进化出了免疫逃逸机制

专家课件


疫苗保护原理：免疫系统实际工作原理
抗体
阻断感染
疫苗
阻止感染
扩大
T细胞
中和抗体阻断感染；
T细胞是清除被感染细胞


疫苗设计的关键要素
免疫原
+
佐剂
=
疫苗
免疫原设计
疫苗载体
新型佐剂
疫苗载体
接种路径
接种策略
B细胞
T细胞
APC
Antibodies
IgG1 IgG3 IgG2
Tc1、Treg
Th1/ Th2/ Tfh
Type I IFNs
IL-12/IL-21
Co-stimulatory signals
CD86/ ICOSL/ CD40L
IgA、TRM
免疫应答的强度、宽度（广谱性）与特征（抗体 vs T细胞，亲和力、增殖能力、表位重要性）
免疫应答的分布

免疫原设计的原理与关键技术

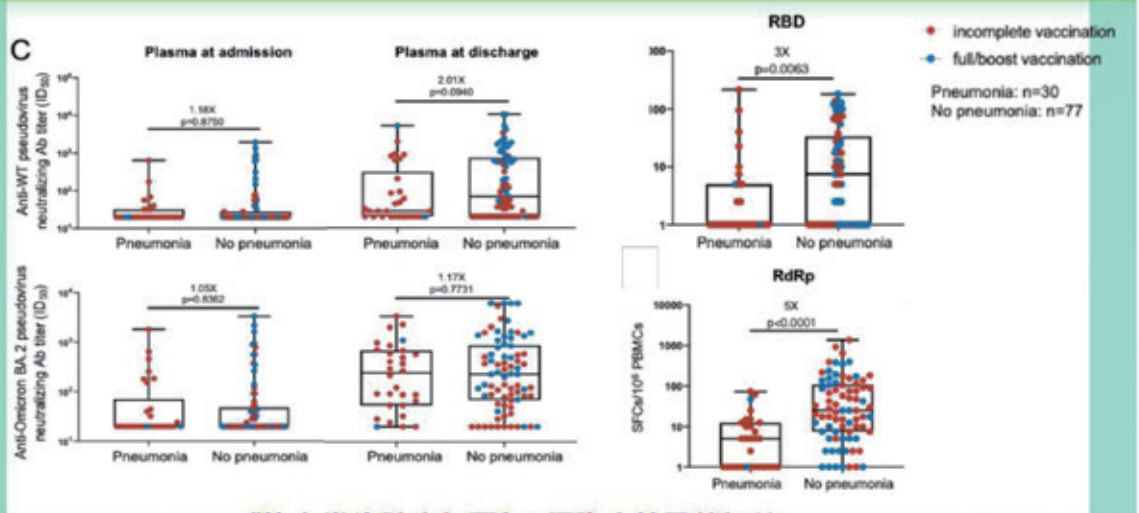


- B细胞免疫原 —活化针对病毒保守表位的广谱中和抗体
- T细胞免疫原 —利用生物信息学技术，对一种病毒的所有毒株和亚型进行分析，获得多种非结构蛋白的保守序列，预测其中的过敏性序列进行删除，获得最终的广谱保守的T细胞免疫原

Nature Communication. 2018;9(1):1772
Journal of Genetics and Genomics. 47, 115-117

训练免疫（Trained immunity）：提供辅助性保护

新冠BA.2的感染时发生肺炎与免疫应答



感染者发生肺炎与否与T细胞应答显著相关

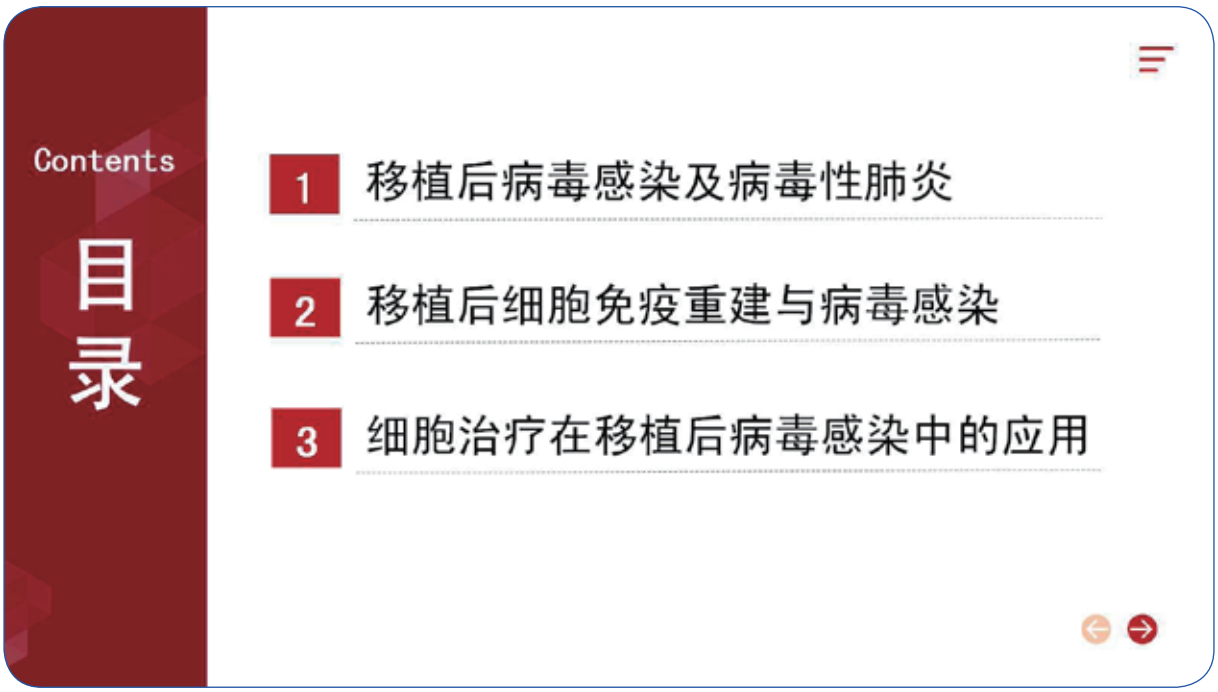
EMI. 2023

专家课件

细胞治疗在病毒性肺炎治疗中的作用

裴旭颖
北京大学人民医院 / 北京大学血液病研究所 , 国家血液系统疾病临床医学研究中心





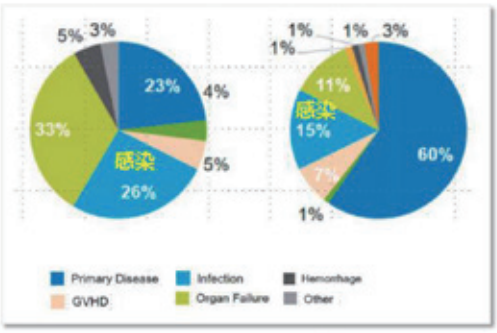
PART 1

移植后病毒感染及病毒性肺炎

病毒感染是导致移植失败的临床难题

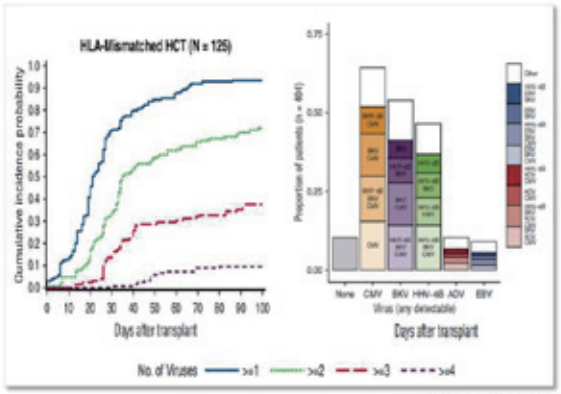
造血干细胞移植后死因分析

- 早期因感染死亡占比：26%
- 晚期因感染死亡占比：15%



Huang XJ, et al.,Blood, 2012, Data from CIBMTR 2021, Data from CBMTR 2022

- 单倍型移植后单一病毒感染率：>90%
- CMV、EBV是移植后最常见的感染病原



Hill JA et al., Blood, 2017.
Liu J, et al.,Clin Microbiol Infect, 2015
Roy F. Chemaly,et al.,Clin Infec Dis, 2019

专家课件

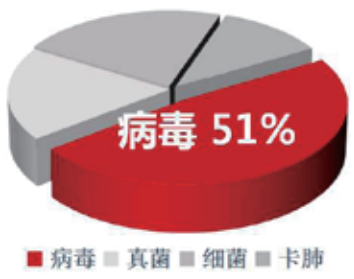
移植后肺部并发症的病因



Chi AK et al. *Chest* 2013

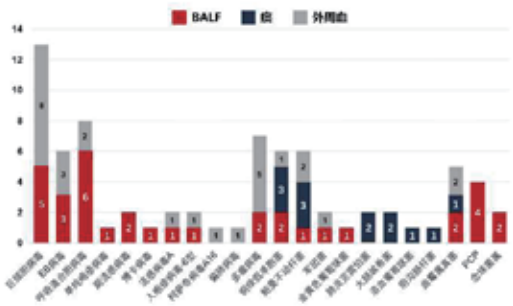
移植后肺炎病原检出率及病原类型

移植后肺炎BALF病原检出率



- 130例Allo-HSCT肺炎患者接受149例次BALF检测，89例次病原学检测阳性，阳性检出率58%
- 呼吸道病毒检出例数最多，占病毒的53%；其次疱疹类病毒，占病毒的38%

肺炎患者检测样本及病原类型



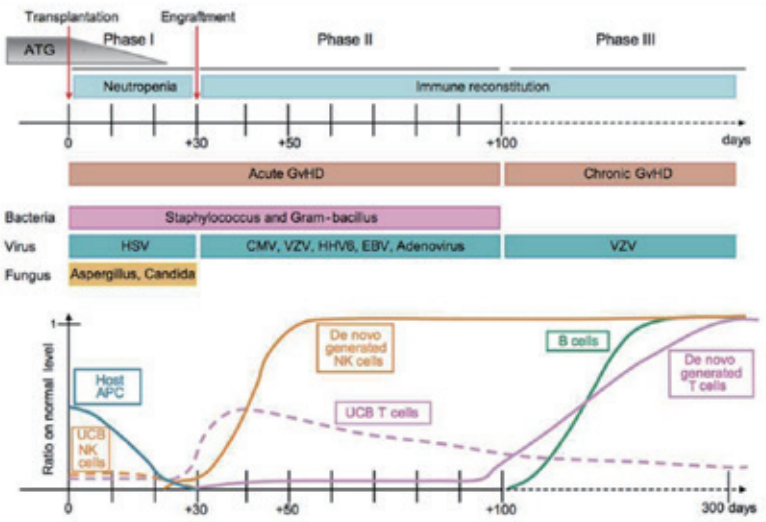
- 100例LOSP患者病原检出分布，BALF标本52例，痰及外周血标本48例
- 55例病原检出阳性，最常见的是病毒（27例）

Tang FF,...X-J Huang* et al., *Clinical Transplantation* 2018
Cao LQ, ...X-J Huang* et al. *Transplant Cell Ther.* 2021

PART 2

移植后细胞免疫重建与病毒感染

移植后细胞免疫重建延迟是病毒感染发生的关键因素



危险因素

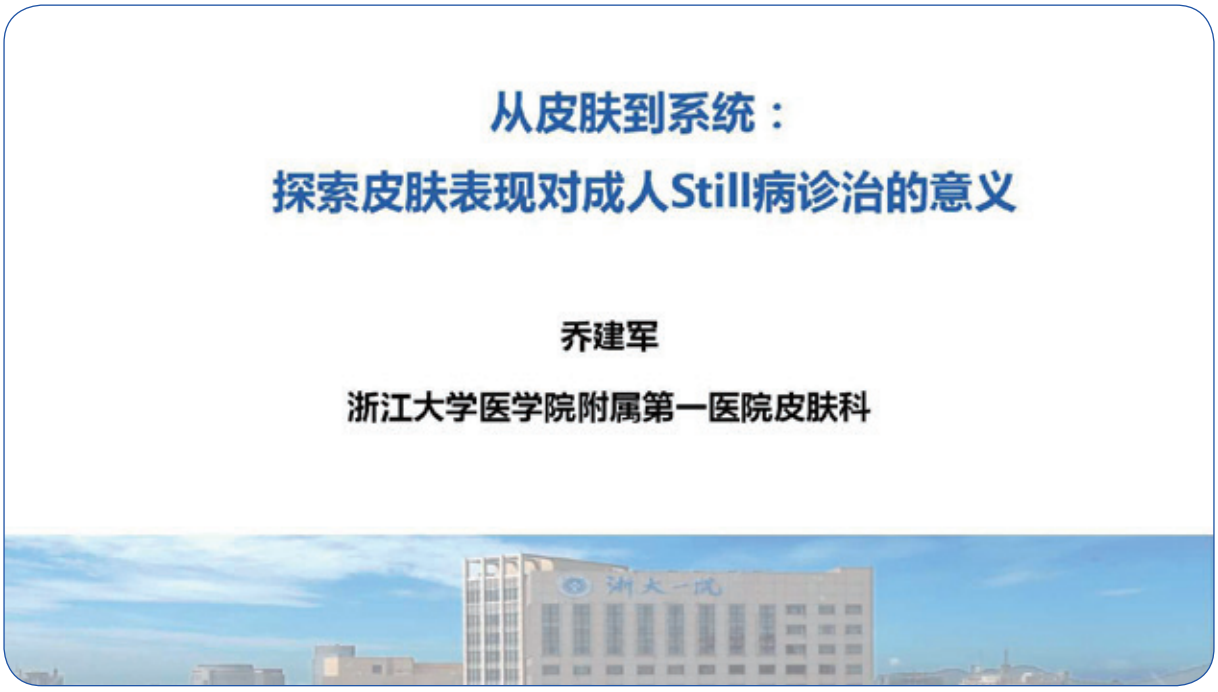
- 移植类型
  自体 vs 全合 vs 单倍型
- 干细胞来源
  PB vs BM vs CB
- 预处理方案
  RIC vs MAC
- GVHD等并发症发生及防治

Robert Danby, Front. Immunol, 2014

专家课件

从皮肤到系统：探索皮肤表现对成人 Still 病诊治的意义

乔建军
浙江大学医学院附属第一医院皮肤科







浙江大学附属第一医院



浙江大学附属第一医院

发热伴皮疹的辅助检查

感染？		
白细胞	19.5×10⁹/L	4-10×10⁹/L
中性粒细胞	88.8%	50-70%
淋巴细胞	4.0%	20-40%
CRP	191.6mg/L	<8mg/L

抗链球菌溶血素“O”：无殊
血培养4次，骨髓培养1次

当地医院头孢
入院后亚胺培南/西司他丁钠*6天

免疫？	
ANA	1:20
dsDNA ,Sm	阴性
SSA，SSB	阴性
类风湿因子	< 20.0U/ml
ESR 98mm/h	<20mm/h

肿瘤？	
腹部B超	无殊
肺部CT	无殊
甲状腺，乳腺	无殊
骨髓穿刺活检	无殊
肿瘤标志物	铁蛋白 13302.4ng/mL

仍反复发热，咽痛，关节痛



浙江大学附属第一医院

成人Still病的持久性瘙痒性皮损

- 瘙痒剧烈
- 条状分布，鞭笞样皮损
- 同形反应阳性
- 发热与皮损的消长之间没有相关性
- 红色、褐色，少数为紫色
- 部分表面有黄白色鳞屑



Kaur S, et al. *Dermatology*. 1994;188(3):241-242.
Lubbe J, et al. *Br J Dermatol*. 1999;141(4):710-713.
Lee JY, et al. *Semin Arthritis Rheum*. 2012;42(3):317-326.
Sun NZ, et al. *J Am Acad Dermatol*. 2015;73(2):294-303.
Qiao J, et al. *Am J Med Sci* 2016; 352:540-1.

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成人Still病

临床特征	实验室检查	严重并发症
• 发热 • 典型皮损（typical rash） • 关节炎/关节痛 • 咽痛 • 淋巴结肿大/肝脾肿大 • 心包炎、心肌炎、胸膜炎、肺部疾病	• 白细胞增高（N>80%） • 铁蛋白升高 • 肝功能异常 • 血沉、C反应蛋白增高 • 类风湿因子、抗核抗体阴性	• 心包填塞、心肌炎、急性呼吸综合征 • 肺动脉高压 • 爆发性肝炎 • 巨噬细胞活化综合征 • DIC/血栓性微血管病

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Bywaters, EG. Still' s disease in the adult. *Ann Rheum Dis* 1971; 30,121-133.
Gerfaud-Valentin M, et al. *Autoimmun Rev* 2014;13(7):708-722.
Feist E, et al. *Nat Rev Rheumatol* 2018;14(10):603-618.
Li S, et al. *Clin Rev Allergy Immunol* 2020; 58: 71-81.

成人Still病的经典皮损--一过性皮损



发热时出皮损



热退时皮损消退

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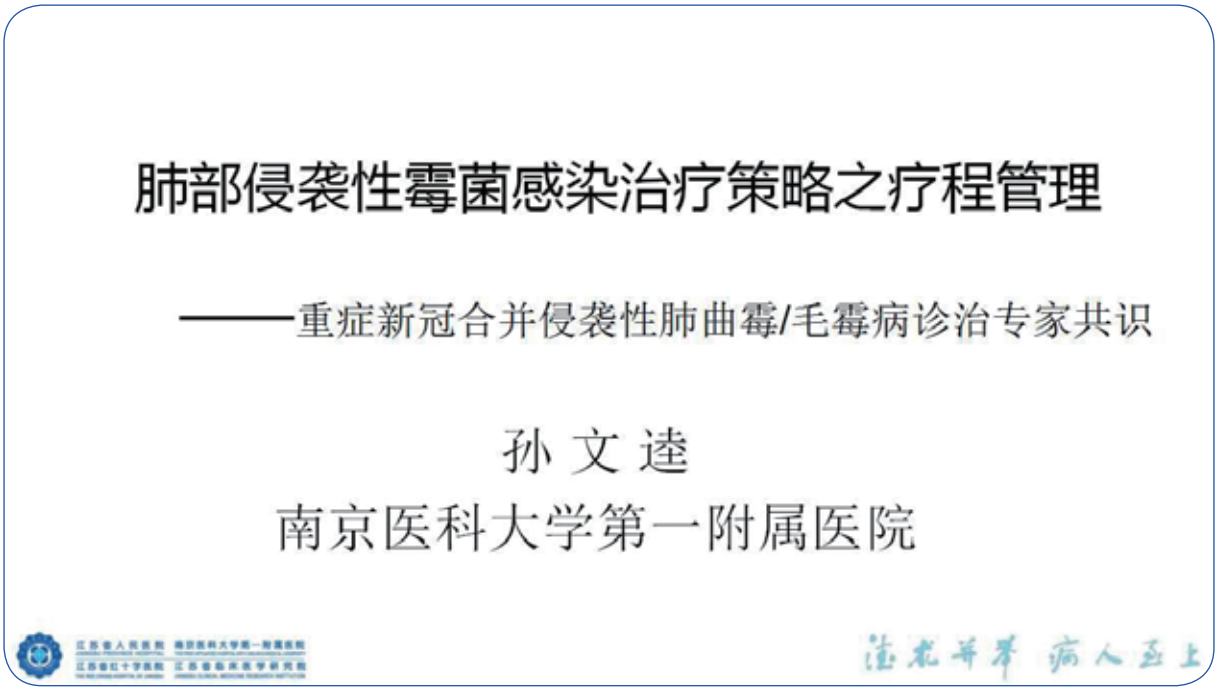
无明显瘙痒

赵辨主编. 中国临床皮肤病学.第2版. 江苏科学技术出版社. 2017年
Blognia J, et al. *Dermatology*. 4th ed. 2017

专家课件

肺部侵袭性霉菌感染治疗策略之疗程管理
——重症新冠合并侵袭性肺曲霉 / 毛霉病诊治专家共识

孙文逵
南京医科大学第一附属医院

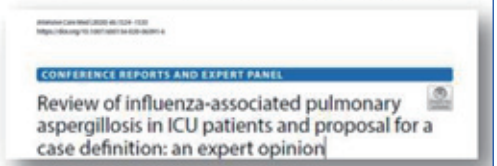




流感纳入肺曲霉病（IAPA）宿主因素



流感合并侵袭性肺曲霉病（IAPA）疾病定义发布[7]



- **EORTC-MSG ICU（2021）工作组将其纳入IAPA临床诊断宿主因素**
  - 定量或定性中性粒细胞异常（原发性中性粒细胞缺乏，中性粒细胞绝对计数≤500 cell/mm³）
  - 血液恶行肿瘤/造血干细胞移植受者
  - 糖皮质激素治疗剂量≥20mg/d的强的松等效剂量
  - 既往90天内接受常用免疫抑制剂治疗（如，钙调神经磷酸酶或人体靶向雷帕霉素（mTOR）抑制剂，肿瘤坏死因子（TNF）阻滞剂,以及干扰抗真菌免疫通路药物，阿仑单抗，依鲁替尼，核苷类似物）
  - 实体器官移植受者
  - 慢性气道病变（慢性阻塞性肺疾病（COPD）,支气管扩张）
  - 失代偿肝硬化
  - HIV 感染患者
  - **重症流感（或其他严重病毒性肺炎，如COVID-19感染）**

- 流感合并肺曲霉病（IAPA）定义逐渐清晰
- 定义：
- 表现为流感相关肺曲霉病(IAPA)的患者可能具有典型的欧洲癌症研究和治疗组织(EORTC)/真菌病研究组教育和研究联盟(MSGERC)定义的宿主因素
- 大部分患者被认为是IPA的低风险患者，包括以前健康的人
- 其临床和影像学表现通常不典型

7. Verweij PE, et al. Intensive Care Med. 2020 Aug;46(8):1524-1535.
8. Matteo Bassetti, Et al. Clin Infect Dis. 2021 Mar 12;72(Supplement_2):S121-S127.

流行病学



- 研究报道的重症COVID-19患者CAPA患病率为**2.4%~34.3%** [3-4-5-6]；
- 有创机械通气患者CAPA患病率**3.2%~37.2%** [6-7-8]；
- **CAPA主要病原体以烟曲霉为主，其次是黄曲霉** [1，6，9，10]；
- 重症CAPA预后差，病死率高达**22.2%~71.4%** [4,-5-6]
- 世界范围内CAM多为散发报道，仅印度出现流行 [11]；
- 印度一项多中心回顾性研究显示住院COVID-19患者CAM患病率为**0.27%** [12]，重症COVID-19患者CAM患病率为**1.6%**。
- 印度报道CAM病例中主要以鼻-眶毛霉病为主，病死率**13%** [14]，播散性CAM、CAPM、脑CAM均为个案报道，临床结局差异较大，有报道病死率高达**49%** [13-14]；
- 法国、德国、墨西哥、土耳其报道ICU中CAM患病率为**0.3%~0.8%** [13]；

专家课件

疗效评估——临床表现、影像学、实验室检测是评估疗效的主要指标

- **临床表现：**
  - 侵袭性肺曲霉病患者：干咳、胸膜性胸痛、发热、咯血和呼吸困难等是IPA患者的常见临床表现[1]
  - 肺毛霉病患者：常表现为持续高热、咳嗽、可伴咯血和胸痛、抗细菌治疗无效，早期呈进行性非特异性支气管炎表现[2]
- **CT影像学：**CT的连续评估已被普遍用于肺真菌感染患者的疗效监测；但临床中需要重视不同患者的影像学变化（如：中性粒细胞减少患者中CT检测病变可能随粒细胞恢复而增加），及由其他伴随感染或非感染疾病导致的非特异性改变[3-4]
- **实验室检测：**一项关于调整抗真菌治疗方案的全球专家共识提出，将BALF-GM滴度值由临界阳性或阴性转为阳性，作为8-14天时患者一线抗真菌治疗方案调整的因素；但BALF-GM滴度值的改变可能来自于标本采集得差异，因此BALF-GM滴度值间的比较应通过必要的矫正和标准化的采集[4]

住院期间的疗效评估

出院后的疗效评估

临床表现 | 影像学检查 | 微生物学检测

1. [illegible] 2. 中国医师协会真菌病专业委员会. 中华内科杂志, 2023,62 3. Bassetti M et al. Curr Opin Crit Care 2020; 26:466–472
4. [illegible] 1 Dec 24;77(1):16-23. 5. Patterson TF et al. Clinical Infectious Diseases 2016;63(4):e1–60.

抗真菌治疗反应评估及疗程


重症新型冠状病毒感染合并侵袭性肺曲霉和肺毛霉病诊治专家共识

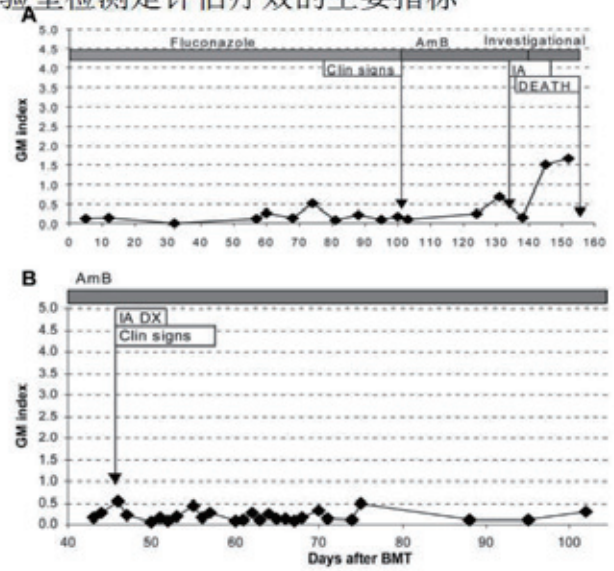
【推荐意见12】推荐根据患者的临床症状/体征、影像学及微生物学检查综合评估治疗反应，CAPA可结合血清GM的动态变化进行评估。

★CAPA患者中，血清GM下降提示治疗有效，血清GM升高提示治疗失败可能[82-83]。但血清GM会受到抗真菌药物的影响[84]，不能独立作为判断疗效的指标。

疗效评估——临床表现、影像学、实验室检测是评估疗效的主要指标

血清GM下降提示治疗有效，血清GM升高提示治疗失败可能

- 在接受骨髓移植的87例患者的986份血清样本中检测了GM EIA的性能。
- 其中：
  - 4例感染存活患者在开始抗真菌治疗后，GM EIA指数明显下降；
  - 5例感染死亡患者中有4例GM 水平持续上升。
- 接受抗真菌药物的EIA动态变化与治疗结果之间存在相关性。



Marr, et al. The Journal of Infectious Diseases 2004; 190:641–9

图：侵袭性曲霉病4例死亡和4例存活患者的血清GM指数变化。

血清GM会受到抗真菌药物的影响

Major caveats	1,3 β-D-glucan (BDG)	Galactomannan (GM)
Cross-reactivity	*Pneumocystis jiroveci*, *Coccidioides immitis*, *Fusarium* sp., *Histoplasma capsulatum*, *Candida* sp., *Acremonium*, *Trichosporon* sp., *Sporothrix schenckii*, *Saccharomyces cerevisiae*, *Aspergillus* sp.	*Aspergillus* sp., *Fusarium* sp., *Paecilomyces* sp., *Penicillium* sp., *Acremonium* sp., *Alternaria* sp., *Wangiella dermatitidis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Cryptococcus neoformans*, *Emmonsia* sp.
False positive results	Semi-synthetic β-lactam antibiotics[a] Hemodialysis or hemofiltration with cellulose membranes Blood stream infections with bacteria (e.g.,*Pseudomonas aeruginosa*) Transfusions of blood or blood-derived products filtered through cellulose membranes Exposure to gauze (specifically packing of serosal surfaces) IV Immunoglobulin infusion Albumin infusion	Semi-synthetic β-lactam antibiotics[a] Severe mucositis or Severe gastrointestinal graft versus host disease Blood products collected using Fresenius Kabi bags Multiple myeloma (IgG type) Plasmalyte used in BAL Cotton swabs Colonization (particularly in lung transplant recipients) Flavored ice-pops/frozen desserts containing sodium gluconate
False negative results	Concomitant use of antifungal prophylaxis or therapy	Concomitant use of antifungal prophylaxis or therapy

假阳性：

- 半合成青霉素，复方电解质溶液，交叉反应；
- 标本器皿污染，摄入含大豆蛋白类食物，双歧杆菌肠道内定植。

假阴性：

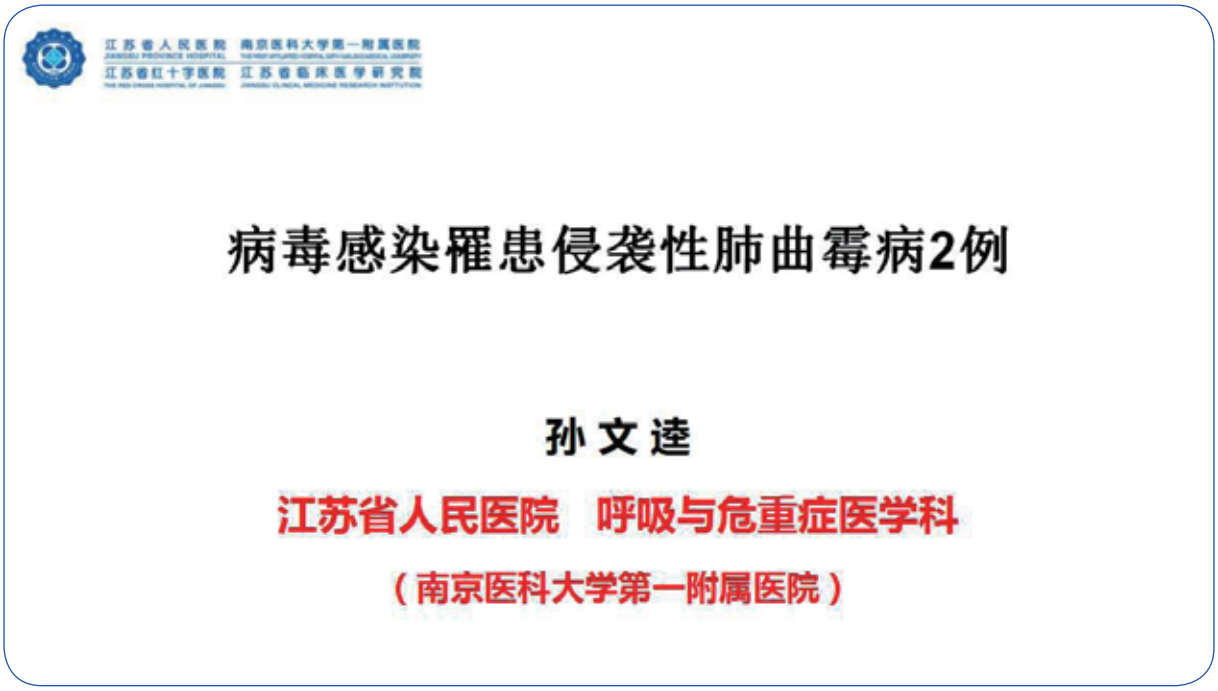
- 有效抗曲霉治疗后，敏感性下降。研究显示GM试验敏感性从89%降至52%。

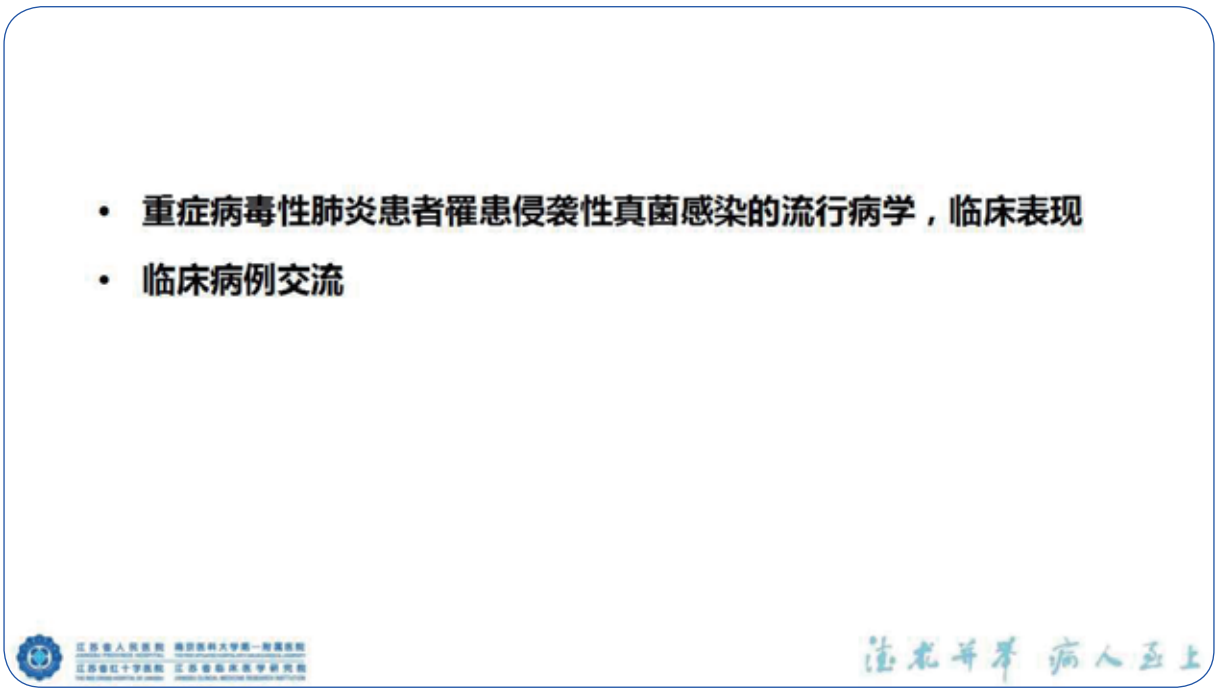
Miceli. et al, Semin Respir Crit Care Med 2015;36:650–661.

专家课件

病毒感染罹患侵袭性肺曲霉病 2 例

孙文逵
江苏省人民医院 呼吸与危重症医学科
（南京医科大学第一附属医院）





病毒性肺炎继发曲霉病--一个久远的话题

- 70年前的病例揭示了流感下IPA的风险
  - **Necrotising aspergillosis complicating fulminating viral pneumonia**

Jariwalla AG等人[2]在Thorax杂志上报道了1例1957年因爆发性病毒性肺炎患者继发坏死性曲霉病的死亡病例。患者为14岁学生，无明显基础疾病。因流感症状接受抗生素治疗无效后入院。入院后患者病情加重死亡，尸检中发现患者肺部巨大的出血性实变伴坏死病灶（如图1）。在组织病理检查中发现，肺部组织在病毒性肺炎的背景下伴有弥漫性坏死性曲霉病的病理表现（如图2）。

这是早期关于病毒性肺炎继发侵袭性曲霉病的案例。



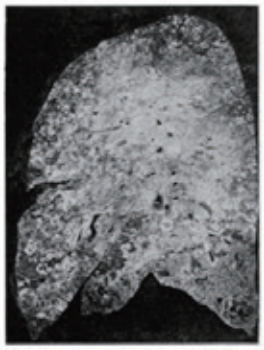


Fig. 1 Cut surface of the lung showing a background of haemorrhagic consolidation with numerous necrotic foci 1 cm to 3 cm in diameter. Some of the larger foci show central cavitation.

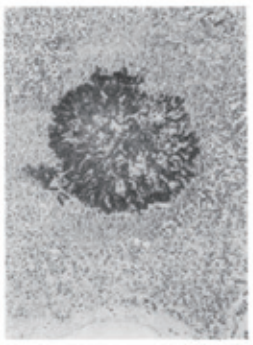


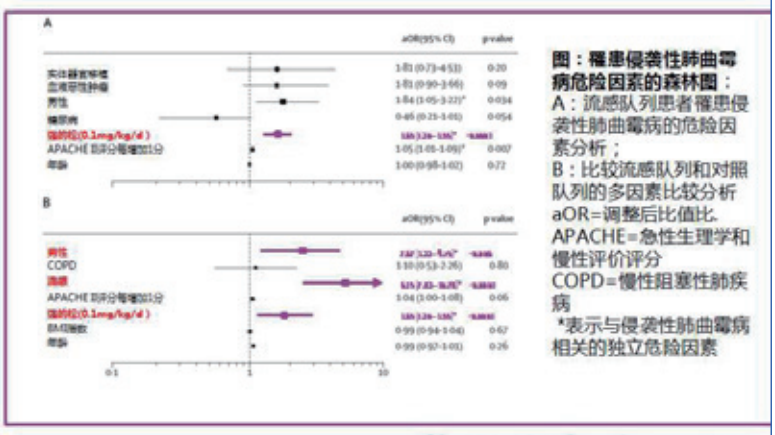
Fig. 2 Mycelial colonies of A fumigatus in necrotic lung tissue. PAS, original magnification ×70.

2Jariwalla AG et al. Thorax. 1980 Mar;35(3):215-6.

重症流感vs 非流感 -ICU队列研究

- **流感是罹患IPA的独立危险因素**
- 一项回顾性队列研究:2009年-2016年期间共纳入432位入住ICU（>24小时）流感患者（流感组），2009-2017年纳入的315位排除流感感染的社区获得性肺炎患者（对照组）进行影响因素回归分析.
- **结果显示：重症流感入住ICU患者IPA发病率为19.2%** (83/432,不同中心发病率介于6-26%）；**流感（aOR 5.19; 95% CI 2.63–10.26; p<0.0001）是罹患侵袭性肺曲霉病的独立危险因素**

Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study



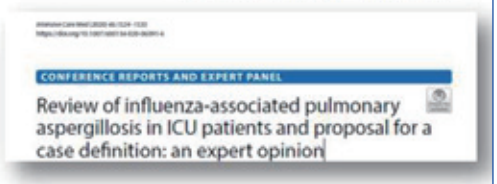
图：罹患侵袭性肺曲霉病危险因素的森林图：
A：流感队列患者罹患侵袭性肺曲霉病的危险因素分析；
B：比较流感队列和对照队列的多因素比较分析
aOR=调整后比值比.
APACHE=急性生理学和慢性评价评分
COPD=慢性阻塞性肺疾病
*表示与侵袭性肺曲霉病相关的独立危险因素

1Schauwvlieghe A, et al. Lancet Respir Med. 2018 Oct;6(10):782-792.

专家课件

流感纳入肺曲霉病（IAPA）宿主因素





- EORTC-MSG ICU（2021）工作组将其纳入IAPA临床诊断宿主因素
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  - 血液恶行肿瘤/造血干细胞移植受者
  - 糖皮质激素治疗剂量≥20mg/d的强的松等效剂量
  - 既往90天内接受常用免疫抑制剂治疗（如，钙调神经磷酸酶或人体靶向雷帕霉素（mTOR）抑制剂，肿瘤坏死因子（TNF）阻滞剂,以及干扰抗真菌免疫通路药物，阿仑单抗，依鲁替尼，核苷类似物）
  - 实体器官移植受者
  - 慢性气道病变（慢性阻塞性肺疾病（COPD）,支气管扩张）
  - 失代偿肝硬化
  - HIV 感染患者
  - **重症流感（或其他严重病毒性肺炎，如COVID-19感染）**

- **流感合并肺曲霉病（IAPA）定义逐渐清晰**
- **定义：**
- 表现为流感相关肺曲霉病(IAPA)的患者可能具有典型的欧洲癌症研究和治疗组织(EORTC)/真菌病研究组教育和研究联盟(MSGERC)定义的宿主因素
- 大部分患者被认为是IPA的低风险患者，包括以前健康的人
- 其临床和影像学表现通常不典型

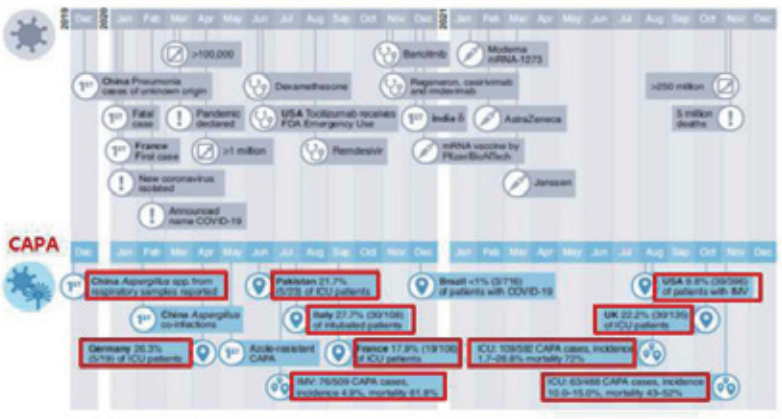
7. Verweij PE et al. Intensive Care Med. 2020 Aug;46(8):1524-1535.
8. Matteo Bassetti. Et al. Clin Infect Dis. 2021 Mar 12;72(Supplement_2):S121-S127

侵袭性曲霉病（IA）成为COVID-19患者的临床挑战

COVID-19合并肺曲霉病（CAPA）病例在2020年早期在中国首先报道，随后在不同地区疫情集中爆发期间相继得到报道。

COVID-19和CAPA关键事件：

- 2019年12月不明病原所致肺炎在中国爆发
- **2019年12月中国报道从患者呼吸道标本中分离到曲霉菌属真菌**
- 2020年1月首例COVID-19死亡病例发表；法国报道欧洲首例COVID-19病例；病毒分离鉴定为新型冠状病毒
- 2020年2月疾病命名为COVID-19
- **中国报道首例COVID-19合并曲霉感染病例**
- 2020年3月感染人数超过10万人；宣布进入疫情；
- 2020年4月超过100万人感染
- **德国ICU患者回顾性研究中CAPA发病率达到26.3%（5/19）**
- 2020年6月妥珠单抗获得FDA紧急授权用于COVID-19患者治疗
- **2020年7月巴基斯坦研究报道ICU患者CAPA发病率为21.7%（5/23）**
- **意大利插管患者CAPA发病率27.7%;另一项研究侵入性机械通气患者CAPA发病率4.9%，死亡率高达61.6%**



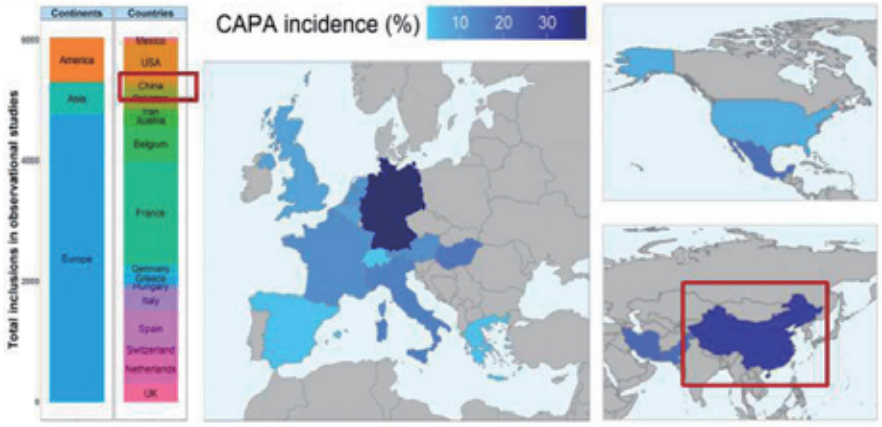
图A：COVID-19，以及合并肺曲霉病（CAPA）关键事件时间线

16. Hoenigl M, et al. Nat Microbiol. 2022 Aug;7(8):1127-1140.

侵袭性曲霉病（IA）成为COVID-19患者的临床挑战

- 重症COVID-19患者罹患CAPA发病率约为7.1-15.1%，中国数据处于中高水平
- Simon Feys等人[11]对观察行研究中患者患者分布和报道的发病率进行了分析。5953例患者多数病例来自于欧洲（79.9%）
- 纳入的中国地区CAPA病例数量不多，值得注意的是中国入住ICU的COVID-19患者仍处于中高水平的发病率。

- 文献报道中不同地区和国家，CAPA发病人数和研究报道发病率
- Regional variation in number of inclusions and CAPA incidence in studies with observational data.
- Bar chart on the left shows the number of patients included in studies with observational data on CAPA, either per continent or per country.
- The maps on the right show the pooled CAPA incidence per country in studies with observational data.
- Only studies with exact information on the countries where patients were recruited were included in this figure
- CAPA incidence is calculated per study for the combination of proven, probable, putative and possible CAPA cases



11. Feys S et al. J Fungi (Basel). 2021 Dec 11;7(12):1067.

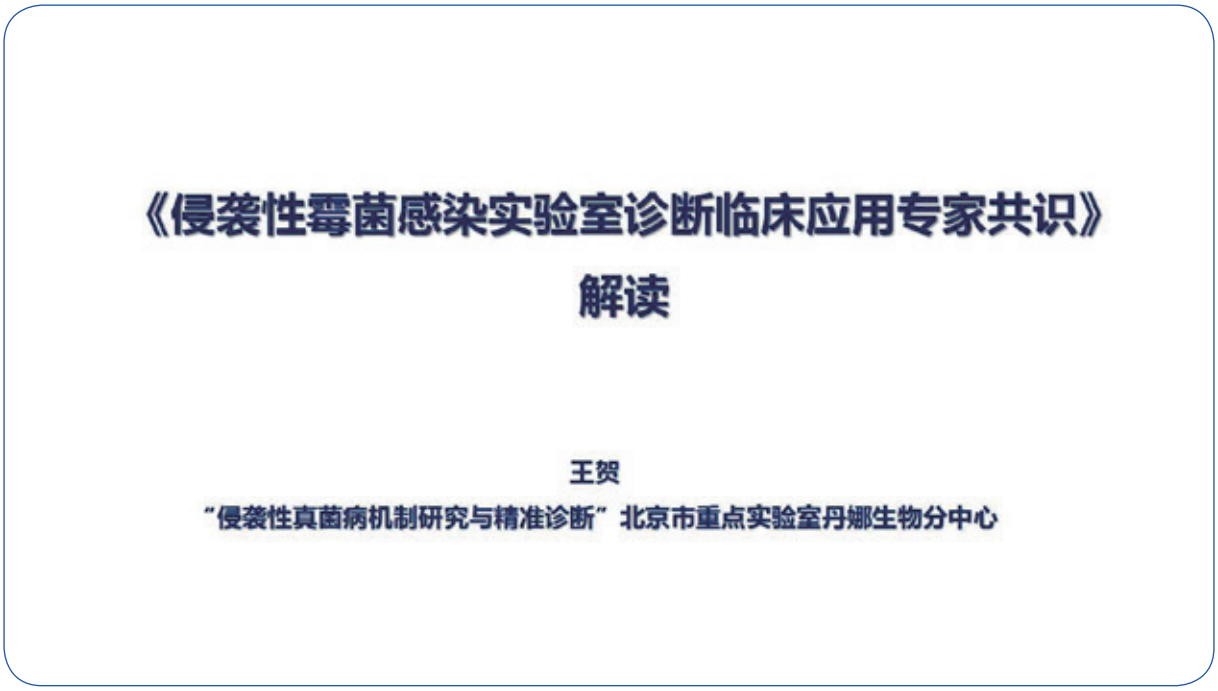
小 结

- 警惕重症病毒性肺炎患者的霉菌感染风险
- 重症病毒性肺炎患者继发侵袭性霉菌感染风险不容忽视，患者伴随高死亡率，重症COVID-19患者罹患CAPA发病率约为7.1-15.1%
- 老年或免疫抑制宿主，肺/肝脏基础疾病和接受糖皮质激素治疗增加新冠患者曲霉感染风险
- 重症COVID-19患者具备曲霉菌和毛霉菌感染的共有危险因素，例如全身糖皮质激素治疗和急性呼吸窘迫综合征等，需警惕混合霉菌感染发生

专家课件

《侵袭性霉菌感染实验室诊断临床应用专家共识》解读

王贺
“侵袭性真菌病机制研究与精准诊断”北京市重点实验室丹娜生物分中心





侵袭性真菌病全球负担重

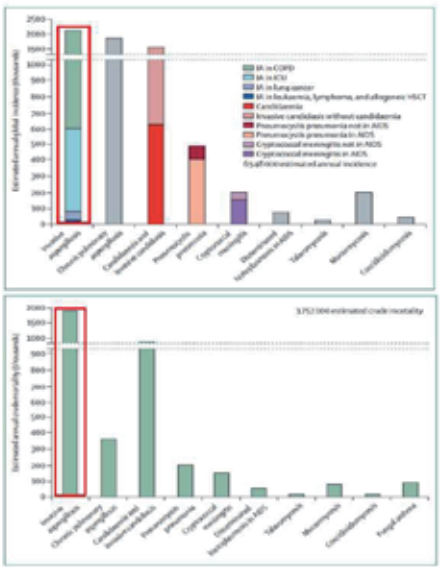
最新报道—全球真菌感染形势严峻，每年高达375万人

Global incidence and mortality of severe fungal disease

Dan A F W Denning 2024年1月发表于《The Lancet Infectious Diseases》

全球每年有超过655万人受到真菌病的威胁，超过375万人死亡。在与真菌病有关的死亡中，大约255万人（68%）可能是由真菌病直接引起的死亡。

- COPD患者中，IA总发病人数约为1,513,000例，合并IA的总死亡率约为43%~72%，归因死亡率约为83%~90%。
- ICU患者确诊IA的粗死亡率约为46%~82%，归因死亡率约为51%。
- 肺癌合并IA的死亡率约为51%（约49 000例），约40%归因于IA。
- 肺结核合并CPA患者发病后第一年死亡率约为20%，5年死亡率约为50%，归因死亡率约为4.8%~85.7%
- 念珠菌病发病率为每10万人中8.05例，治疗后的念珠菌血症死亡率约为35%，未治疗的念珠菌血症死亡率约为90%



Downing DW. *Lancet Infect Dis*. 2024 Jan 12:S1473-

专家课件

WHO首次公布威胁健康的"真菌病原体清单"

2022年10月25日世界卫生组织首次公布威胁健康的"真菌病原体清单"（FPPL），共列出19种构成公共卫生风险的真菌



严重级别组：包括高度耐药、并在全世界引发多起疫情的耳念珠菌、新型隐球菌、烟曲霉和白念珠菌。

高级别组：光滑念珠菌、组织胞浆菌属、真菌性足菌肿病原体、毛霉目、镰刀菌属、热带念珠菌以及近平滑念珠菌。

中级别组：赛多孢子菌属、多育节荚孢霉、球胞子菌属、克柔念珠菌、格特隐球菌、马尔尼菲篮状菌、耶氏肺孢子菌以及副球孢子菌属。

等级划分

- 根据真菌病原体的优先级将其分为三类：严重级别组、高级别组和中级别组。
- 每个优先类别的真菌病原体的排名主要是基于它们对公众健康的影响和/或出现抗真菌耐药性的风险。

世卫组织称，真菌感染及其对治疗日益增加的耐药性是一个越来越大的风险。然而，对这种风险历来缺乏关注意味着在知识方面存在巨大缺口，同时也缺乏监测、治疗和诊断。

真菌病认识周（FDAW）



- 每年，美国疾病控制与预防中心（CDC）及其合作伙伴都会在真菌病认识周（FDAW）期间进行活动和宣传，提高公众对真菌病的认识。
- 今年FDAW（2023年9月18-22日）分为5个主题，从认知、预防、耐药性、环境、未来五个方面引导公众思考真菌。

Day 1	Day 2	Day 3	Day 4	Day 5
提高对真菌的认知	抗击真菌，保护患者	真菌耐药的途径	真菌与环境	真菌感染的未来



国家卫健委全国真菌病监测网建立

国家卫生健康委员会办公厅

国卫办医函〔2019〕481号

国家卫生健康委办公厅关于建立全国真菌病监测网的通知

各省、自治区、直辖市及新疆生产建设兵团卫生健康委：

为贯彻落实《关于持续规范抗菌药物临床应用管理有关工作的通知》（国卫办医发〔2019〕12号）要求，提高医疗机构真菌病诊疗能力及抗真菌药物临床应用管理水平，我委决定建立全国真菌病监测网（以下简称监测网）。委托中国医学科学院北京协和医院负责监测网的总体规划设计和日常运行管理工作。在建立全国真菌病监测网的同时，有条件的地区和医疗机构也应当适步开展相应监测工作。

现将全国真菌病监测网方案（2019版，见附件1）印发给你们，请按照方案要求，于2019年6月30日前确定出辖区内符合条件的医疗机构，填写《全国真菌病监测网监测单位情况信息表》（见附件2）并报送至指定邮箱。在确定监测网监测单位后，监督指导辖区内入选的监测单位按照方案和工作安排开展监测网有关工作。

联系人：医政医管局医疗管理处　王爱莉

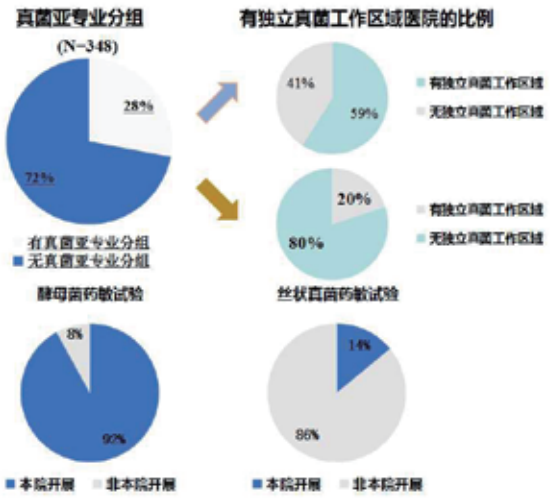
CFDSS已成立31个省级监测中心和超700多家监测单位，搭建出一个覆盖全国、科学分级的真菌病监测网络，并开展定期监测、主动防控、开展研究、提出建议、推进发展五项主要工作。

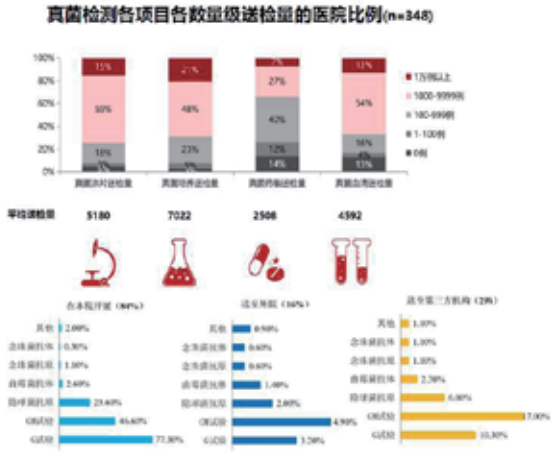


2019.10.18 全国真菌病监测网成立仪式

三甲医院真菌检测能力调研

国内三甲综合医院真菌检测能力调研结果堪忧，不能满足临床需要





血清学送至第三方机构进行检测的医院比例较高

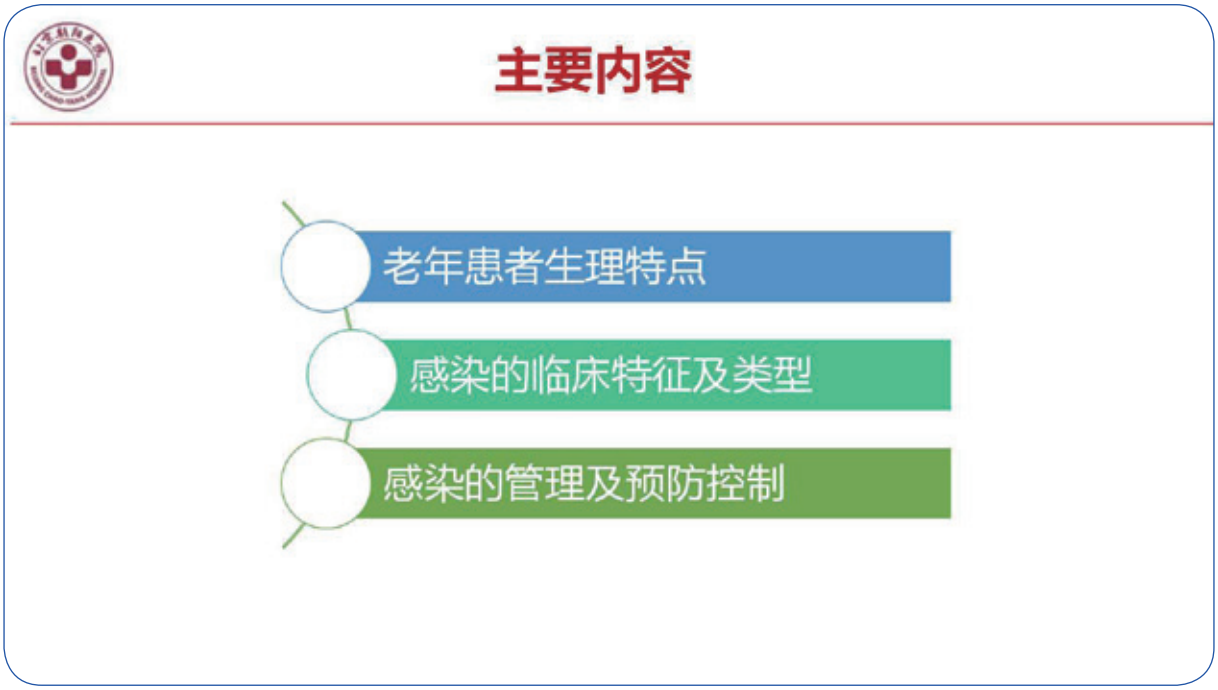
Wang H, et al. J Microbiol Immunol Infect 2020;53):845-853.

专家课件

老年视角谈感染预防

王晓娟
首都医科大学附属北京朝阳医院





第一部分：老年患者生理特点

中国老龄化问题严重

◆ 二十一世纪的中国将是一个老龄化社会

◆ 中国国家卫生健康委报道：

- 截至2022年底我国60岁及以上老年人口为2.8亿，占总人口的19.8%
- 65岁及以上老年人口为2.1亿，占总人口的14.9%
- 据测算，到2035年左右，60岁及以上老年人口将突破4亿

专家课件

老年患者的生理变化



阶段性、渐进性、不可逆性、多样性

1.免疫衰老

- **免疫衰老：随着年龄增长，免疫系统功能逐渐下降，导致机体免疫力下降的过程**

T细胞	B细胞	NK细胞
• 随着年龄的增长，T细胞的产生和功能逐渐减弱，对病原体的反应能力下降	• B细胞的产生和功能也随年龄下降，抗体生成减弱，对疫苗接种的反应减弱	• NK细胞的数量和功能下降，对肿瘤和病原体的识别和杀伤能力降低

1.免疫衰老

免疫屏障

- 皮肤和粘膜构成机体防御生物的第一道防线。
- 呼吸道粘膜主要靠复层柱状纤毛运动，并借助分泌物粘附微生物，通过喷嚏、咳嗽、咯痰等方式将病原体排出体外。
- 胃酸则可杀灭大多数细菌，肠道中的大肠杆菌能分泌细胞素抑制某些厌氧菌和革兰氏阳性细菌。
- 呼吸道及消化道粘液中还含有溶菌酶、补体和抗体，协同起抗菌作用。
- 尿液中的氨和尿道粘膜上的sIgA对微生物均有抑制作用。
- **老年人上述非特异性免疫屏障常遭损害，呼吸道、胃肠道、泌尿道粘膜的免疫活力和功能下降，均可成为多种病原入侵的门户。**

2.慢性基础疾病

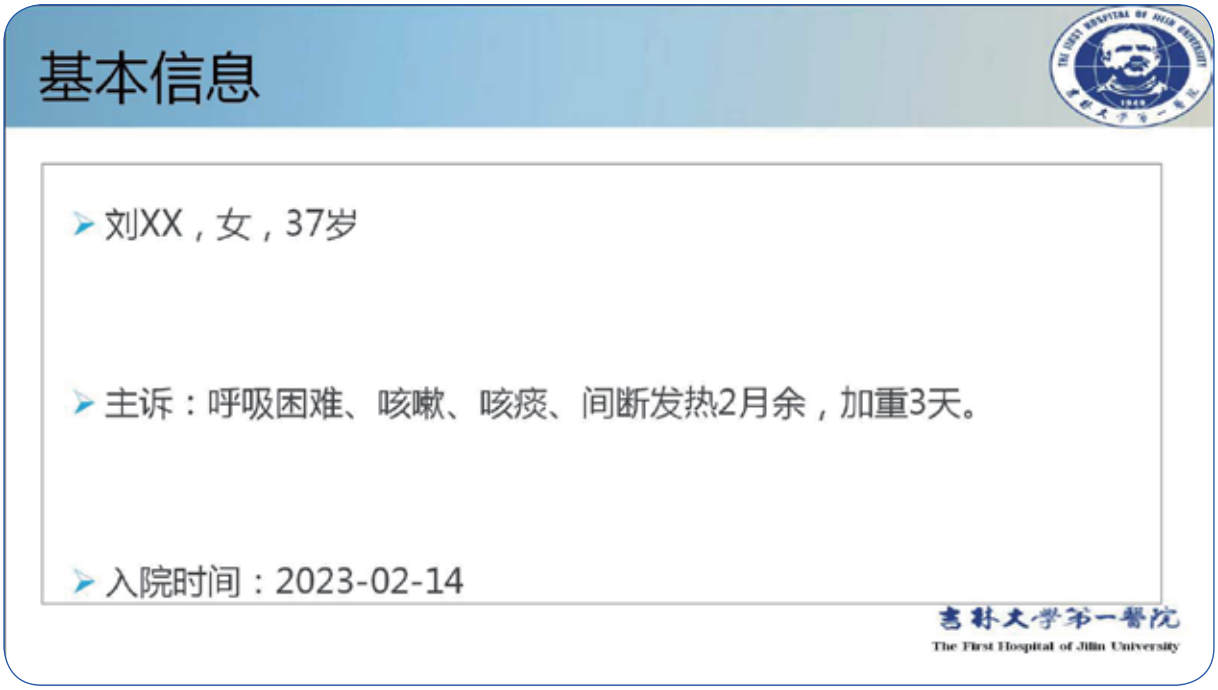
- 老年患者常见的并发症：糖尿病、高血压、骨质疏松症、尿失禁、慢性支气管炎、心衰和认知功能损害等，其中糖尿病和慢性心衰与感染的关系最为密切。
- 住院的老年患者往往同时存在以上多种慢性疾病，随着年龄的增加，其发生院内感染的风险、以及感染发生后的并发症和死亡率都会增加。

专家课件

”根“本不能忽视，mNGS 主力下的精准治疗

温中梅
吉林大学第一医院呼吸与危重症医学科





现病史

患者缘于2个月余前出现活动后呼吸困难，阵发性咳嗽、咳痰，痰为白色粘痰，并伴有间断发热、体温波动于38.5℃左右，自行口服退热药物及”头孢类抗生素”，体温可降至正常，但间隔10余天患者会再次发热，且呼吸困难有加重的趋势，1周前患者再次出现发热，于当地医院行肺部CT提示“双肺肺炎”予以“β内酰胺类抗生素“静点抗感染治疗，上述症状未缓解，3天前患者呼吸困难加重，并出现持续发热，现患者为求进一步诊治，遂就诊于我院。急诊以“肺炎”收入我科。病程中，有全身乏力，无头晕，无头痛，无恶心、呕吐，无腹痛、腹泻，近期体重较前无明显变化。

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既往史

- 肾移植术后、长期口服激素及免疫抑制剂，
- 一侧卵巢切除术
- 否认其他既往史

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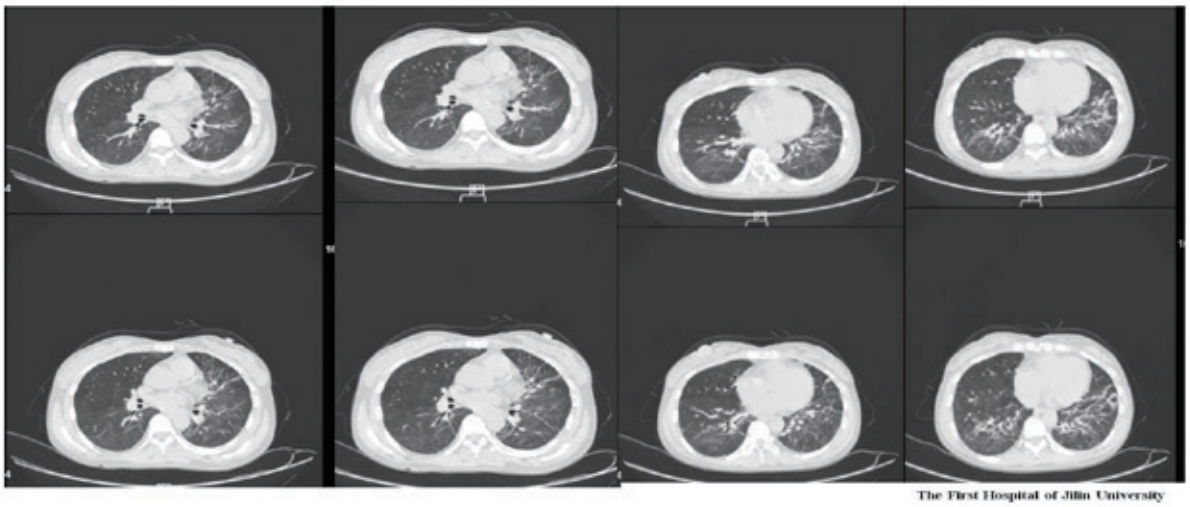
专家课件

查体

- 体温36.8℃，脉博113次/分，血压115/70mmHg，呼吸25次/分。气管居中，叩诊清音，双肺呼吸音粗，双下肺可闻及散在湿罗音。心率113次/分，律整，无额外心音及杂音，腹平软，无压痛、反跳痛及肌紧张，肝脾肋下未触及，双下肢无水肿。

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2023-02-13肺CT



The First Hospital of Jilin University

辅助检查

- 血常规：WBC:7.12*109/L NE#:6.14 LY#:0.51*109/L ,HGB:110g/L
- CRP:38.35 PCT:<0.05;ESR:32MM/1h
- D-D:0.64 FDP:2.50;
- 呼吸道病原菌核酸检测（痰):流感嗜血杆菌（+）
- 新冠核酸：阴性
- 血巨细胞病毒核酸：＜500

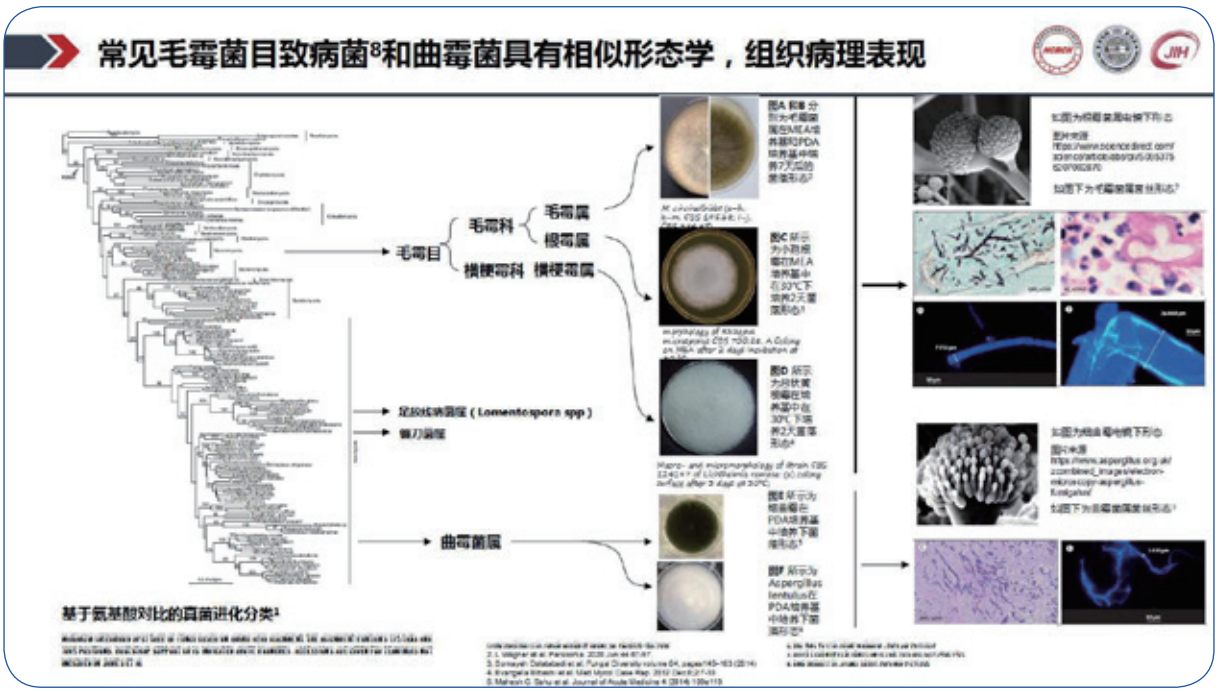
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专家课件

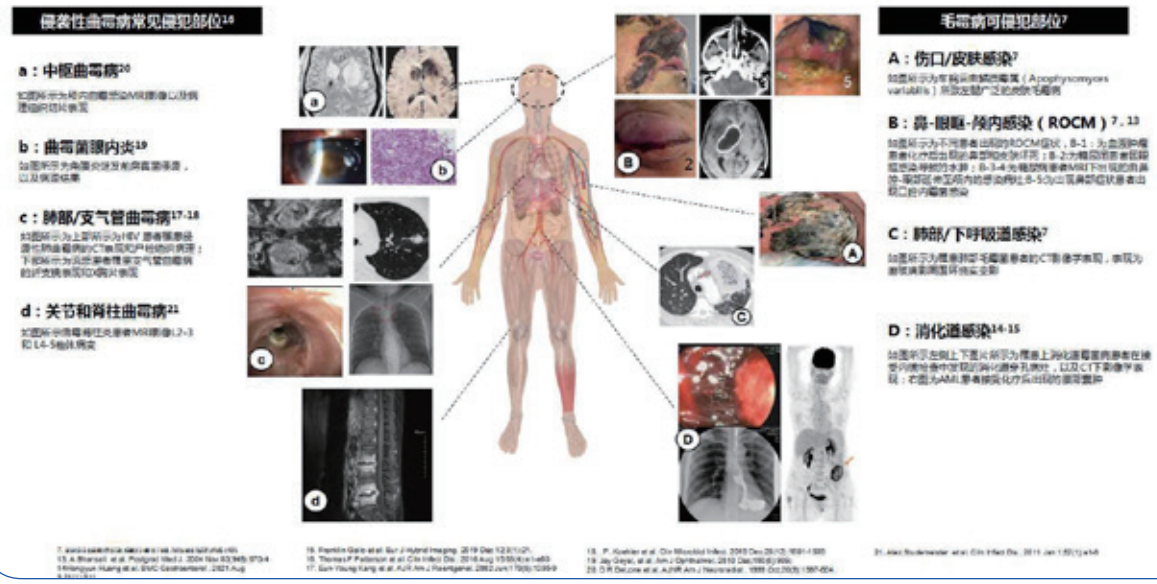
异基因造血干细胞移植患者的毛霉感染诊治

吴德沛
国家血液系统疾病临床医学研究中心
苏州大学附属第一医院



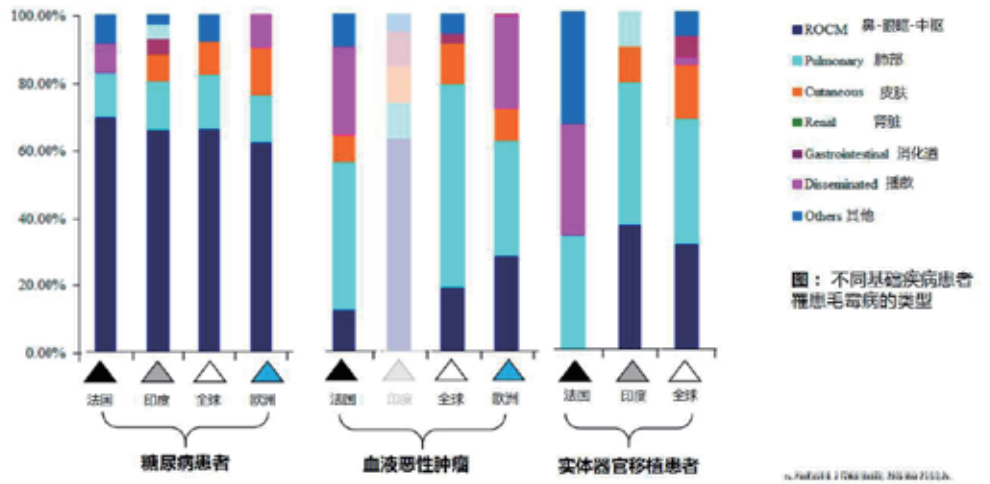


毛霉病可表现为皮肤，鼻-眼眶-中枢，肺部/呼吸道感染累及多个器官



血液恶性肿瘤患者罹患IM伴随更高的肺部感染比率和播散性感染

- Prakash H教授[20]对全球毛霉病的流行病学基于基础疾病和感染类型进行了进一步的分析（如下图），血液肿瘤患者相较于糖尿病基础疾病患者伴随更高的肺部侵袭性和全身播散性感染比率。糖尿病患者主要以ROC(鼻-眼眶-中枢)累及为主

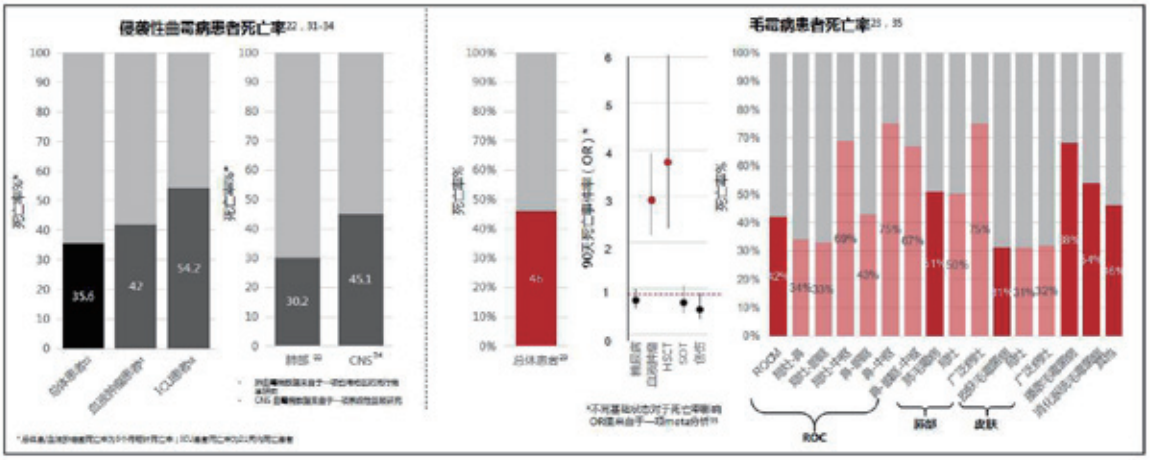


图：不同基础疾病患者罹患毛霉病的类型

专家课件

约半数毛霉病患者死亡，免疫抑制患者增加毛霉病死亡风险

- 一项系统性回顾研究[33]对2000年1月-2017年1月期间发表的毛霉病病例进行分析，来自600篇文献报道的851例患者总体死亡率接近50%（血液肿瘤伴随更高死亡风险）；研究者在另一文献[35]中对患者的治疗和临床预后进行进一步的分析，肺部感染和累及中枢系统伴随极高的死亡率~70%。

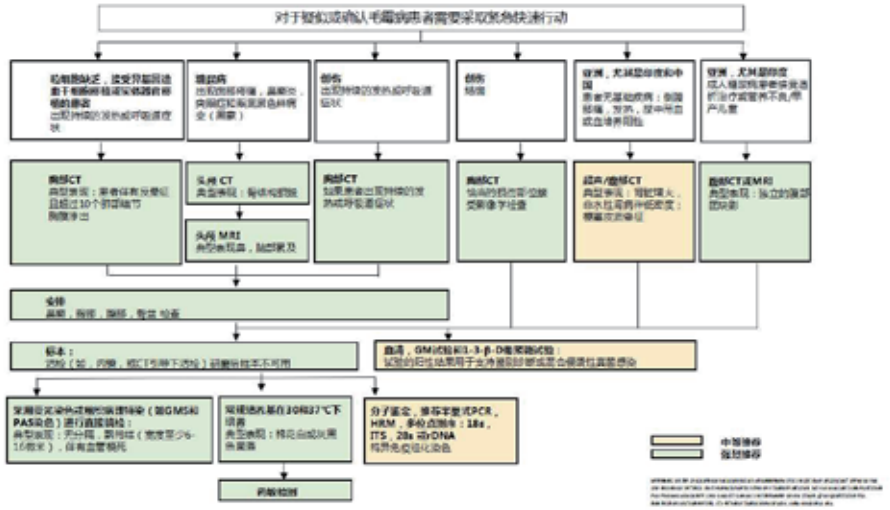


EORTC-MGS对于侵袭性霉菌感染临床诊断的定义

2019年EORTC/MSGERC更新了侵袭性霉菌病确诊和临床诊断标准[19]，对侵袭性霉菌感染临床诊断定义进行了调整；

临床诊断宿主因素	临床表现	微生物学证据
• 近期发生中性粒细胞缺乏（中性粒细胞计数<0.5×10⁹/L）并持续超过10天 • 接受异基因造血干细胞移植 • 血液系统肿瘤患者 既往60天内，长时间使用皮质类固醇（除外支持性支气管肺曲霉病）：超过3周的平均最低剂量为0.3mg/kg/d泼尼松的类似剂量 • 既往90天内接受T细胞免疫抑制剂治疗，如：如环孢素、TNF-α阻滞剂、特异的单克隆抗体（如阿仑单抗），或抗胸腺细胞球蛋白 接受B细胞免疫抑制剂治疗，如布鲁顿酪氨酸激酶抑制剂（如：依鲁替尼） • 实体器官移植受者 • 遗传性严重免疫缺陷（如慢性肉芽肿、STAT 3缺陷或严重联合免疫缺陷） • 累及肠、肺或肝的III级或IV级GVHD，且对一线皮质类固醇治疗无效	**肺曲霉病：** 患者存在以下4种CT特征中的一种： 1)结节、边界清晰的病灶，伴或不伴晕征;2)空气新月征;3)空洞;3)楔形和节段性或大叶性实变 **其他霉菌肺部感染：**与肺曲霉病相似，加上反晕征 **鼻窦气管炎型：**鼻下可见气管支气管溃疡，结节，伪膜，斑块，或坏疽 **鼻腔病变：**局部急性疼痛（包括伴随脑脓肿性疼痛）；鼻部溃疡伴黑色坏痂；从鼻黏膜穿过骨质蔓延至邻近颅腔	• 从痰液、支气管肺泡灌洗液、支气管毛刷或抽吸液中培养检出任何霉菌，如曲霉、镰刀菌、接合菌、威氏霉菌 • 慢病鼻窦抽吸液、支气管肺泡灌洗液、支气管毛刷或抽吸液中检测到真菌成分 **鼻支气管炎：** 1)支气管肺泡灌洗液或支气管毛刷培养检出曲霉;2) BAL或支气管毛刷获得标本中直接显微镜检发现真菌成份，提示存在霉菌 **鼻腔病变：** 1）鼻腔吸引物霉菌培养阳性；2）鼻腔吸引物镜检发现真菌成分提示霉菌 **仅对曲霉菌病：** **半乳甘露聚糖抗原（GM）：**血浆、血清、BAL或脑脊液中检测到抗原结果为以下任意一项：1）单血清或血浆≥1.0；2）BAL液≥1.0；3）单血清或血浆≥0.7，且BAL液≥0.8；4）CSF: ≥1.0) **曲霉PCR检测：**(以下任意一项1）血浆、血清或全血两次或2次或以上PCR检测阳性；2）BAL液重复2次或以上PCR检测阳性；3）血浆、血清或全血至少1次PCR检测阳性，同时BAL液至少1次PCR检测阳性 痰、BAL、支气管毛刷、或脓吸液培养检出曲霉 **曲霉培养：**从痰液、支气管肺泡灌洗液、支气管毛刷或抽吸液中培养检出丝霉属真菌

ECMM 推荐的毛霉病诊断流程



侵袭性毛霉菌感染治疗药物的推荐：最新的国际指南推荐

"2019年ECMM-MSG更新的毛霉病诊断和治疗指南

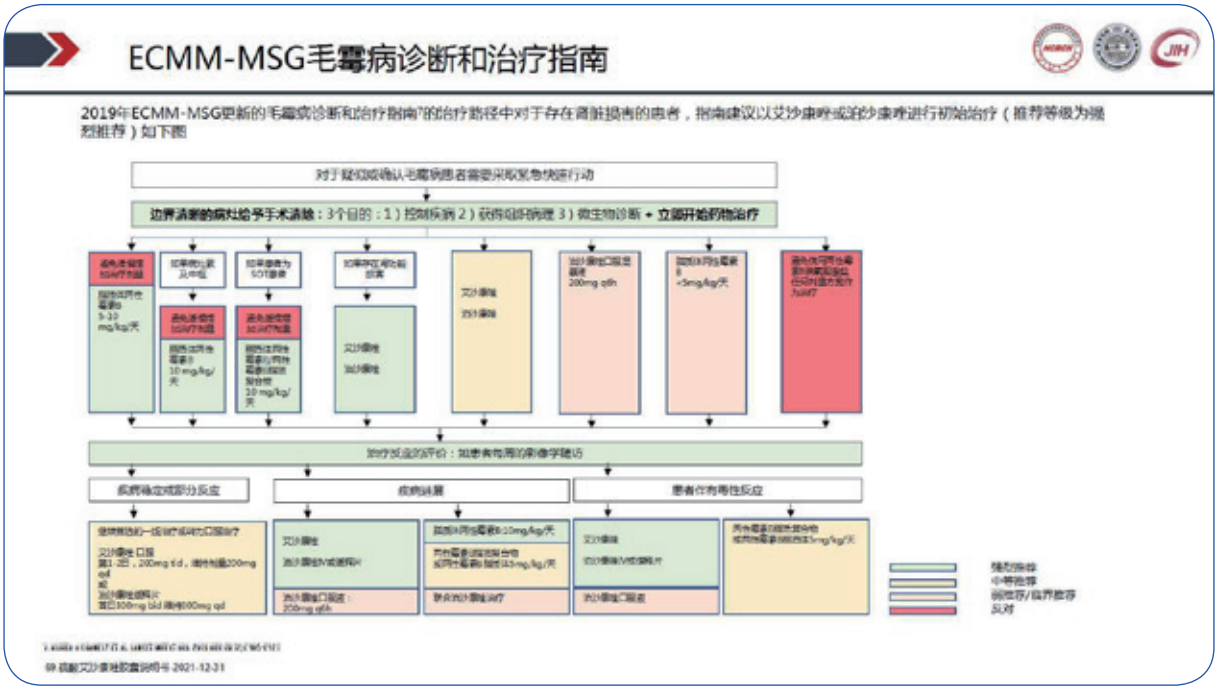
表2：ECMM-MSG推荐毛霉菌一线单药治疗

	目的	治疗药物	推荐级别	证据等级
所有患者	治愈和降低患者生存率	两性霉素B，任何制剂，首日剂量必须加倍实施治疗剂量	D	BIII
所有患者	治愈和降低患者生存率	两性霉素B脂质体，5-10mg/kg/天	A	BII
累及CNS	治愈	两性霉素B脂质体，10mg/kg/天，起始疗程28天	A	BII
成人SOT	治愈	两性霉素B脂质体，10mg/kg/天	A	BII
成人SOT	治愈	两性霉素B脂质复合物，10mg/kg/天	A	BII
所有患者未累及中枢	治愈	两性霉素B脂质复合物，5mg/kg/天	B	BIII
血液恶性肿瘤患者	治愈	两性霉素B脂质体：1-<5mg/kg/天 +手术治疗	C	BII
所有患者*	治愈	艾沙康唑	B	BIb
所有患者	治愈	艾沙康唑缓释片或静脉制剂	B	BIIa
所有患者	治愈	艾沙康唑口服悬液	C	BIII
所有患者	治愈	任何剂量的两性霉素B脱氧胆酸盐（如有其他任何可替代方案）	D	BIII
创伤考虑病	治愈	两性霉素B脂质复合物预防注射联合全身治疗	D	BII

*

对于难治性/毒性不耐受毛霉病患者（包括存在肾脏损害患者），指南强烈推荐艾沙康唑作为治疗药物选择（A-IIb）

专家课件

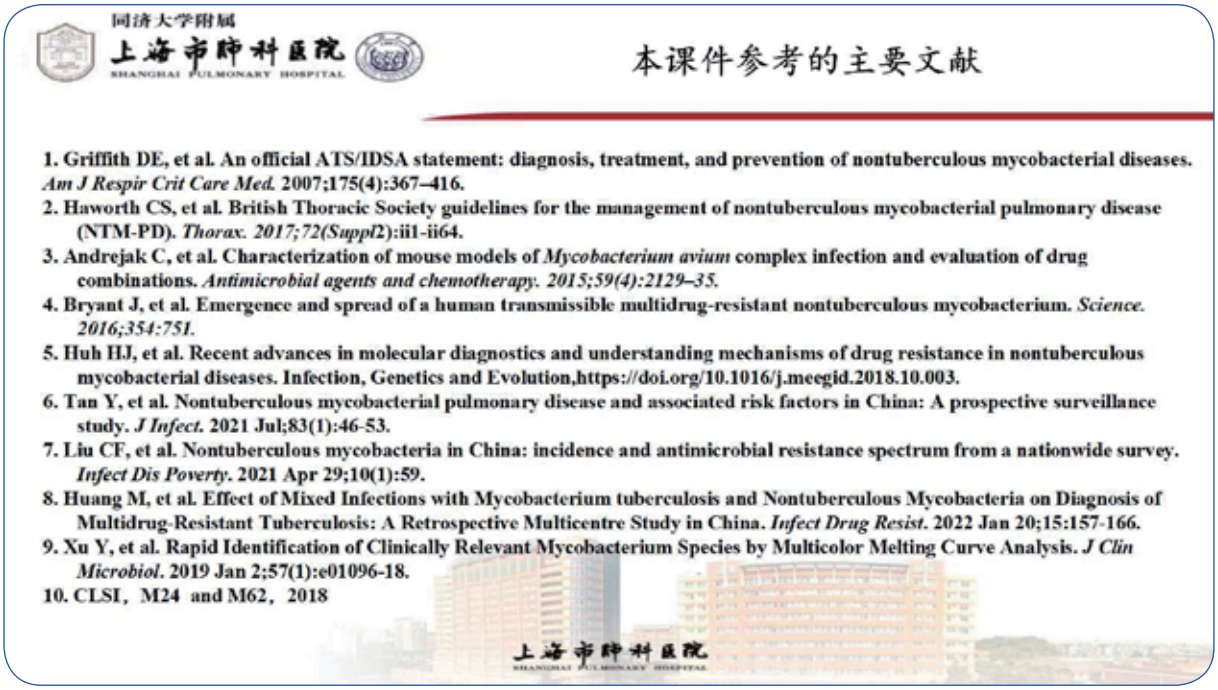

ECMM-MSG毛霉病诊断和治疗指南
2019年ECMM-MSG更新的毛霉病诊断和治疗指南中的治疗路径中对于存在胃肠损害的患者，指南建议以艾沙康唑或泊沙康唑进行初始治疗（推荐等级为强烈推荐）如下图
对于疑似或确认毛霉病患者需要采取紧急处理行动
边界清楚的病灶给予手术清除：3个目的：1）控制疾病 2）获得组织病理 3）微生物诊断 + 立即开始药物治疗
治疗反应的评价：如患者有用的病理学随访
疾病稳定或部分反应
疾病进展
患者仍有毒性反应
强烈推荐
中等推荐
弱推荐/临界推荐
反对


谢谢
THANKS FOR YOUR ATTENTION

非结核分枝杆菌感染与实验室检测

余方友
同济大学附属上海市肺科医院 检验科





1. Griffith DE, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med.* 2007;175(4):367–416.
2. Haworth CS, et al. British Thoracic Society guidelines for the management of nontuberculous mycobacterial pulmonary disease (NTM-PD). *Thorax. 2017;72(Suppl2):*ii1-ii64.
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5. Huh HJ, et al. Recent advances in molecular diagnostics and understanding mechanisms of drug resistance in nontuberculous mycobacterial diseases. Infection, Genetics and Evolution,https://doi.org/10.1016/j.meegid.2018.10.003.
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8. Huang M, et al. Effect of Mixed Infections with Mycobacterium tuberculosis and Nontuberculous Mycobacteria on Diagnosis of Multidrug-Resistant Tuberculosis: A Retrospective Multicentre Study in China. *Infect Drug Resist.* 2022 Jan 20;15:157-166.
9. Xu Y, et al. Rapid Identification of Clinically Relevant Mycobacterium Species by Multicolor Melting Curve Analysis. *J Clin Microbiol.* 2019 Jan 2;57(1):e01096-18.
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专家课件


同济大学附属
上海市肺科医院
SHANGHAI PULMONARY HOSPITAL
内容提要
W
F
S
C
Step 1
Step 2
Step 3
Step 4
Step 5
NTM概述
NTM病与病原体
NTM检测方法
上海市肺科医院


同济大学附属
上海市肺科医院
SHANGHAI PULMONARY HOSPITAL
分枝杆菌属（抗酸染色阳性）
结核分枝杆菌复合群
麻风分枝杆菌
非结核分枝杆菌（NTM）
上海市肺科医院

同济大学附属上海市肺科医院 SHANGHAI PULMONARY HOSPITAL

NTM概述

NTM普遍存在于环境中，由于其细胞壁具有较强的疏水性，能天然耐受多种消毒剂、抗生素以及重金属，使其常生存于饮水系统中。

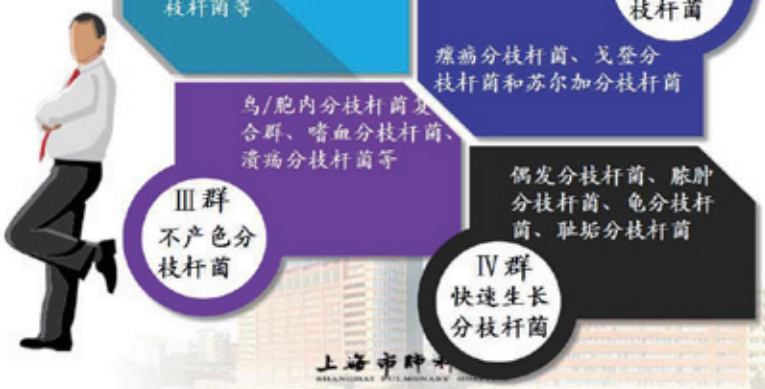
NTM可以在很多物体表面形成生物膜，从而使其能够抵御外界不利因素，帮助其在自然界或者物体表面长期存活。

已经发现的NTM超过190余种，仅少部分与人类致病相关，分疾病来源与非疾病来源。

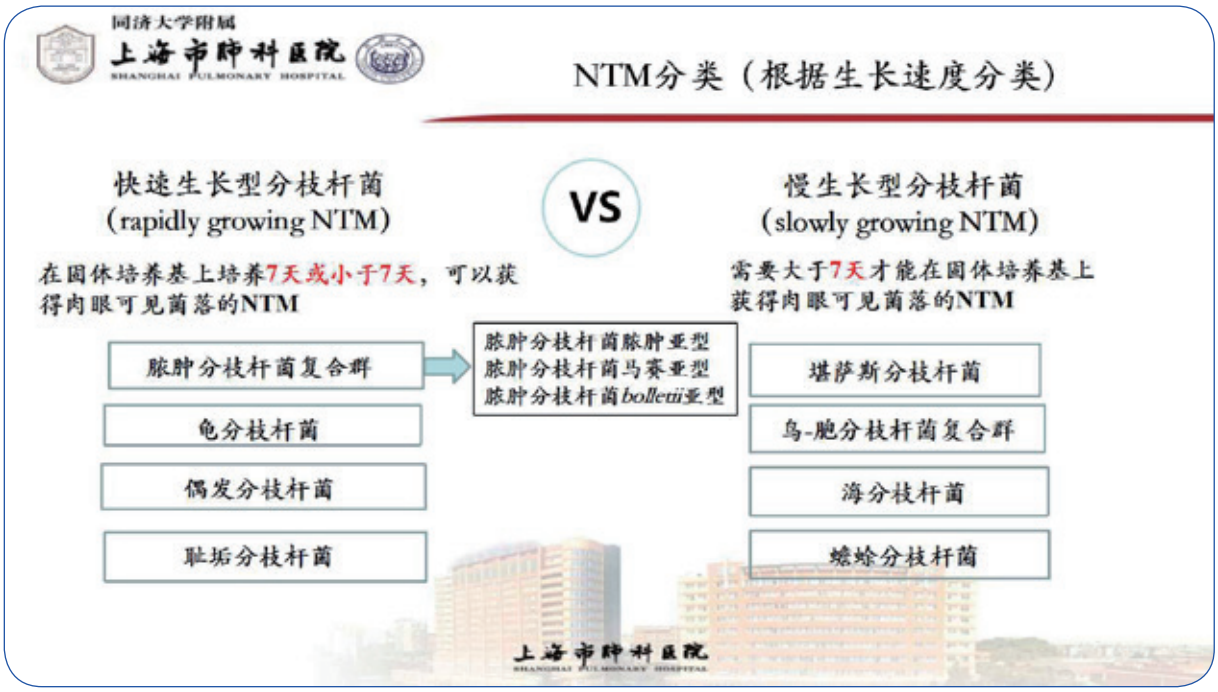
标本采集过程或者实验室操作过程中导致污染，应正确区别。

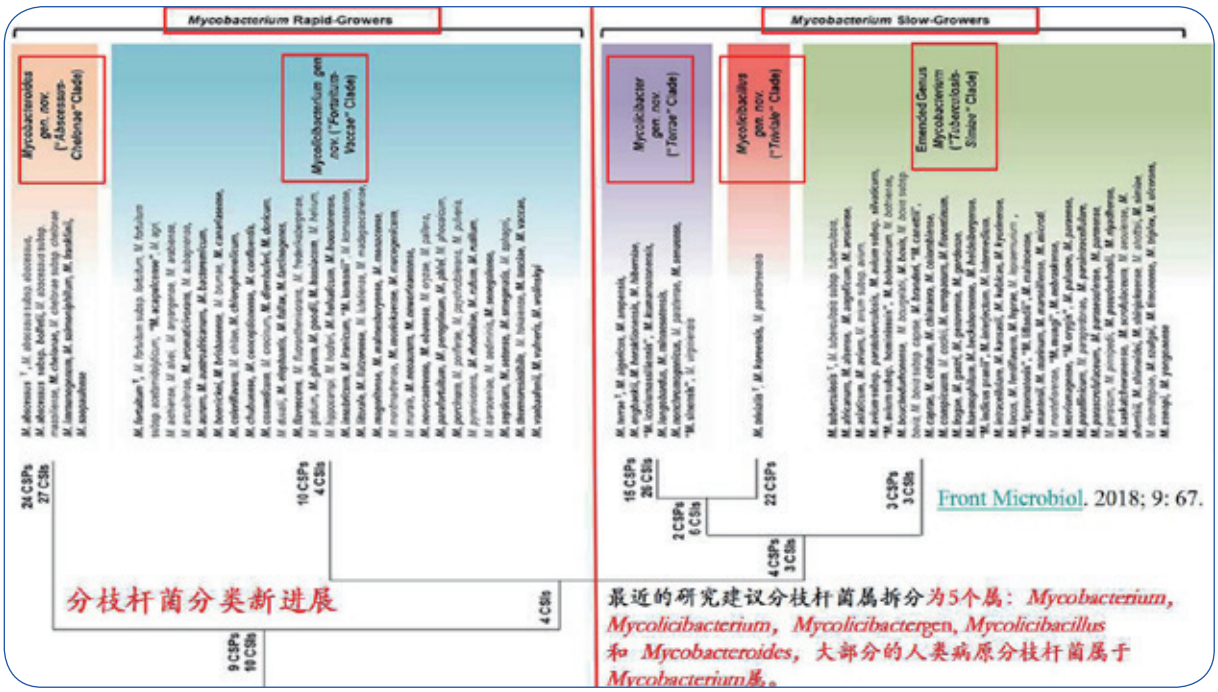
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根据NTM生长速度及产色情况分类



专家课件

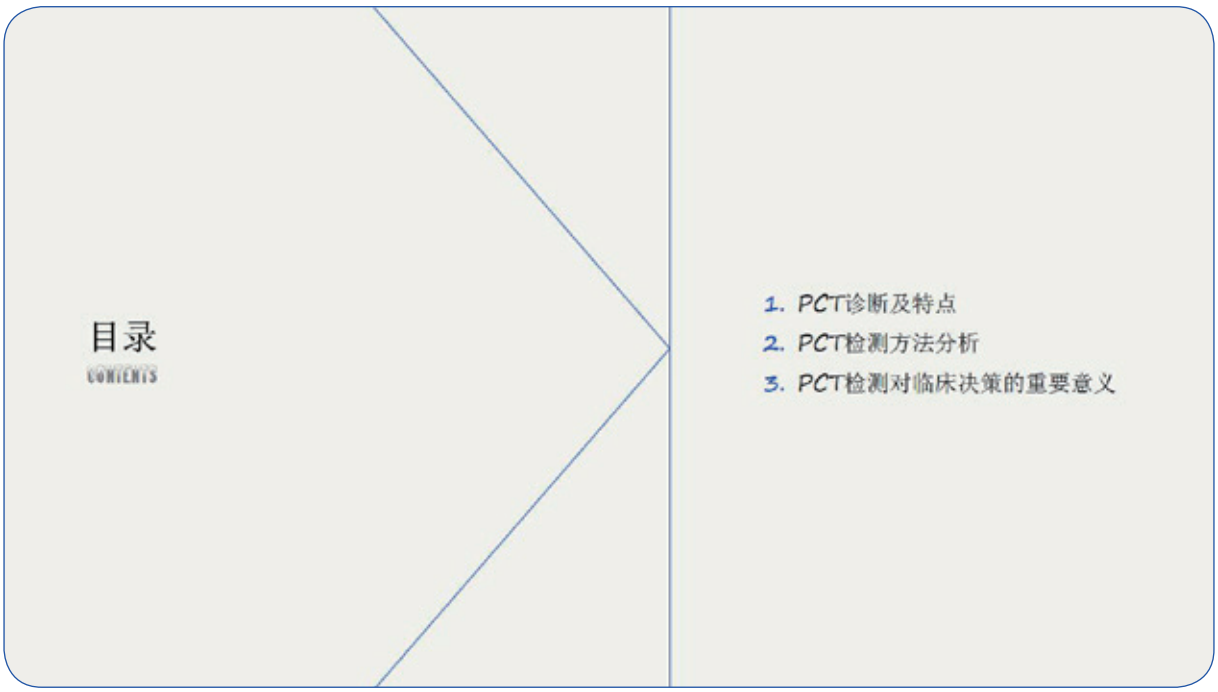

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NTM分类（根据生长速度分类）
快速生长型分枝杆菌
(rapidly growing NTM)
VS
慢生长型分枝杆菌
(slowly growing NTM)
在固体培养基上培养7天或小于7天，可以获得肉眼可见菌落的NTM
需要大于7天才能在固体培养基上获得肉眼可见菌落的NTM
脓肿分枝杆菌复合群
龟分枝杆菌
偶发分枝杆菌
耻垢分枝杆菌
脓肿分枝杆菌脓肿亚型
脓肿分枝杆菌马赛亚型
脓肿分枝杆菌bolletii亚型
堪萨斯分枝杆菌
鸟-胞分枝杆菌复合群
海分枝杆菌
蟾蜍分枝杆菌
上海市肺科医院


Mycobacterium Rapid-Growers
Mycobacterium Slow-Growers
Mycobacteroides gen. nov. ("Abscessus-Chelonae" Clade)
Mycolicibacterium gen. nov. ("Fortuitum-Vaccae" Clade)
Mycolicibacter gen. nov. ("Terrae" Clade)
Mycolicibacillus gen. nov. ("Triviale" Clade)
Emended Genus Mycobacterium ("Tuberculosis-Simiae" Clade)
24 CSPs 27 CSIs
10 CSPs 4 CSIs
15 CSPs 26 CSIs
22 CSPs
3 CSPs 3 CSIs
2 CSPs 6 CSIs
4 CSPs 3 CSIs
4 CSIs
9 CSPs 10 CSIs
分枝杆菌分类新进展
Front Microbiol. 2018; 9: 67.
最近的研究建议分枝杆菌属拆分为5个属：Mycobacterium, Mycolicibacterium, Mycolicibactergen, Mycolicibacillus 和 Mycobacteroides，大部分的人类病原分枝杆菌属于Mycobacterium属。

感染标志物的质量管理对临床诊疗的意义

俞颖
浙江省中医院





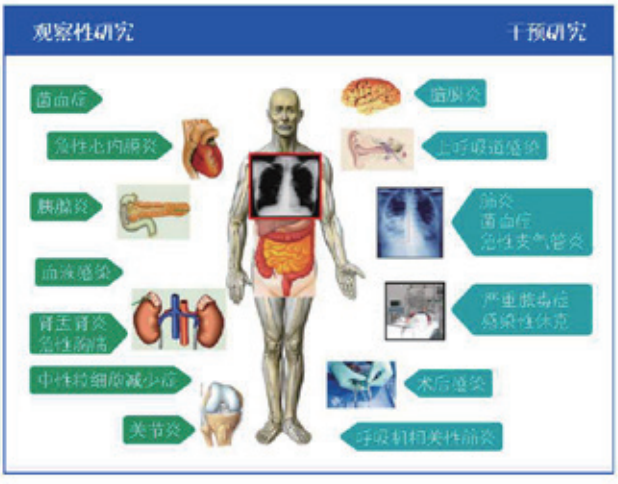
专家课件

1.PCT诊断及特点

PCT——感染的可靠标志物

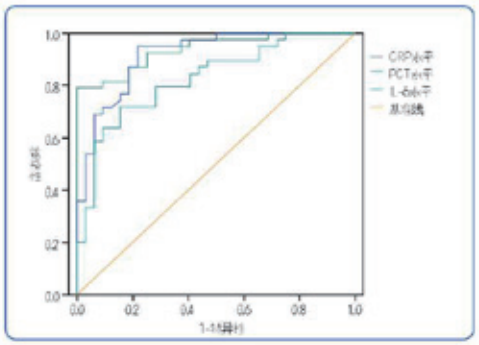
- 指导细菌感染后的抗生素管理

- 感染可伴随任何疾病发生，感染性疾病是严重的公共卫生问题和造成人类死亡的重要因素；
- 据世界卫生组织（WHO）数据统计，全球每年约有1500万人死于感染，约占全球每年总体死亡率的25%；
- 降钙素原（procalcitonin, PCT）是降钙素的前肽物质，在感染和脓毒血症时产生，与细菌感染内毒素和炎症介质的释放密切相关。PCT在全球大部分地区已成为感染和脓毒血症管理中至关重要的生物学标志物。



PCT——系统性细菌感染和脓毒症的标志物

- 敏感性与特异性高于其他炎症反应因子



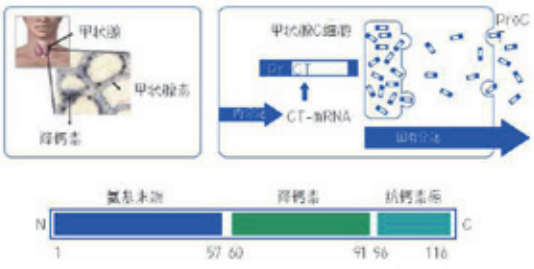
引起PCT升高的非感染因素	
系统性疾病	湿疹相关综合征：川崎病；中暑；DRESS综合征/伴嗜酸粒细胞增多和系统症状的药疹；高IgD综合征；成人Still病
特定状态的急性期	多发伤、大手术和严重烧伤早期；急性胰腺炎；亚急性甲状腺炎
肿瘤	喹来胰酸注射后；小细胞肺癌；甲状髓样癌；类癌；多发性肝转移
移植	移植物抗宿主病；抗CD3治疗(器官移植后)

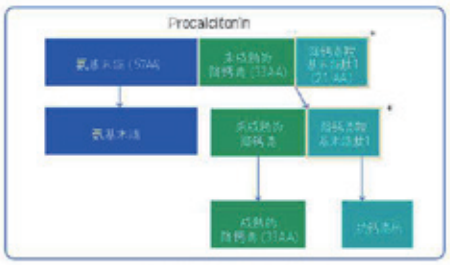
- 一项诊断荟萃分析对细菌感染研究中，PCT曲线下面积为0.974(P<0.05)，敏感性96.8%，特异性93.5%；CRP曲线下面积为0.953(P<0.05)，敏感性94.2%，特异性91.7%；IL-6曲线下面积为0.925(P<0.05)，敏感性93.6%，特异性90.5%；PCT>CRP>IL-6。
- 尽管PCT对细菌感染的诊断具有较高的特异性，但一些非感染因素同样会影响PCT的生成和清除，尤其在影响PCT水平的非感染因素与细菌感染并存时，需谨慎解读检测结果。

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PCT——结构性质

- PCT在细菌感染后可快速生成入血，半衰期短，3h后即可在外周血中检出





PCT分子及其组成肽的示意图

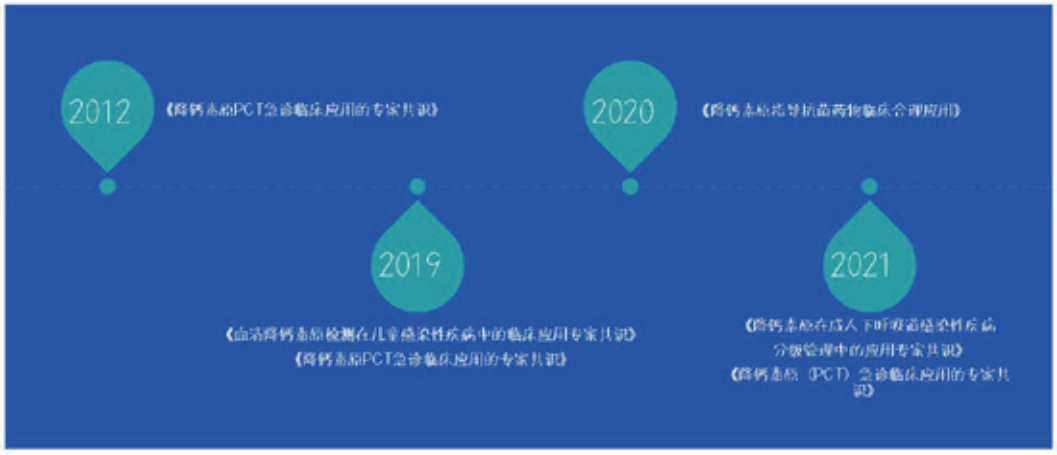
- PCT是一种116-氨基酸肽，分子量为14.5 kDa；正常生理条件下由甲状腺C细胞产生。
- 生成后的前体本被切割成抗钙素原、降钙素和N端片段。只有少量PCT被释放到循环中，故其在健康成人外周血中的含量很低：<0.05 ng/L。
- 细菌感染时几乎所有的外周组织都参与PCT的产生。
- 组成PCT的三部分包括：氨基末端（57个氨基酸），未成熟的降钙素（33个氨基酸）和降钙素原基因编码1（CCP-1）也称为片钙素（21个氨基酸）。
- 市售的检测方法一般使用抗钙素原和CCP-1多肽的抗体，如图标有*的形式。
- 识别PCT肽链两个部位的双抗双位点结合相比单位点结合大大降低了假阳性率，检测结果更精准。

1. Leonhardt K, Gebuhr K, Balzer K G, et al. Endocrinology, 2003, 144(12): 5519-5525.
2. Schneider H G, Lee G T. Pathology, 2007, 39(4): 369-380.
3. Fernández J, Fernández E R. Bol Cientif Biochemist Arrieta, 2017, 28(2): 56.

专家课件

PCT临床应用历程

- 2012年美国危重病医学会首次将PCT纳入改善脓毒血症诊断、抗菌药物管理流程的参考指标



2.PCT检测方法分析