

· 论著 ·

2017 年 CHINET 中国细菌耐药性监测

胡付品¹, 郭燕¹, 朱德妹¹, 汪复¹, 蒋晓飞^{*}, 徐英春², 张小江², 张朝霞³, 季萍³, 谢轶⁴, 康梅⁴, 王传清⁵, 王爱敏⁵, 徐元宏⁶, 沈继录⁶, 孙自镛⁷, 陈中举⁷, 倪语星⁸, 孙景勇⁸, 褚云卓⁹, 田素飞⁹, 胡志东¹⁰, 李金¹⁰, 俞云松¹¹, 林洁¹¹, 单斌¹², 杜艳¹², 郭素芳¹³, 魏莲花¹⁴, 邹凤梅¹⁴, 张泓¹⁵, 王春¹⁵, 胡云建¹⁶, 艾效曼¹⁶, 卓超¹⁷, 苏丹虹¹⁷, 汪瑞忠¹⁸, 房华¹⁸, 俞碧霞¹⁹, 赵勇²⁰, 龚萍²⁰, 郭大文²¹, 赵金英²¹, 刘文恩²², 李艳明²², 金炎²³, 邵春红²³, 温开镇²⁴, 张贻荣²⁴, 徐雪松²⁵, 鄢超²⁵, 喻华²⁶, 黄湘宁²⁶, 王山梅²⁷, 楚亚菲²⁷, 张利侠²⁸, 马娟²⁸, 周树平²⁹, 周艳²⁹, 朱镭³⁰, 孟晋华³⁰, 董芳³¹, 郑红艳³¹, 沈瀚³², 周万青³², 贾伟³³, 李刚³³, 吴劲松³⁴, 卢月梅³⁴,

摘要: **目的** 了解国内主要地区临床分离菌对临床常用抗菌药物的敏感性和耐药性。**方法** 对国内主要地区34所医院(29所综合性医院、5所儿童医院)临床分离菌采用纸片扩散法或自动化仪器法按统一方案进行抗菌药物敏感性试验。按CLSI 2017版判断结果。**结果** 收集2017年1—12月上述医院临床分离菌共190 610株,其中革兰阳性菌55 649株,占29.2%,革兰阴性菌134 951株,占70.8%。金黄色葡萄球菌和凝固酶阴性葡萄球菌中甲氧西林耐药株(MRSA和MRCNS)的平均检出率分别为35.3%和80.3%。MRSA和MRCNS对绝大多数测试药物的耐药率均显著高于甲氧西林敏感株(MSSA和MSCNS)。MRSA中有91.6%菌株对甲氧苄啶-磺胺甲噁唑敏感;MRCNS中有86.2%的菌株对利福平敏感。未发现万古霉素耐药株。肠球菌属中粪肠球菌对多数测试抗菌药物(除外氯霉素)的耐药率均显著低于屎肠球菌,两者中均有少数万古霉素耐药株,根据对50株万古霉素耐药肠球菌的表型推测或基因型检测结果,显示主要为*vanA*型(36株)、*vanB*型(8株)或*vanM*型(6株)耐药。肺炎链球菌非脑膜炎株儿童株中青霉素敏感株(86.8%)和耐药株(2.2%)所占比例较2016年有所下降,中介株的检出率(11.0%)有所上升。肠杆菌科细菌对碳青霉烯类抗生素仍高度敏感,多数菌属的耐药率低于10.0%(除外克雷伯菌属)。肺炎克雷伯菌对亚胺培南和美罗培南的耐药率分别从2005年的3.0%和2.9%上升到了2017年的20.9%和24.0%,耐药率上升幅度高达8倍,与此同时,肺炎克雷伯菌每年的分离率亦呈稳步上升趋势。不动杆菌属(鲍曼不动杆菌占91.5%)对亚胺培南和美罗培南的耐药率分别为66.7%和69.3%。与2016年耐药性数据相比,铜绿假单胞菌对碳青霉烯

作者单位: 1.复旦大学附属华山医院抗生素研究所,上海 200040; *检验科;

2.北京协和医院;

3.新疆医科大学第一附属医院;

4.四川大学华西医院;

5.复旦大学附属儿科医院;

6.安徽医科大学第一附属医院;

7.华中科技大学同济医学院附属同济医院;

8.上海交通大学医学院附属瑞金医院;

9.中国医科大学附属第一医院;

10.天津医科大学总医院;

11.浙江大学医学院附属邵逸夫医院;

12.昆明医科大学第一附属医院;

13.内蒙古医科大学附属医院;

14.甘肃省人民医院;

15.上海交通大学附属儿童医院,上海市儿童医院;

16.北京医院;

17.广州医科大学附属第一医院;

18.上海市浦东新区人民医院;

19.宁波市镇海龙赛医院;

20.湖北省秭归县人民医院;

21.哈尔滨医科大学附属第一医院;

22.中南大学湘雅医院;

23.山东省立医院;

24.福建省晋江医院;

25.吉林大学中日联谊医院;

26.四川省人民医院;

27.河南省人民医院;

28.陕西省人民医院;

29.江西省儿童医院;

30.山西省儿童医院;

31.首都医科大学附属北京儿童医院;

32.南京大学医学院附属鼓楼医院;

33.宁夏医科大学总医院;

34.深圳市人民医院。

作者简介: 胡付品(1975—),男,博士,副研究员,主要从事抗菌药物药理学、细菌耐药性监测和耐药机制研究。

通信作者: 朱德妹, E-mail: zhu_dm@fudan.edu.cn。

类抗菌药物的耐药率(23.6%对20.9%)继续呈下降趋势。**结论** 临床分离菌对常见抗菌药物的耐药率仍呈增长趋势,尤其是碳青霉烯类耐药肺炎克雷伯菌,应加强医院感染防控措施和抗菌药物临床应用管理措施,在继续做好细菌耐药监测工作的同时加强实验室与临床的沟通,以发挥耐药监测工作的最大价值。

关键词: 细菌耐药监测; 药物敏感性试验; 万古霉素耐药肠球菌; 甲氧西林耐药葡萄球菌; 青霉素耐药肺炎链球菌; 碳青霉烯类耐药革兰阴性菌

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Antimicrobial resistance profile of clinical isolates in hospitals across China: report from the CHINET Surveillance Program, 2017

HU Fupin, GUO Yan, ZHU Demei, WANG Fu, JIANG Xiaofei, XU Yingchun, ZHANG Xiaojiao, ZHANG Zhaoxia, JI Ping, XIE Yi, KANG Mei, WANG Chuanqing, WANG Aimin, XU Yuanhong, SHEN Jilu, SUN Ziyong, CHEN Zhongju, NI Yuxing, SUN Jingyong, CHU Yunzhuo, TIAN Sufei, HU Zhidong, LI Jin, YU Yunsong, LIN Jie, SHAN Bin, DU Yan, GUO Sufang, WEI Lianhua, ZOU Fengmei, ZHANG Hong, WANG Chun, HU Yunjian, AI Xiaoman, ZHUO Chao, SU Danhong, WANG Ruizhong, FANG Hua, YU Bixia, ZHAO Yong, GONG Ping, GUO Dawen, ZHAO Jinying, LIU Wenen, LI Yanming, JIN Yan, SHAO Chunhong, WEN Kaizhen, ZHANG Yirong, XU Xuesong, YAN Chao, YU Hua, HUANG Xiangning, WANG Shanmei, CHU Yafei, ZHANG Lixia, MA Juan, ZHOU Shuping, ZHOU Yan, ZHU Lei, MENG Jinhua, DONG Fang, ZHENG Hongyan, SHEN Han, ZHOU Wanqing, JIA Wei, LI Gang, WU Jinsong, LU Yuemei. (Institute of Antibiotics, Huashan Hospital, Fudan University, Shanghai 200040, China)

Abstract: **Objective** To investigate the antimicrobial resistance profile of the clinical isolates collected from selected hospitals across China. **Methods** Twenty-nine general hospitals and five children's hospitals were involved in this program. Antimicrobial susceptibility testing was carried out according to a unified protocol using Kirby-Bauer method or automated systems. Results were interpreted according to CLSI 2017 breakpoints. **Results** A total of 190 610 clinical isolates were collected from January to December 2017, of which gram negative organisms accounted for 70.8% (134 951/190 610) and gram positive cocci 29.2% (55 649/190 610). The prevalence of methicillin-resistant strains was 35.3% in *S. aureus* (MRSA) and 80.3% in coagulase negative *Staphylococcus* (MRCNS) on average. MR strains showed much higher resistance rates to most of the other antimicrobial agents than MS strains. However, 91.6% of MRSA strains were still susceptible to trimethoprim-sulfamethoxazole, while 86.2% of MRCNS strains were susceptible to rifampin. No staphylococcal strains were found resistant to vancomycin. *E. faecalis* strains showed much lower resistance rates to most of the drugs tested (except chloramphenicol) than *E. faecium*. Vancomycin-resistant *Enterococcus* (VRE) was identified in both *E. faecalis* and *E. faecium*. The identified VRE strains were mainly *vanA*, *vanB* or *vanM* type based on phenotype or genotype. The proportion of PSSP or PRSP strains in the non-meningitis *S. pneumoniae* strains isolated from children decreased but the proportion of PISP strains increased when compared to the data of 2016. *Enterobacteriaceae* strains were still highly susceptible to carbapenems. Overall, less than 10% of these strains (excluding *Klebsiella* spp.) were resistant to carbapenems. The prevalence of imipenem-resistant *K. pneumoniae* increased from 3.0% in 2005 to 20.9% in 2017, and meropenem-resistant *K. pneumoniae* increased from 2.9% in 2005 to 24.0% in 2017, more than 8-fold increase. About 66.7% and 69.3% of *Acinetobacter* (*A. baumannii* accounts for 91.5%) strains were resistant to imipenem and meropenem, respectively. Compared with the data of year 2016, *P. aeruginosa* strains showed decreasing resistance rate to carbapenems. **Conclusions** Bacterial resistance is still on the rise. It is necessary to strengthen hospital infection control and stewardship of antimicrobial agents. The communication between laboratorians and clinicians should be further improved in addition to surveillance of bacterial resistance.

Key words: bacterial resistance surveillance; antimicrobial susceptibility testing; vancomycin-resistant *Enterococcus*; methicillin-resistant *Staphylococcus*; penicillin-resistant *Streptococcus pneumoniae*; carbapenem-resistant gram-negative bacterium

近年来,以革兰阴性杆菌为代表的多重耐药细菌的检出率呈快速上升趋势,为临床抗感染治疗带来巨大挑战。细菌耐药监测工作是了解耐药菌变迁、遏制耐药菌进一步流行播散最重要的基础工作之一。现将2017年CHINET细菌耐药监测结果报道如下。

1 材料与方法

1.1 材料

1.1.1 细菌收集 2017年1月1日—2017年12月31日临床分离株,剔除同一患者分离的重复菌株,按统一方案进行细菌对抗菌药物的敏感性试验。

1.1.2 培养基 药敏试验用Mueller-Hinton琼脂,肺炎链球菌及各组链球菌用含5%脱纤维羊血MH琼脂,流感嗜血杆菌用嗜血杆菌属培养基(HTM)加SR0158营养补充剂。上述试剂均为英国OXOID公司商品。

1.1.3 抗菌药物纸片和E试验条 抗菌药物纸片为美国BBL公司或英国OXOID公司商品。青霉素、万古霉素和替考拉宁E试验条为法国生物梅里埃公司商品。

1.2 方法

1.2.1 药敏试验 参照2017年美国临床和实验室标准化协会(CLSI)推荐的纸片扩散法进行^[1],部分参与单位采用自动化仪器法。药敏试验质控菌为:金黄色葡萄球菌(金葡萄)ATCC 25923(纸片法)、ATCC 29213(机器法)、大肠埃希菌ATCC 25922、铜绿假单胞菌ATCC 27853、肺炎链球菌ATCC 49619和流感嗜血杆菌ATCC 49247。

1.2.2 判断标准 参照2017年CLSI M100-s27th版推荐的折点标准^[1]。其中磷霉素的判断标准仅针对尿标本分离的大肠埃希菌和粪肠球菌。替加环素的判断标准按美国FDA推荐的折点标准。多黏菌素对肠杆菌科细菌的判断标准参考CLSI流行病学界值(MIC≤2 mg/L野生株, MIC≥4 mg/L为非野生株)。

1.2.3 β内酰胺酶检测 采用头孢硝噻吩试验定性检测流感嗜血杆菌中的β内酰胺酶。按CLSI推荐的纸片法酶抑制剂增强试验确证大肠埃希菌、肺炎克雷伯菌、产酸克雷伯菌和奇异变形杆菌中产超广谱β内酰胺酶(ESBL)菌株。

1.2.4 青霉素不敏感肺炎链球菌检测 经1 μg/片苯唑西林纸片法测定抑菌圈直径≤19 mm的肺炎链

球菌菌株,采用青霉素E试验条测定其MIC,脑膜炎株和非脑膜炎株按CLSI 2017年标准判定为青霉素敏感、中介和耐药(PSSP、PISP和PRSP)。

1.2.5 耐万古霉素肠球菌(VRE)检测 经万古霉素纸片法或自动化仪器法测定结果为不敏感株者,用万古霉素和替考拉宁E试验条测定MIC值,部分菌株采用PCR法确认VRE的基因型。

1.2.6 特殊耐药菌株定义 碳青霉烯类耐药肠杆菌科细菌(CRE)定义为对亚胺培南、美罗培南或厄他培南中任一药物耐药者。

1.2.7 数据统计分析 数据统计分析采用WHONET 5.6软件。

2 结果

2.1 细菌分布

2017年共收集临床分离株190 610株,其中革兰阳性菌55 649株,占29.2%,革兰阴性菌134 951株,占70.8%。住院患者和门急诊患者分离的菌株分别占87.3%、12.7%。标本分布中痰液等呼吸道标本占40.0%、尿液19.2%、血液15.2%、伤口脓液11.7%、脑脊液1.4%、其他无菌体液5.1%、生殖道分泌物1.4%、粪便1.0%和其他标本4.9%。肠杆菌科细菌占有分离菌株的43.3%(82 754/190 610),其中最多见者依次为大肠埃希菌(44.4%)、肺炎克雷伯菌(31.7%)、阴沟肠杆菌(6.6%)、奇异变形杆菌(3.5%);不发酵糖革兰阴性杆菌占有分离菌株的24.1%(45 985/190 610),其中最多见者依次为鲍曼不动杆菌(38.3%)、铜绿假单胞菌(36.0%)、嗜麦芽窄食单胞菌(11.9%)和洋葱伯克霍尔德菌(3.9%)。革兰阳性菌中最多见者依次为金葡萄菌、肠球菌属和凝固酶阴性葡萄球菌(只包括血液、脑脊液等无菌体液分离菌)。主要细菌菌种分布见表1。

2.2 革兰阳性球菌对抗菌药物的敏感率和耐药率

2.2.1 葡萄球菌属 34所医院金葡萄菌中甲氧西林耐药株(MRSA)的平均检出率为35.3%(10.3%~62.1%),其中5所儿童医院MRSA的检出率范围为10.3%~47.1%。凝固酶阴性葡萄球菌甲氧西林耐药株(MRCNS)的检出率平均为80.3%(49.3%~100%)。见表2。MRSA和MRCNS对大环内酯类、氨基糖苷类和喹诺酮类等抗菌药物的耐药率均显著高于甲氧西林敏感株(MSSA和MSCNS)。但MRSA对甲氧苄啶-磺胺

表1 CHINET细菌耐药监测的菌种分布

Table 1 Distribution of bacterial species

Organism	No. of strains	%
<i>E. coli</i>	36 735	19.27
<i>Klebsiella</i> spp	27 977	14.68
<i>Acinetobacter</i> spp	19 246	10.10
<i>S. aureus</i>	17 213	9.03
<i>P. aeruginosa</i>	16 562	8.69
<i>Enterococcus</i> spp	16 043	8.42
Coagulase-negative <i>Staphylococcus</i> (from blood, CSF and other sterile body fluid)	8 369	4.39
<i>Enterobacter</i> spp	7 491	3.93
β -hemolytic <i>Streptococcus</i>	7 404	3.88
<i>S. maltophilia</i>	5 471	2.87
<i>H. influenzae</i>	5 070	2.66
<i>S. pneumoniae</i>	4 595	2.41
<i>Proteus</i> spp	3 646	1.91
<i>Serratia</i> spp	2 330	1.22
<i>S. viridans</i> (from blood, CSF and other sterile body fluid)	1 990	1.04
<i>Burkholderia</i> spp	1 921	1.01
<i>Citrobacter</i> spp	1 689	0.89
<i>Moraxella catarrhalis</i>	1 543	0.81
<i>Salmonella</i> spp	1 236	0.65
<i>Morganella</i> spp	943	0.49
Other <i>Pseudomonas</i> spp	870	0.46
Other <i>Haemophilus</i> spp	466	0.24
<i>Helicobacter nemestrinae</i>	362	0.19
<i>Neisseria</i> spp	208	0.11
<i>Alcaligenes</i> spp	112	0.06
<i>Listeria monocytogenes</i>	87	0.05
<i>Providencia</i> spp	54	0.03
<i>Shigella</i> spp	49	0.03
Others*	928	0.49
Total	190 610	100

CSF, cerebrospinal fluid.

* Including *Elizabethkingia meningosepticum*, *Chryseobacterium* spp, *Aerococcus* spp, *Flavobacterium* spp, *Chryseomonas luteola*, and *Vibrio* spp, *Bacillus* spp, *Pasteurella* spp.

甲氧唑的耐药率低于MSSA (8.2%对17.9%)。MRCNS对甲氧苄啶-磺胺甲噁唑的耐药率明显高于MRSA (58.2%对8.2%)，但对庆大霉素和克林霉素的耐药率则显著低于MRSA (27.5%对37.3%和43.2%对65.0%)。91.6%的MRSA对甲氧苄啶-磺胺甲噁唑敏感，86.2%的MRCNS对利福平敏感。

葡萄球菌属中未发现万古霉素耐药。见表3。

2.2.2 肠球菌属 16 043株肠球菌属中粪肠球菌6 693株，屎肠球菌8 173株，分别占41.7%和50.9%；其他肠球菌1 177株，占7.3%。粪肠球菌对绝大多数测试抗菌药物的耐药率均显著低于屎肠球菌，但对氯霉素的耐药率高于屎肠球菌 (30.7%对7.5%)。粪肠球菌对呋喃妥因、磷霉素和氨苄西林的耐药率较低，分别为1.8%、3.8%和3.9%，屎肠球菌对测试药物的耐药率均较高；两者对高浓度庆大霉素的耐药率分别为35.8%和49.0%。粪肠球菌和屎肠球菌中均有少数万古霉素和利奈唑胺耐药株。见表4。121株耐万古霉素的粪肠球菌 (5株) 和屎肠球菌 (116株) 中，根据耐药表型推测或经PCR检测万古霉素耐药相关基因，可分型的50株VRE中，产*vanA*、*vanB*和*vanM*型基因的菌株分别为36株 (粪肠球菌1株，屎肠球菌35株)、8株 (粪肠球菌1株，屎肠球菌7株) 和6株 (全部为屎肠球菌)。

2.2.3 链球菌属 分离到A、B、C、F、G各组 β 溶血链球菌分别为3 589、3 010、362、57和72株，分离自血液或脑脊液等无菌体液标本中的草绿色链球菌1 990株，7.9%的草绿色链球菌对青霉素耐药。各组链球菌属对红霉素和克林霉素的耐药率均近60%或以上：其中A组链球菌对该两药的耐药率可达90%以上。除B组链球菌外，其他链球菌属对左氧氟沙星均较敏感。未发现万古霉素和利奈唑胺耐药株。见表5。

2.2.4 肺炎链球菌 4 595株肺炎链球菌中，84株为脑膜炎分离株 (儿童组66株，成人组18株)，其中PSSP和PRSP菌株分别为10株、74株。4 511株非脑膜炎分离肺炎链球菌根据青霉素药敏试验结果，其中3 212株儿童株中PSSP、PISP和PRSP的检出率分别为86.8%、11.0%和2.2%；成人株中分别为94.7%、3.4%和1.9%。见表6。显示儿童株中PSSP检出率较成人株低，但PISP和PRSP检出率则较成人高。儿童株和成人株对红霉素、克林霉素和甲氧苄啶-磺胺甲噁唑耐药率均较高。儿童株中出现少数左氧氟沙星和莫西沙星的耐药株，耐药株较成人株少。未发现万古霉素和利奈唑胺耐药株。见表7。

2.3 革兰阴性杆菌对抗菌药物的敏感率和耐药率

2.3.1 肠杆菌科细菌 大肠埃希菌对头孢噻肟、环丙沙星、左氧氟沙星、庆大霉素、哌拉西林和甲氧苄啶-磺胺甲噁唑的耐药率均接近或高于

表2 2017年CHINET 监测网各医院葡萄球菌甲氧西林耐药菌株的检出率
Table 2 Prevalence of methicillin-resistant *Staphylococcus* in 2017 CHINET by hospital

Hospital	<i>S. aureus</i>		Coagulase-negative <i>Staphylococcus</i>	
	MR strains/total	%	MR strains/total	%
Shanxi Provincial Children's Hospital	36/349	10.3	37/49	75.5
The First Affiliated Hospital of Harbin Medical University	153/943	16.2	633/855	74.0
The First Affiliated Hospital of Inner Mongolia Medical University	100/527	19.0	125/152	82.2
People's Hospital of Zigui County, Hubei Province	38/199	19.1	5/5	100
The First Hospital of China Medical University	57/261	21.8	234/276	84.8
Tianjin Medical University General Hospital	106/480	22.1	253/297	85.2
First Affiliated Hospital of Xinjiang Medical University	111/491	22.6	87/127	68.5
Shenzhen People's Hospital	74/313	23.6	227/315	72.1
Jinjiang Hospital, Fujian Province	46/185	24.9	18/18	100
Sino-Japanese Friendship Hospital of Jilin University	85/339	25.1	185/231	80.1
Peking Union Medical College Hospital	183/712	25.7	215/292	73.6
General Hospital of Ningxia Medical University	188/715	26.3	66/78	84.6
Sichuan Provincial People's Hospital	133/491	27.1	269/343	78.4
Xiangya Hospital of Central South University	149/545	27.3	406/513	79.1
Beijing Children's Hospital, Capital Medical University	245/884	27.7	541/652	83.0
First Affiliated Hospital of Kunming Medical University	97/346	28.0	145/174	83.3
West China Hospital, Sichuan University	269/953	28.2	300/369	81.3
Shandong Provincial Hospital	149/511	29.2	41/51	80.4
People's Hospital of Pudong New Area, Shanghai	89/254	35.0	35/71	49.3
Sir Run Run Shaw Hospital, Zhejiang University School of Medicine	122/334	36.5	117/156	75.0
Children's Hospital of Fudan University	183/496	36.9	242/293	82.6
Jiangxi Provincial Children's Hospital	71/172	41.3	26/39	66.7
Beijing Hospital	77/164	47.0	163/190	85.8
Shanghai Children's Hospital	160/340	47.1	230/274	83.9
Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School	377/787	47.9	296/381	77.7
Ruijin Hospital, Shanghai JiaoTong University School of Medicine	269/551	48.8	46/53	86.8
Gansu Provincial Hospital	113/230	49.1	25/31	80.6
The First Affiliated Hospital of Anhui Medical University	224/439	51.0	260/315	82.5
Ningbo Longsai Hospital	30/58	51.7	16/23	69.6
The First Affiliated Hospital of Guangzhou Medical College	181/348	52.0	76/91	83.5
Henan Provincial People's Hospital	275/516	53.3	275/310	88.7
Huashan Hospital, Fudan University	230/426	54.0	115/146	78.8
Tongji Hospital, Tongji Medical college of HUST	624/1 042	59.9	178/212	84.0
Shaanxi Provincial People's Hospital	254/409	62.1	114/139	82.0
Total	6 084/17 213	35.3	6 717/8 371	80.2

50%。肠杆菌科细菌对替加环素的耐药率均低于2.3%，对3种碳青霉烯类的耐药率仍较低，除克雷伯菌属的耐药率高于14.4%外，不同菌种的耐药率多在10%以下。见表8。肺炎克雷伯菌对亚胺培南和美罗培南的耐药率分别从2005年的3.0%和

2.9%上升到了2017年的20.9%和24.0%，耐药率上升幅度高达8倍（图1），与此同时，肺炎克雷伯菌每年的分离率亦呈稳步上升趋势。沙门菌属细菌对氨苄西林的耐药率均超过50%，伤寒沙门菌和副伤寒沙门菌对环丙沙星和氯霉素的耐药率高

表3 葡萄球菌属对抗菌药物的耐药率和敏感率

Table 3 Susceptibility of *Staphylococcus* strains to antimicrobial agents

Antimicrobial agent	(%)							
	MRSA (n=6 084)		MSSA (n=11 120)		MRCNS (n=6 717)		MSCNS (n=1 586)	
	R	S	R	S	R	S	R	S
Vancomycin	0	100	0	100	0	100	0	100
Teicoplanin	0	100	0	100	0	100	0	100
Linezolid	0	100	0	100	0	100	0	100
Rifampin	16.2	82.1	1.0	98.5	13.1	86.2	1.9	97.7
Levofloxacin	50.3	48.8	9.8	89.2	56.2	40.9	10.2	88.6
Gentamicin	37.3	60.9	11.9	85.3	27.5	65.7	3.5	93.6
Trimethoprim-sulfamethoxazole	8.2	91.6	17.9	81.9	58.2	40.9	21.7	77.7
Clindamycin	65.0	33.2	26.5	71.7	43.2	54.3	17.3	80.3
Erythromycin	82.9	14.9	53.3	45.5	85.1	13.4	64.6	32.9
Penicillin G	100	0	89.9	10.1	100	0	71.3	28.7
Oxacillin	100	0	0	100	100	0	0	100

表4 粪肠球菌和屎肠球菌对抗菌药物的耐药率和敏感率

Table 4 Susceptibility of *Enterococcus faecalis* and *Enterococcus faecium* to antimicrobial agents

Antimicrobial agent	(%)			
	<i>E. faecalis</i> (n=6 693)		<i>E. faecium</i> (n=8 173)	
	R	S	R	S
Vancomycin	0.1	99.8	1.4	98.5
Teicoplanin	0	99.9	1.1	98.8
Linezolid	1.2	97.4	0.2	99.5
Nitrofurantoin	1.8	96.5	45.4	29.5
Ampicillin	3.9	96.1	90.2	9.8
Chloramphenicol	30.7	67.0	7.5	90.5
Levofloxacin	26.1	71.6	84.7	10.0
Ciprofloxacin	24.7	64.8	88.3	7.5
Gentamicin-High	35.8	62.7	49.0	49.8
Erythromycin	65.0	6.9	88.9	3.9
Fosfomycin	3.8*	92.6*	NA	NA

* Results of urinary tract isolates only. NA, not available.

于其他沙门菌属细菌。沙门菌属细菌对碳青霉烯类和头孢哌酮-舒巴坦的敏感率最高, 超过90%, 见表9。82 754株肠杆菌科细菌对11种常用抗菌药物的总耐药率和敏感率见表10。其中细菌对替加环素、3种碳青霉烯类和阿米卡星的耐药率最低, 为1.5%~9.8%, 对两种酶抑制剂复合剂(哌拉西林-他唑巴坦和头孢哌酮-舒巴坦)的耐药率分别为11.7%和13.0%。

2.3.2 不发酵糖革兰阴性杆菌 16 562株铜绿假单胞菌对亚胺培南和美罗培南的耐药率分别为23.6%和20.9%; 对多黏菌素B和阿米卡星的耐药率分别为0.9%和6.1%; 对所测试的两种酶抑制剂复合剂、庆大霉素、环丙沙星、左氧氟沙星、头孢吡肟和哌拉西林的耐药率<20%。19 246株不动杆菌属中91.5% (17 602/19 246) 为鲍曼不动杆菌, 该菌对亚胺培南和美罗培南的耐药率分别

表5 链球菌属对抗菌药物的耐药率

Table 5 Prevalence of antibiotic-resistant strains in *Streptococcus* spp.

Antimicrobial agent	(%)					
	Group A (n=3 589)	Group B (n=3 010)	Group C (n=362)	Group F (n=57)	Group G (n=72)	<i>S. viridans</i> * (n=1 990)
Penicillin	0.2	0.6	3.0	0	0	7.9
Erythromycin	94.1	73.7	71.2	78.9	66.7	65.4
Clindamycin	92.8	66.0	63.7	82.5	70.8	58.3
Cefotaxime	0.2	5.3	2.3	0	0	11.5
Ceftriaxone	2.5	7.3	2.2	1.9	1.6	8.6
Vancomycin	0	0	0	0	0	0
Linezolid	0	0	0	0	0	0
Levofloxacin	0.4	53.6	3.4	0	11.8	14.0

* Isolates from blood, cerebrospinal fluid or other sterile body fluids.

表6 儿童和成人患者中非脑膜炎肺炎链球菌的分布

Table 6 The distribution of nonmeningitis *S. pneumoniae* isolates from children and adults in terms of penicillin susceptibility in three years

Strains	Isolates from children						Isolates from adults					
	2015		2016		2017		2015		2016		2017	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
PSSP	900	86.5	2 263	89.6	2 787	86.8	426	91.8	788	95.4	1 288	94.7
PISP	66	6.3	186	7.4	355	11.0	26	5.6	28	3.4	46	3.4
PRSP	75	7.2	78	3.1	70	2.2	12	2.6	10	1.2	26	1.9
Total	1 041	100	2 527	100	3 212	100	464	100	826	100	1 360	100

PSSP: penicillin susceptible *S. pneumoniae*; PISP: penicillin intermediate *S. pneumoniae*; PRSP: penicillin resistant *S. pneumonea*.

表7 儿童和成人患者中非脑膜炎肺炎链球菌对抗菌药物的耐药率

Table 7 Prevalence of antibiotic-resistant strains in the nonmeningitis *S. pneumoniae* isolated from children and adults

(%)

Antimicrobial agent	Isolates from children			Isolates from adults		
	PSSP (n=2 787)	PISP (n=355)	PRSP (n=70)	PSSP (n=1 288)	PISP (n=46)	PRSP (n=26)
Penicillin G	0	0	100	0	0	100
Vancomycin	0	0	0	0	0	0
Linezolid	0	0	0	0	0	0
Erythromycin	98.1	100	97.1	93.0	100	100
Clindamycin	96.3	99.4	98.5	89.8	94.3	95.7
Trimethoprim-sulfamethoxazole	73.4	85.4	91.2	62.4	97.3	82.6
Levofloxacin	0.3	0	2.4	3.1	4.7	16.0
Moxifloxacin	0.4	0	0	1.4	0	22.2
Chloramphenicol	6.9	4.3	2.8	11.7	3.2	0

PSSP: penicillin susceptible *S. pneumoniae*; PISP: penicillin intermediate *S. pneumoniae*; PRSP: penicillin resistance *S. pneumonea*.

表8 肠杆菌科细菌对抗菌药物的耐药率和敏感率

Table 8 Susceptibility of *Enterobacteriaceae* species to antimicrobial agents

(%)

Antimicrobial agent	<i>E. coli</i> (n=36 735)		<i>Klebsiella</i> spp (n=27 977)		<i>Proteus</i> spp (n=3 646)		<i>Enterobacter</i> spp (n=7 491)		<i>Serratia</i> spp (n=2 330)		<i>Citrobacter</i> spp (n=1 689)		<i>Morganella</i> spp(n=943)	
	R	S	R	S	R	S	R	S	R	S	R	S	R	S
Tigecycline	0.2	99.5	2.1	93.4	NA	NA	2.3	94.5	0.7	96.0	0.5	97.5	2.3	89.5
Polymyxin B ^a	4.6	95.4	3.6	96.4	NA	NA	9.5	90.5	NA	NA	13.1	86.9	NA	NA
Imipenem	1.9	97.8	20.0	79.1	4.2 ^b	86.9 ^b	6.9	89.5	5.5	90.6	8.1	89.7	19.9	55.2
Meropenem	2.3	97.6	23.1	76.4	2.5	97.3	7.0	92.3	4.6	95.0	7.9	91.4	2.5	97.2
Ertapenem	2.0	97.8	14.4	85.4	1.1	98.0	8.2	90.4	5.3	94.3	7.9	92.0	2.2	97.6
Cefepime	22.2	68.0	27.9	68.1	7.2	84.6	12.1	84.5	7.6	89.2	12.7	84.0	3.0	92.9
Ceftazidime	27.1	68.0	34.3	63.0	7.0	91.6	31.7	65.7	5.2	92.9	30.0	66.4	14.9	81.4
Cefotaxime	59.3	40.1	45.6	53.2	33.8	64.3	39.0	55.3	19.1	76.3	39.2	57.6	23.9	72.8
Ceftriaxone	56.4	42.8	42.1	57.3	27.0	69.1	37.1	61.4	16.5	82.9	36.4	61.6	15.2	78.2
Cefoperazone-sulbactam	6.4	81.1	25.3	66.1	1.7	95.9	11.2	78.1	8.1	85.8	10.8	77.9	3.7	93.2
Cefuroxime	60.5	37.0	46.1	51.2	43.8	55.5	47.8	39.4	88.9	2.5	41.7	53.2	79.8	7.8
Cefazolin	71.3	21.4	59.4	34.2	69.0	21.7	95.9	3.2	99.0	1.0	85.4	13.5	99.1	0.7
Cefoxitin	12.4	80.6	28.6	69.1	4.6	91.8	93.9	4.6	26.9	28.0	61.3	34.9	16.3	42.4
Piperacillin	71.9	20.7	50.9	41.2	25.8	62.2	34.1	59.6	14.1	82.8	39.9	50.2	19.8	71.9
Piperacillin-tazobactam	4.7	91.3	23.6	71.8	1.8	97.0	11.7	76.5	4.0	92.3	12.1	78.1	3.6	93.7
Ampicillin	85.9	13.0	89.1	1.3	64.5	34.7	74.5	9.5	69.9	9.6	NA	NA	NA	NA
Ampicillin-sulbactam	46.3	32.6	46.4	46.8	30.5	58.7	55.2	34.9	59.8	23.6	42.7	51.6	58.8	18.7

表8 (续)
Table 8 (continued)

(%)

Antimicrobial agent	<i>E. coli</i> (n=36 735)		<i>Klebsiella</i> spp (n=27 977)		<i>Proteus</i> spp (n=3 646)		<i>Enterobacter</i> spp (n=7 491)		<i>Serratia</i> spp (n=2 330)		<i>Citrobacter</i> spp (n=1 689)		<i>Morganella</i> spp(n=943)	
	R	S	R	S	R	S	R	S	R	S	R	S	R	S
Amikacin	2.8	96.4	14.1	85.7	3.4	95.4	1.5	97.7	1.2	98.1	3.6	95.7	2.0	97.6
Gentamicin	41.5	57.9	29.2	70.2	26.0	64.2	11.2	87.0	9.5	89.8	18.3	80.6	22.7	73.3
Ciprofloxacin	57.0	40.7	31.1	65.4	39.8	51.7	11.6	84.2	10.6	85.7	19.5	74.7	22.2	68.2
Levofloxacin	54.4	42.9	26.6	71.0	25.2	65.7	9.1	87.8	7.2	89.5	16.2	78.7	10.4	82.4
Nitrofurantoin	2.7	90.2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Trimethoprim-sulfamethoxazole	55.7	44.1	35.0	64.7	56.3	43.5	21.1	78.6	5.7	94.0	27.3	72.4	41.0	58.5
Fosfomycin	4.9 ^c	94.2 ^c	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

^a R=non-wild-type, S=wild-type.^b Results by Kirby-Bauer method.^c Results of urinary tract isolates only.

NA, not available.

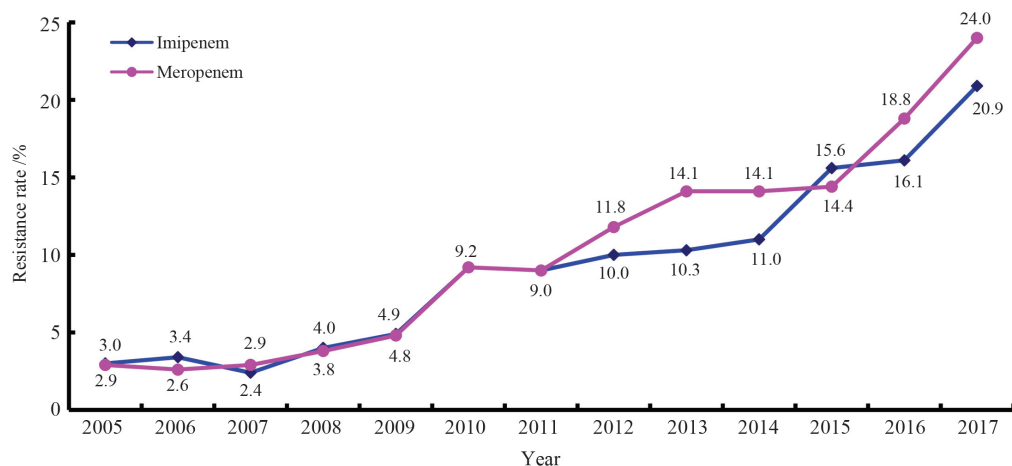


图1 2005—2017年肺炎克雷伯菌对亚胺培南和美罗培南的耐药变迁菌株数量范围 (2 136~26 268株)

Figure 1 Increasing prevalence of imipenem- and meropenem-resistant *Klebsiella pneumoniae* isolates during the period from 2005 to 2017 (the annual number of isolates ranging from 2 136 to 26 268)

表9 沙门菌属对抗菌药物的耐药率和敏感率

Table 9 Susceptibility of *Salmonella* spp. to antimicrobial agents

(%)

Antimicrobial agent	<i>S. typhimurium</i> (n=362)		<i>S. enteritidis</i> (n=214)		<i>S. typhi</i> & <i>S. paratyphi</i> (n=95)	
	R	S	R	S	R	S
Ampicillin	82.1	17.4	75.9	23.6	51.6	48.4
Ampicillin-sulbactam	24.4	56.5	36.3	33.0	30.0	53.3
Amoxicillin-clavulanic acid	24.4	48.3	21.3	48.3	11.5	59.6
Cefoperazone-sulbactam	1.7	93.4	1.0	98.0	0	89.7
Ceftriaxone	26.0	72.2	13.2	86.8	7.1	91.4
Ciprofloxacin	13.6	52.5	7.5	42.0	22.7	39.4
Trimethoprim-sulfamethoxazole	38.0	61.4	8.1	91.5	17.4	82.6
Chloramphenicol	45.5	53.7	1.5	98.5	45.9	54.1
Imipenem	0	100	0	98.8	3.3	96.7
Meropenem	NA	NA	0	100	2.1	97.9

NA, not available.

表10 82 754株肠杆菌科细菌对抗菌药物的耐药率和敏感率

Antimicrobial agent	No. of strains	R /%	S /%
Tigecycline	41 162	1.5	95.3
Amikacin	80 197	6.6	92.8
Ertapenem	50 380	7.0	92.6
Imipenem	79 656	9.4	89.1
Meropenem	62 113	9.8	89.8
Piperacillin-tazobactam	79 334	11.7	83.4
Cefoperazone-sulbactam	51 914	13.0	76.9
Cefepime	81 352	21.6	71.8
Ceftazidime	71 997	28.1	68.2
Gentamicin	78 771	31.8	67.0
Ciprofloxacin	78 246	39.7	56.9

为66.7%和69.3%；对头孢哌酮-舒巴坦和米诺环素的耐药率分别为 43.5%和44.4%，对多黏菌素B和替加环素的耐药率较低（0.1%和6.0%），对其他测试药的耐药率多在40%以上。嗜麦芽窄食单胞菌对甲氧苄啶-磺胺甲噁唑、米诺环素和左氧氟沙星的耐药率低，细菌敏感率近90%或以上。洋葱伯克霍尔德菌对CLSI推荐的美罗培南、头孢他啶、米诺环素、甲氧苄啶-磺胺甲噁唑和氯霉素等抗菌药物的耐药率亦低，细菌敏感率均在82.9%~92.2%；但对左氧氟沙星的敏感率仅为67.6%。见表11。

2.4 其他革兰阴性杆菌

2.4.1 流感嗜血杆菌 5 070株流感嗜血杆菌中，儿童分离株3 161株，成人分离株1 898株。流感嗜血杆菌对氨苄西林的耐药率均近45%或以上，除甲

表11 不发酵糖革兰阴性菌对抗菌药物的耐药率和敏感率

Table 11 Susceptibility of non-fermentative gram-negative bacilli to antimicrobial agents

Antimicrobial agent	(%)							
	<i>P. aeruginosa</i> (n=16 562)		<i>Acinetobacter</i> spp (n=19 246)		<i>S.maltophilia</i> (n=5 471)		<i>B.cepacia</i> (n=1 804)	
	R	S	R	S	R	S	R	S
Amikacin	6.1	91.9	48.6	49.8	NA	NA	NA	NA
Gentamicin	10.7	85.7	63.2	34.5	NA	NA	NA	NA
Piperacillin	19.1	80.9	70.5	22.8	NA	NA	NA	NA
Piperacillin-tazobactam	13.4	86.6	64.5	31.8	NA	NA	NA	NA
Cefoperazone-sulbactam	14.8	71.1	43.5	37.3	18.0	57.4	13.0	66.7
Ampicillin-sulbactam	NA	NA	62.1	32.3	NA	NA	NA	NA
Ceftazidime	21.4	71.1	72.0	24.9	38.1	52.7	8.0	87.6
Cefepime	18.7	62.1	67.7	24.5	NA	NA	NA	NA
Aztreonam	31.4	51.1	NA	NA	NA	NA	NA	NA
Imipenem	23.6	72.7	66.7	32.1	NA	NA	NA	NA
Meropenem	20.9	74.9	69.3	29.7	NA	NA	10.3	82.2
Ciprofloxacin	14.8	79.8	68.3	30.9	NA	NA	NA	NA
Levofloxacin	15.8	77.6	50.8	33.9	9.3	87.3	17.4	67.6
Trimethoprim-sulfamethoxazole	NA	NA	52.6	45.6	5.5	93.9	6.5	92.2
Minocycline	NA	NA	44.4	38.1	1.8	95.2	3.8	83.9
Polymyxin B	0.9	99.1	0.1	99.9	NA	NA	NA	NA
Tigecycline	NA	NA	6.0	74.8	NA	NA	NA	NA
Chloramphenicol	NA	NA	NA	NA	19.8	50.2	11.6	82.9

NA, not available.

氧苄啶-磺胺甲噁唑外，流感嗜血杆菌对其他抗菌药物的敏感率均近70%或以上。儿童分离株对氨苄西林、头孢呋辛、阿奇霉素和甲氧苄啶-磺胺甲噁唑的敏感率低于成人株。流感嗜血杆菌对抗菌药物的敏感率见表12。

3 讨论

2017年CHINET细菌耐药性监测结果：①参加本次细菌耐药性监测的医院较2016年^[2]新增4所（1所儿童专科医院，3所三级综合性医院）。

表12 流感嗜血杆菌对抗菌药物的耐药率和敏感率
Table 12 Susceptibility of *H. influenzae* to antimicrobial agents

Antimicrobial agent	Total (n=5 070)		Isolates from children (n=3 161)		Isolates from adults (n=1 898)	
	R	S	R	S	R	S
Ampicillin	52.2	42.9	56.4	38.6	44.9	50.5
Amoxicillin-clavulanic acid	14.8	85.2	13.9	86.1	17.6	82.4
Ampicillin-sulbactam	22.6	77.4	22.2	77.8	23.0	77.0
Cefuroxime	26.4	68.9	28.6	65.9	21.5	75.3
Ceftriaxone	2.8 ^a	97.2	1.7 ^a	98.3	5.4 ^a	94.6
Chloramphenicol	6.3	90.4	5.2	92.3	8.1	87.4
Azithromycin	22.2 ^a	77.7	26.1 ^a	73.9	14.2 ^a	85.9
Levofloxacin	1.3 ^a	98.1	0.3 ^a	99.6	2.8 ^a	95.6
Trimethoprim-sulfamethoxazole	63.6	33.3	66.6	30.2	59.3	37.7
Meropenem	1.6 ^a	98.4	1.3 ^a	98.6	1.9 ^a	98.0

^a percentage of non-susceptible isolates.

2017年收集的总菌株数为190 610株,较2016年的153 059株增加24.5%。除大肠埃希菌外,肠杆菌科细菌中大多数菌属的检出率较2016年略有上升,以克雷伯菌属为最多(增加0.87%)。不发酵糖革兰阴性杆菌中不动杆菌属的检出率略有增加,但铜绿假单胞菌持平。革兰阳性球菌中金葡萄、肠球菌属和β溶血链球菌均略有增加,但凝固酶阴性葡萄球菌减少。流感嗜血杆菌略减少但肺炎链球菌增多。②金葡萄中甲氧西林耐药株检出率由2016年的38.4%继续下降至35.3%,但儿童分离金葡萄中MRSA的检出率呈上升趋势,应引起重视。MRSA对甲氧苄啶-磺胺甲噁唑的耐药率略上升(7.4%对8.2%)。凝固酶阴性葡萄球菌中甲氧西林耐药株检出率由2016年的77.6%上升至80.3%;MRCNS对利福平的耐药率略有上升(12.7%对13.1%)。③121株耐万古霉素粪肠球菌(5株)和屎肠球菌(116株)中,根据耐药表型推测或经PCR检测万古霉素耐药相关基因,可分型的50株VRE中,产*vanA*、*vanB*或*vanM*型基因的菌株分别为36株(粪肠球菌1株,屎肠球菌35株)、8株(粪肠球菌1株,屎肠球菌7株)和6株耐药(全部为屎肠球菌)。发现少数利奈唑胺耐药粪肠球菌和屎肠球菌。由于不同耐药基因导致其对万古霉素和替考拉宁的敏感性有差别,实验室应加强对VRE耐药基因型的检测。④常规药敏试验结果显示,部分CRE菌株报告ESBL检测结果为阴性。由于碳青霉烯酶的存在可干扰ESBL的检测,导致假阴性结果。对CRE菌株检测相关β内酰胺酶耐药基

因结果发现,90%以上的菌株同时产碳青霉烯酶和ESBL。因此,建议实验室对于CRE菌株的ESBL检测结果不做报告。

革兰阴性菌的细菌耐药性问题日趋严重,临床上对于某些耐药菌感染的治疗方法极为有限^[3-5]。在过去的10年中,碳青霉烯类药物被认为是治疗耐药革兰阴性菌感染的最后一道防线。随着碳青霉烯类耐药菌株尤其是肺炎克雷伯菌、铜绿假单胞菌和鲍曼不动杆菌检出率的快速上升,已成为当前临床抗感染治疗的难题。历年CHINET细菌耐药性监测数据显示,肺炎克雷伯菌对亚胺培南和美罗培南的耐药率分别从2005年的3.0%和2.9%上升到了2017年的20.9%和24.0%,耐药率上升幅度达8倍,与此同时,肺炎克雷伯菌每年的分离率亦呈稳步上升趋势。本次监测结果显示,肺炎克雷伯菌对碳青霉烯类的耐药率均>20%;5所儿童医院中除1所医院分离的肺炎克雷伯菌对亚胺培南的耐药率为2.5%外,其余4所的耐药率范围为32.1%~45.5%。而铜绿假单胞菌和鲍曼不动杆菌对亚胺培南的耐药率分别已接近23.6%和66.7%。从细菌分布看,8 247株CRE菌株中,分离率占前三位的是肺炎克雷伯菌(68.8%, 5 673/8 274)、大肠埃希菌(10.9%, 896/8 274)和阴沟肠杆菌(6.9%, 568/8 274)。34所医院分离的克雷伯菌属细菌对亚胺培南的耐药率范围为0~42.2%;铜绿假单胞菌对亚胺培南的耐药率范围为1.7%~41.5%;不动杆菌属对亚胺培南的耐药率范围为3.8%~90.7%。研究显示,碳青霉烯

类耐药菌株对多数临床常用抗菌药物高度耐药,多数为仅对替加环素和多黏菌素敏感的广泛耐药菌株。为应对此类超级耐药细菌所致感染,实验室需要积极与临床沟通,增做其他可能有效的抗菌药物如多黏菌素、替加环素和头孢他啶-阿维巴坦的药敏试验。但微生物实验室人员在药敏试验时,需特别注意多黏菌素和替加环素的药敏试验方法存在的问题。多黏菌素药敏试验方法目前CLSI不推荐纸片法、琼脂稀释法等其他药敏方法,必须用微量肉汤稀释法进行测定。替加环素体外药敏结果受多种因素的影响,包括培养基类型、配制时间、检测方法、菌种类型、折点选择等^[6]。因此,实验室用纸片扩散法和自动化仪器测定替加环素敏感性时,若出现中度敏感或耐药结果时,需采用微量肉汤稀释法确认其敏感性。

产生KPC型碳青霉烯酶或NDM-1型金属酶是肠杆菌科细菌对碳青霉烯类耐药最主要的耐药机制,且不同人群来源和不同地区来源菌株的耐药机制有所不同。研究结果显示,儿童患者分离的CRE菌株主要产生NDM-1型金属酶,而成人患者分离的菌株主要产生KPC型碳青霉烯酶。从地域分布看,与南方相比,我国北方医院临床分离的CRE菌株中产NDM-1金属酶菌株多些,而产KPC型碳青霉烯酶菌株少些^[7]。除此之外,临床实验室需加强对CRE菌株中D类碳青霉烯酶的检测,尤其是OXA-48型碳青霉烯酶家族包括OXA-181和OXA-232型碳青霉烯酶。由于目前CLSI以及相关文献推荐的方法均无法有效检测OXA型碳青霉烯酶,可能导致检测结果假阴性。研究显示,我国已有产OXA型碳青霉烯酶肺炎克雷伯菌所致感染的克隆菌株流行报道,且此类耐药菌株主要出现

于儿童患者分离菌株^[8]。未来需要开展全国范围内的关于OXA型碳青霉烯酶的流行病学调查研究,以替莫西林为基础的表型检测结合耐药基因检测方法明确该类酶在临床分离肠杆菌科细菌中的检出率,为后续采取有效的感染预防控制措施提供参考。

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