

2012 年中国 CHINET 细菌耐药性监测

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摘要: **目的** 了解国内主要地区临床分离菌对常用抗菌药物的敏感性和耐药性。**方法** 对国内主要地区(13 所综合性医院、2 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细菌药敏试验,按 CLSI 2012 年版标准判断结果。**结果** 2012 年 1—12 月收集各医院临床分离菌共 72 397 株,其中革兰阳性菌 20 354 株,占 28.1%,革兰阴性菌 52 043,占 71.9%。金葡菌和凝固酶阴性葡萄球菌中甲氧西林耐药株(MRSA 和 MRCNS)的检出率平均分别为 47.9%和 77.1%。甲氧西林耐药株对 β 内酰胺类抗生素和其他测试抗菌药物的耐药率显著高于甲氧西林敏感株。MRSA 中 87.0% 菌株对甲氧苄啶-磺胺甲噁唑敏感;MRCNS 中 89.1% 菌株对利福平敏感,发现 0.4% 菌株对替考拉宁耐药。葡萄球菌属细菌中未发现对万古霉素、利奈唑胺耐药株。肠球菌属细菌中粪肠球菌对所测试的抗菌药物(除氯霉素外)的耐药率均显著低于屎肠球菌。两者中均检出少数万古霉素耐药株,根据表型推测多数为 VanA 型耐药;此外两者中均有少数替考拉宁和利奈唑胺耐药株。大肠埃希菌、克雷伯菌属(肺炎克雷伯菌和产酸克雷伯菌)和奇异变形杆菌中产 ESBLs 株平均分别为 55.3%、33.9%和 20.7%。肠杆菌科细菌对碳青霉烯类抗生素仍高度敏感,总耐药率 4.4%~6.3%。不动杆菌属细菌(鲍曼不动杆菌占 89.6%)对亚胺培南和美罗培南耐药率分别为 57.0%和 61.0%。肠杆菌科细菌中仍有少数碳青霉烯类抗生素耐药株,尤以肺炎克雷伯菌为多。**结论** 细菌耐药性仍是临床重要问题,尤其耐碳青霉烯类肠杆菌科细菌应引起高度关注。

关键词: 细菌耐药性; 药敏试验; 多重耐药; 碳青霉烯类耐药肠杆菌科细菌; 耐万古霉素肠球菌; 甲氧西林耐药葡萄球菌; 青霉素耐药肺炎链球菌; 超广谱 β 内酰胺酶

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2012 CHINET surveillance of bacterial resistance in China

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Abstract: **Objective** To investigate the susceptibility and resistance of clinical bacterial isolates from hospitals in several major regions of China. **Methods** Thirteen general hospitals and two children's hospitals were involved in this pro-

gram. Antimicrobial susceptibility testing was carried out according to a unified protocol using Kirby-Bauer method or automated systems. Results were analyzed according to the breakpoints of CLSI 2012. **Results** A total of 72 397 clinical isolates were collected from January through December 2012, of which Gram negative organisms and Gram positive cocci accounted for 71.9% (52 043/72 397) and 28.1% (20 354/72 397) respectively. The average prevalence of methicillin-resistant strains in *S. aureus* (MRSA) and coagulase-negative *Staphylococcus* (MRCNS) was 47.9% and 77.1%, respectively. The resistance rates of MR strains to beta-lactams and other antimicrobial agents were much higher than those of MS strains. However, nearly 87.0% of MRSA strains were still susceptible to trimethoprim-sulfamethoxazole, while 89.1% of MRCNS strains were susceptible to rifampin. No staphylococcal strain was found resistant to vancomycin, teicoplanin or linezolid. Nearly 0.4% of the MRCNS strains were found resistant to teicoplanin. In *Enterococcus* spp., the resistance rates of *E. faecalis* strains to most antimicrobial agents tested (except chloramphenicol) were much lower than those of *E. faecium*. Some strains of both species were resistant to vancomycin, most of which were VanA type based on their phenotype. Some strains resistant to teicoplanin or linezolid were identified in both species. The prevalence of ESBLs producing strains was 55.3% in *E. coli*, 33.9% in *Klebsiella* spp. (*K. pneumoniae* and *K. oxytoca*) and 20.7% in *Proteus mirabilis* on average. ESBLs producing *Enterobacteriaceae* strains were more resistant than non-ESBLs-producing strains to all the antimicrobial agents tested. *Enterobacteriaceae* strains were still highly susceptible to the three carbapenems tested, the overall resistance rates being 4.4%-6.3%. The resistance rates of *Acinetobacter* spp. (*A. baumannii* accounted for 89.6%) to imipenem and meropenem were up to 57.0% and 61.0%, respectively. Some carbapenem resistant strains were found in various *Enterobacteriaceae* spp., especially in *K. pneumoniae*. **Conclusions** Bacterial resistance is still an important problem in clinical setting in China, especially the carbapenem resistant *Enterobacteriaceae*, which is of great concern.

Key words: bacterial resistance; antimicrobial susceptibility testing; multi-drug resistant; carbapenem-resistant *Enterobacteriaceae*; vancomycin-resistant *Enterococcus*; methicillin-resistant *Staphylococcus*; penicillin-resistant *Streptococcus pneumoniae*; extended-spectrum beta-lactamase

随着抗菌药物在临床的广泛应用,多重耐药和泛耐药菌株日益增多,已成为公共卫生领域的严重问题。

现将 2012 年中国 CHINET 细菌耐药性监测结果报道如下。

材料与方 法

一、材料

(一)细菌 收集国内主要地区 13 所综合性和 2 所儿童医院 2012 年 1 月 1 日至 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。

(二)培养基 药敏试验用 Mueller-Hinton (MH)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 SR158 营养补充剂。上述试剂均为英国 OXOID 公司产品。

(三)抗菌药物纸片和 E 试验条 抗菌药纸片为美国 BBL 公司或英国 OXOID 公司产品。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产品。

二、方法

参照 2012 年 CLSI 推荐的药敏试验方法进行。

(一)药敏试验 采用 Kirby-Bauer 纸片扩散法或自动化仪器法。质控菌为金葡萄菌 ATCC 25923、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。药敏试验结果判断标准为 CLSI 2012 年版^[1]。尿分离大肠埃希菌和肠球菌属细菌对磷霉素的药敏试验判断标准按 CLSI 2012 版($S \leq 64$ mg/L)^[2]。

(二) 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 推荐的纸片法筛选和酶抑制剂增强确证试验检测大肠埃希菌、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(ESBLs)菌株。

(三)青霉素不敏感肺炎链球菌检测 经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 值,脑膜炎株和非脑膜炎株分别按 CLSI 2012 年标准判定为青霉素敏感、中介或耐药株。

(四)耐万古霉素肠球菌检测 经万古霉素纸片法测定结果为非敏感株者,用万古霉素和替考拉宁

E 试验条测定 MIC 值,并根据表型推测或采用 PCR 确认万古霉素耐药基因型别。

(五)统计分析 试验结果采用 WHONET5.6 软件统计分析。

结 果

一、细菌及其分布

2012 年共收集临床分离菌 72 397 株,其中革兰阳性菌 20 354 株,占 28.1%,革兰阴性菌 52 043 株,占 71.9%。87.3% 菌株自住院患者中分离,12.7% 菌株自门诊急诊患者中分离。痰液等呼吸道标本占 44.4%、尿液 21.4%、血液 11.7%、无菌体液 5.4%、伤口脓液 5.6%、粪便 1.8%、生殖道分泌物 1.7%、其他标本 7.9%。肠杆菌科细菌(31 278 株)占革兰阴性杆菌的 60.1%,其中最多见者依次为大肠埃希菌、克雷伯菌属、肠杆菌属、变形杆菌属;不发酵糖革兰阴性杆菌 19 620 株,占革兰阴性杆菌的 37.7%,其中最多见者依次为不动杆菌属、铜绿假单胞菌和嗜麦芽窄食单胞菌(表 1)。革兰阳性菌中最多见者依次为金葡菌、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)(表 2)。

二、革兰阳性球菌对抗菌药物的敏感率和耐药率

(一)葡萄球菌属 15 所医院分离的金葡菌中甲氧西林耐药株(MRSA)的平均检出率为 47.9%(18.4%~82.9%),其中 2 所儿童医院 MRSA 的检出率较低,分别为 18.4%和 29.4%。凝固酶阴性葡萄球菌甲氧西林耐药株(MRCNS)的检出率平均为 77.1%(59.0%~89.5%),儿童分离株与成人分离株中甲氧西林耐药(MR)菌株的检出率差异无统计学意义(表 3)。MRSA 和 MRCNS 对 β 内酰胺类、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)。MRCNS 对甲氧苄啶-磺胺甲噁唑的耐药率明显高于 MRSA(分别为 60.8%和 11.5%);但对利福平的耐药率则显著低于 MRSA(分别为 10.5%和 57.5%)。MRSA 中约 87.0% 菌株对甲氧苄啶-磺胺甲噁唑敏感。MRCNS 中有 89.1% 菌株对利福平敏感。MRCNS 中有 0.4% 菌株对替考拉宁耐药,葡萄球菌属细菌中均未发现对万古霉素、利奈唑胺耐药的菌株(表 4)。

表 1 CHINET 耐药监测革兰阴性菌菌种分布

Table 1 Distribution of gram negative bacterial species in CHINET resistance surveillance during 2012

Organism	No. of strains	%
<i>E. coli</i>	14 154	27.20
<i>Klebsiella</i> spp.	9 621	18.49
<i>Acinetobacter</i> spp.	8 739	16.79
<i>P. aeruginosa</i>	7 270	13.97
<i>Enterobacter</i> spp.	3 031	5.82
<i>S. maltophilia</i>	2 156	4.14
<i>Proteus</i> spp.	1 565	3.01
<i>Serratia</i> spp.	997	1.92
<i>H. influenzae</i>	960	1.84
<i>Salmonella</i> spp.	639	1.23
<i>Burkholderia</i> spp.	608	1.17
<i>Citrobacter</i> spp.	596	1.15
Other <i>Pseudomonas</i> spp.	464	0.89
<i>Morganella</i> spp.	298	0.57
<i>Moraxella</i> spp.	224	0.43
<i>Raoultella</i>	121	0.23
Other <i>Hemophilus</i> spp.	102	0.20
<i>Pantoea</i> spp.	97	0.19
<i>Shigella</i> spp.	81	0.16
<i>Alcaligenes</i> spp.	50	0.10
<i>Comamonas</i> spp.	40	0.08
<i>Providencia</i> spp.	37	0.07
<i>Ralstonia</i> spp.	26	0.05
<i>Neisseria</i> spp.	21	0.04
<i>Flavobacterium</i> spp.	16	0.03
<i>Bordetella</i> spp.	15	0.03
<i>Aeromonas</i> spp.	11	0.02
<i>Kingella</i> spp.	5	0.01
Others	99	0.19
Total	52 043	100

表 2 CHINET 耐药监测革兰阳性菌菌种分布

Table 2 Distribution of gram positive bacterial species in CHINET resistance surveillance during 2012

Organism	No. of strains	%
<i>S. aureus</i>	7 339	36.06
<i>Enterococcus</i> spp.	6 228	30.60
Coagulase-negative <i>Staphylococcus</i> (from blood, CSF or other body fluid)	3 725	18.30
<i>S. pneumoniae</i>	1 343	6.60
Beta-hemolytic <i>Streptococcus</i>	1 170	5.75
<i>S. viridans</i> (from blood, CSF or other body fluid)	495	2.43
Others	54	0.27
Total	20 354	100

表 3 2012 年 CHINET 监测网各医院葡萄球菌甲氧西林耐药菌株检出率

Table 3 Prevalence of methicillin-resistant *Staphylococcus* by hospital in CHINET resistance surveillance during 2012

Hospital	<i>S. aureus</i>		Coagulase-negative <i>Staphylococcus</i>	
	MR strains/total	%	MR strains/total	%
Shanghai Huashan Hospital	266/435	61.1	112/146	76.7
Shanghai Ruijin Hospital	255/434	58.8	66/89	74.2
Beijing Union Hospital	297/745	39.9	163/222	73.4
Wuhan Tongji Hospital	733/1 143	64.1	303/371	81.7
First Affiliated Hospital of Guangzhou Medical University	188/313	60.1	78/95	82.1
Beijing Hospital	350/422	82.9	74/92	80.4
Children's Hospital of Fudan University	90/489	18.4	403/683	59.0
Shanghai Children's Hospital	163/554	29.4	357/399	89.5
People's Hospital of Gansu Province	190/496	38.3	54/68	79.4
First Affiliated Hospital of Xinjiang Medical University	186/381	48.8	122/143	85.3
First Affiliated Hospital of Anhui Medical University	175/326	53.7	190/233	81.5
First Affiliated Hospital of Kunming Medical University	52/138	37.7	132/190	69.5
Sir Run Run Shaw Hospital of Zhejiang Province	167/365	45.8	315/378	83.3
First Affiliated Hospital of China Medical University	224/524	42.7	294/353	83.3
General Hospital of Tianjin Medical University	183/574	31.9	209/263	79.5
Total	3 519/7 339	47.9	2 872/3 725	77.1

表 4 葡萄球菌属细菌对抗菌药物的耐药率和敏感率(%)

Table 4 Resistance and sensitivity rates of *Staphylococcus* spp. to antimicrobial agents (%)

Antimicrobial agent	MSSA (3 686)		MRSA (3 519)		MSCNS (733)		MRCNS (2 872)	
	R	S	R	S	R	S	R	S
Vancomycin	0	100	0	100	0	100	0	100
Teicoplanin	0	100	0	100	0	100	0.4	99.3
Linezolid	0	100	0	100	0	100	0	100
Penicillin G	89.9	10.1	100	0	70.6	29.4	100	0
Oxacillin	0	100	100	0	0	100	100	0
Ampicillin-sulbactam	1.3	96.2	75.2	13.5	0.7	99.0	25.6	66.2
Cefazolin	0.9	98.5	85.7	11.6	1.4	98.6	34.8	61.2
Cefuroxime	0.7	99.1	86.7	10.1	1.2	97.8	37.8	56.4
Erythromycin	51.1	44.2	85.7	12.0	58.2	38.4	87.8	10.9
Clindamycin	25.6	67.7	71.3	27.1	14.3	78.0	44.0	50.5
Rifampin	1.7	97.9	57.5	41.6	1.9	97.5	10.5	89.1
Gentamicin	15.1	82.7	74.2	24.0	5.9	91.3	37.8	55.0
Levofloxacin	6.2	92.6	80.6	17.8	6.9	89.7	44.9	47.4
Ciprofloxacin	11.0	85.7	85.4	13.3	8.1	88.6	58.2	35.0
Trimethoprim-sulfamethoxazole	13.7	85.2	11.5	87.0	23.0	76.4	60.8	37.1

(二) 肠球菌属 6 228 株肠球菌属细菌中粪肠球菌 3 131 株, 屎肠球菌 2 609 株, 分别占肠球菌属细菌的 50.3% 和 41.9%; 其他肠球菌属 488 株, 占 7.8%。粪肠球菌对所测试的大多数抗菌药物的耐药率显著低于屎肠球菌, 但对氯霉素的耐药率高于屎肠球菌(29.7% 对 5.7%)。粪肠球菌尿标本分离株对磷霉素耐药率为 2.8%, 其余菌株对呋喃妥因、

氨苄西林的耐药率较低, 分别为 4.6% 和 9.0%。屎肠球菌除尿标本分离株对磷霉素的耐药率为 11.3% 外, 对其他测试的抗菌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 33.6% 和 57.9%。粪肠球菌和屎肠球菌中均有少数万古霉素、替考拉宁和利奈唑胺耐药株。粪肠球菌中 8 株对万古霉素耐药, 其中 VanA 型 6 株, VanB 型 2 株。

屎肠球菌中 65 株对万古霉素耐药,其中 VanA 型 37 株, VanB 型 27 株, VanM 型 1 株(表 5)。

表 5 粪肠球菌和屎肠球菌对抗菌药物的耐药率和敏感率(%)

Table 5 Resistance and sensitivity rates of *Enterococcus* spp. to antimicrobial agents (%)

Antimicrobial agent	<i>E. faecalis</i> (3 131)		<i>E. faecium</i> (2 609)	
	R	S	R	S
Vancomycin	0.3	99.7	2.5	97.1
Teicoplanin	0.2	99.8	1.3	98.2
Linezolid	0.3	99.3	0	99.8
Ampicillin	9.0	91.0	91.4	8.6
Chloramphenicol	29.7	64.0	5.7	73.7
Erythromycin	69.8	9.5	89.9	3.1
Rifampin	61.2	18.4	87.6	10.2
Gentamicin-High	33.6	60.5	57.9	40.4
Levofloxacin	26.5	68.7	84.3	9.9
Ciprofloxacin	29.6	47.7	89.4	5.8
Nitrofurantoin	4.6	92.2	44.8	34.5
Fosfomycin*	2.8	95.4	11.0	81.8

* 1 538 strains of *E. faecalis* isolated from urine; 1 414 strains of *E. faecium* isolated from urine.

(三)链球菌属 分离到 A、B、C、G 各组 β 溶血链球菌分别为 248、649、84、73 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 495 株。各组 β 溶血链球菌对青霉素均极敏感,15.4% 草绿色链球菌对之耐药。各组链球菌属细菌对红霉素和克林霉素的耐药率均 >50.0%;其中 A 组链球菌对两药的耐药率接近 90.0%。少数 β 溶血链球菌对头孢呋辛、头孢噻肟、头孢曲松和左氧氟沙星耐药,但草绿色链球菌对上述抗菌药物的耐药率可达 10.0%~17.0%。未发现万古霉素、利奈唑胺耐药株(表 6)。

(四)肺炎链球菌 1 343 株肺炎链球菌中有 11 株脑膜炎株(儿童 4 株,成人 7 株)和 1 332 株非脑膜炎株(儿童 930 株,成人 402 株)。儿童株中青霉素敏感、中介和耐药肺炎链球菌(PSSP、PISP 和 PRSP)的检出率分别为 77.1%、12.7%和 10.2%,成人株中分别为 93.9%、5.4%和 0.7%(表 7)。药敏试验结果显示,儿童株和成人株对红霉素和克林霉素耐药率均较高。儿童株中已出现少数对左氧氟沙星耐药的菌株,但较成人株的耐药率为低。未发现万古霉素和利奈唑胺耐药株(表 8)。

表 6 链球菌属细菌对抗菌药物的耐药率(%)

Table 6 Percentage of the strains resistant to antimicrobial agents in various *Streptococcus* species (%)

Antimicrobial agent	Group A (248)	Group B (649)	Group C (84)	Group G (73)	<i>S. viridans</i> * (495)
Penicillin	1.3	2.6	5.6	1.6	15.4
Erythromycin	88.8	60.9	65.8	54.3	57.4
Clindamycin	87.4	55.3	63.8	58.0	58.0
Cefuroxime	0.8	0.7	0	0	10.3
Cefotaxime	1.2	2.4	1.5	0	15.3
Ceftriaxone	2.5	3.0	5.6	0	17.4
Levofloxacin	0.9	43.8	9.2	1.6	16.3
Vancomycin	0	0	0	0	0
Linezolid	0	0	0	0	0

* Isolated from blood, CSF or other sterile body fluids.

三、革兰阴性杆菌对抗菌药物的敏感率和耐药率

(一)肠杆菌科细菌 大肠埃希菌、克雷伯菌属细菌(肺炎克雷伯菌和产酸克雷伯菌)以及奇异变形杆菌中产 ESBLs 菌株的检出率分别为 55.3%、33.9%和 20.7%。上述产 ESBLs 株对青霉素类、头孢菌素类、氨基糖苷类、喹诺酮类、甲氧苄啶-磺胺甲噁唑的耐药率均显著高于非产 ESBLs 株。大肠埃希菌对环丙沙星、庆大霉素和哌拉西林的耐药率均接近或高于 50.0%。肠杆菌科细菌对 3 种碳青霉烯类抗生素的耐药率较低,不同菌种的耐药率大多 <10.0%。变形杆菌属、摩氏摩根菌和普罗威登菌对亚胺培南的耐药率均明显高于对美罗培南的耐药率(表 9)。副伤寒甲沙门菌对氨苄西林的耐药率(8.8%)显著低于伤寒沙门菌(57.1%)、肠炎沙门菌(64.5%)和鼠伤寒沙门菌(73.3%)。除鼠伤寒沙门菌外(耐药率 51.3%),其他沙门菌对甲氧苄啶-磺胺甲噁唑的耐药率均 <20.0%,副伤寒甲沙门菌和肠炎沙门菌对氯霉素的耐药率(<10.0%)显著低于伤寒沙门菌和鼠伤寒沙门菌(≥50.0%)。所有沙门菌属细菌对头孢曲松和环丙沙星均较敏感(表 10)。志贺菌属细菌 81 株,其中福氏志贺菌 46 株、宋氏志贺菌 30 株,其他志贺菌 5 株。宋氏志贺菌对氨苄西林-舒巴坦、环丙沙星、氯霉素耐药率较福氏志贺菌显著为低(表 11)。肠杆菌科细菌对 3 种碳青霉烯类抗生素的总耐药率最低,为 4.4%~6.3%,其次为阿米卡星、两种酶抑制剂复方制剂(表 12)。

表 7 儿童和成人医院中肺炎链球菌的分布

Table 7 Distribution of *S. pneumoniae* isolates in children and adults by year

Strains	Isolates from children				Isolates from adults			
	2011		2012		2011		2012	
	Number	%	Number	%	Number	%	Number	%
PSSP	582	73.6	720	77.1	310	93.1	384	93.9
PISP	107	13.5	119	12.7	16	4.8	22	5.4
PRSP	102	12.9	95	10.2	7	2.1	3	0.7
Total	791	100	934	100	333	100	409	100

表 8 儿童和成人患者非脑脊液标本肺炎链球菌对抗菌药物的耐药率(%)

Table 8 Prevalence of various resistant *S. pneumoniae* (nonmeningitis strains) in the isolates from children or adults (%)

Antimicrobial agent	Isolates from children			Isolates from adults		
	PSSP (720)	PISP (119)	PRSP(94)	PSSP (384)	PISP(22)	PRSP(3)*
Penicillin	0	0	100	0	0	3
Erythromycin	96.4	97.5	98.9	88.8	100	2
Clindamycin	95.1	96.6	98.9	85.9	88.9	1
Levofloxacin	0.3	0	1.1	1.9	5.3	0
Moxifloxacin	0.2	0	0	1.8	0	0
Vancomycin	0	0	0	0	0	0
Linezolid	0	0	0	0	0	0

* The figures are number of strains when $n < 10$.

表 9 肠杆菌科细菌对抗菌药物的耐药率和敏感率(%)

Table 9 Resistance and sensitivity rates of *Enterobacteriaceae* species to antimicrobial agents (%)

Antimicrobial agent	<i>E. coli</i> (14 154)		<i>Klebsiella</i> spp. (9 621)		<i>Proteus</i> spp. (1 249)		<i>Enterobacter</i> spp. (3 031)		<i>Citrobacter</i> spp. (596)		<i>Morganella</i> spp. (298)		<i>Serratia</i> spp. (997)		<i>Providencia</i> spp. (37)	
	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S
	Piperacillin	76.0	17.8	52.0	36.4	24.8	65.4	42.9	50.6	48.7	42.2	23.7	63.7	24.2	71.1	25.0
Cefazolin	70.5	9.8	53.7	16.2	48.8	10.7	94.0	1.8	81.7	6.4	98.7	0.8	96.3	1.2	76.5	8.8
Cefuroxime	63.3	34.4	50.1	47.1	35.4	63.8	54.4	39.4	46.6	48.0	78.9	12.4	86.8	7.9	20.7	75.9
Cefotaxime	63.2	35.8	48.5	49.3	30.2	67.0	47.5	45.4	46.7	47.2	28.5	66.3	29.6	60.8	19.4	77.4
Ceftazidime	30.0	63.4	32.6	62.9	6.1	91.9	34.3	60.6	33.6	59.6	18.4	78.3	9.4	86.7	5.6	83.3
Cefepime	25.0	66.2	20.7	74.1	5.9	90.2	12.2	83.4	11.5	84.9	4.1	93.8	7.8	88.8	2.9	97.1
Cefoxitin	15.5	76.8	16.0	81.4	4.0	91.1	89.2	8.5	73.0	21.2	20.0	49.0	31.7	35.6	20.0	80.0
Piperacillin-tazobactam	4.8	89.2	14.1	77.2	0.8	98.5	12.0	74.6	11.2	76.2	5.8	91.8	5.7	90.7	2.7	91.9
Cefoperazone-sulbactam	7.6	73.3	17.0	69.6	2.5	94.3	10.6	73.5	12.1	72.2	4.2	88.3	9.0	82.2	0	85.3
Imipenem	0.9	98.3	8.9	89.3	18.0	72.1	3.5	90.1	4.0	90.7	25.5	42.9	6.0	87.5	11.8	73.5
Meropenem	1.0	98.4	10.8	87.8	0.7	98.3	3.7	94.5	4.3	94.3	1.2	96.5	6.3	93.1	0	97.1
Ertapenem	1.5	97.4	12.9	85.1	1.1	95.9	10.3	85.4	4.6	94.0	2.4	97.1	7.9	90.6	3.3	96.7
Gentamicin	48.0	50.7	28.5	70.4	30.8	63.7	17.8	79.7	25.6	72.6	35.5	59.7	16.9	82.4	45.9	40.5
Amikacin	5.4	92.1	11.4	87.6	5.3	93.5	6.6	90.1	6.7	92.1	3.1	95.5	4.8	94.4	32.4	67.6
Ciprofloxacin	58.1	38.2	24.1	68.4	43.2	50.0	12.0	81.9	23.3	69.1	25.1	60.3	13.7	80.4	43.2	35.1
Trimethoprim-sulfamethoxazole	60.1	39.1	31.9	66.5	54.9	44.3	26.3	72.6	33.4	66.2	50.9	48.0	9.1	89.6	62.9	31.4
Fosfomycin*	6.5	92.5														

* 7 257 strains of *E. coli* isolated from urine.

表 10 沙门菌属和志贺菌属细菌对抗菌药物的耐药率和敏感率(%)

Table 10 Resistance and sensitivity rates of *Salmonella* spp. to antimicrobial agents (%)

Antimicrobial agent	<i>Salmonella typhi</i>		<i>Salmonella paratyphi A</i>		<i>Salmonella enteritidis</i>		<i>Salmonella typhimurium</i>	
	(14)		(38)		(206)		(195)	
	R	S	R	S	R	S	R	S
Ampicillin	57.1	42.9	8.8	85.3	64.5	35.5	73.3	25.7
Ampicillin-sulbactam	25.0	75.0	6.5	87.1	35.6	40.7	42.4	35.6
Amoxicillin-clavulanic acid	0	85.7	10.0	90.0	2.4	59.8	9.4	53.9
Ceftriaxone	0	100	0	100	12.6	86.3	15.3	83.1
Cefoperazone-sulbactam	0	100	0	92.3	2.3	85.5	4.4	82.9
Chloramphenicol	50.0	50.0	0	88.5	7.9	91.5	52.9	46.0
Trimethoprim-sulfamethoxazole	14.3	85.7	18.8	81.2	9.8	89.3	51.3	46.6
Ciprofloxacin	0	78.6	0	89.5	2.0	86.8	15.5	56.5

表 11 76 株志贺菌属细菌对抗菌药物的耐药率和敏感率(%)

Table 11 Resistance and sensitivity rates of 76 *Shigella* spp. to antimicrobial agents (%)

Antimicrobial agent	<i>Shigella flexneri</i> (46)		<i>Shigella sonnei</i> (30)	
	R	S	R	S
	Ampicillin	97.7	2.3	85.7
Ampicillin-sulbactam	75.6	7.3	20.0	52.0
Ceftriaxone	48.7	38.5	36.0	60.0
Chloramphenicol	88.9	11.1	4.5	90.9
Trimethoprim-sulfamethoxazole	84.1	13.6	80.0	20.0
Ciprofloxacin	52.2	32.6	3.3	90.0

表 12 31 277 株肠杆菌科细菌对抗菌药物的耐药率和敏感率(%)

Table 12 Resistance and sensitivity rates of 31 277 strains of *Enterobacteriaceae* to antimicrobial agents (%)

Antimicrobial agent	R	S
Imipenem	5.0	92.2
Meropenem	4.4	94.6
Ertapenem	6.3	91.8
Amikacin	7.4	90.7
Piperacillin-tazobactam	8.4	84.2
Cefoperazone-sulbactam	10.5	73.9
Cefepime	20.2	73.2
Ceftazidime	29.1	65.3
Gentamicin	36.0	62.4

(二)不发酵糖革兰阴性杆菌 7 271 株铜绿假单胞菌对亚胺培南和美罗培南的耐药率分别为

29.0%和 27.1%;对其他测试抗菌药物(除阿米卡星、多黏菌素 B 外)的耐药率为 17.0%~35.0%。519 株铜绿假单胞菌对多黏菌素 B 的耐药率仅 1.0%(5/519)。499 株不动杆菌属细菌对多黏菌素 B 的耐药率为 1.4%(7/499),对黏菌素耐药率 0.2%(1/499)。8 739 株不动杆菌属细菌中 89.6%为鲍曼不动杆菌,该菌对亚胺培南和美罗培南的耐药率均>56.0%;除对头孢哌酮-舒巴坦、阿米卡星、左氧氟沙星和米诺环素的耐药率分别为 33.0%、40.2%、45.5%和 42.2%外,对其他测试抗菌药物的耐药率均>50.0%,对多黏菌素 B 和黏菌素的敏感率均>90.0%。嗜麦芽窄食单胞菌对甲氧苄啶-磺胺甲噁唑、米诺环素、左氧氟沙星敏感率均>80.0%。伯克霍尔德菌对甲氧苄啶-磺胺甲噁唑、头孢他啶、美罗培南和米诺环素的敏感率均近 80.0%或>80.0%(表 13)。不发酵糖革兰阴性杆菌对 8 种常用抗菌药物的敏感率均在 50.0%以上(表 14)。

(三)肠杆菌科细菌中碳青霉烯类抗生素耐药株

历年肠杆菌科细菌中均出现少数对碳青霉烯类抗生素耐药菌株,近二三年来在肺炎克雷伯菌和变形杆菌属中此种耐药株有显著增多(表 15)。

四、其他革兰阴性杆菌

960 株流感嗜血杆菌中,儿童分离株 613 株,成人分离株 347 株。产 β 内酰胺酶株的总检出率为 26.3%,其中儿童株和成人株的产酶率分别为 28.5%和 22.5%。除阿奇霉素和环丙沙星外,儿童株对其他抗菌药物的耐药率均较成人株高(表 16)。

表 13 不发酵糖革兰阴性杆菌对抗菌药物的耐药率和敏感率(%)

Table 13 Resistance and sensitivity rates of non-fermentative gram-negative bacilli to antimicrobial agents (%)

Antimicrobial agent	<i>P. aeruginosa</i> (7 271)		<i>Acinetobacter</i> spp. (8 739)		<i>S. maltophilia</i> (2 156)		<i>Burkholderia</i> spp. (470)	
	R	S	R	S	R	S	R	S
Piperacillin	24.6	62.6	69.6	21.2				
Ceftazidime	19.6	74.0	64.5	31.7			9.9	85.2
Cefoperazone	34.5	49.6	81.9	6.9				
Cefepime	18.3	71.7	59.4	37.7				
Aztreonam	29.4	49.9	72.6	5.4				
Imipenem	29.1	66.6	56.8	41.9				
Meropenem	27.1	67.7	61.4	37.9			10.6	79.1
Piperacillin-tazobactam	17.5	68.4	58.3	37.6				
Ticarcillin-clavulanic acid	38.3	19.7	74.9	22.4				
Cefoperazone-sulbactam	19.8	62.5	33.0	44.7	24.4	49.2		
Minocycline			42.2	42.5	3.8	89.6	9.3	80.6
Chloramphenicol								
Gentamicin	20.9	71.3	60.9	37.7				
Amikacin	13.5	82.3	40.2	57.7				
Levofloxacin	20.6	72.5	45.5	44.0	10.5	85.5		
Ciprofloxacin	17.9	75.2	60.8	37.7				
Fosfomycin	28.5	53.6	64.6	15.3				
Trimethoprim-sulfamethoxazole			56.8	41.7	10.0	89.0	11.7	86.8
Polymyxin B ^a	1.0	99.0	1.4	98.6				
Colistin ^b			2.6	97.4				

^a310 strains of *P. aeruginosa* tested against polymyxin B.

^b499 strains of *Acinetobacter* spp. tested against polymyxin B and 307 strains against colistin.

表 14 19 613 株不发酵糖革兰阴性杆菌对抗菌药物的耐药率和敏感率(%)

Table 14 Resistance and sensitivity rates in 19 613 strains of non-fermentative gram-negative bacilli to antimicrobial agents (%)

Antimicrobial agent	R	S
Cefoperazone-sulbactam	26.5	52.8
Amikacin	28.9	67.9
Piperacillin-tazobactam	38.5	52.5
Ciprofloxacin	40.0	55.0
Cefepime	40.4	53.3
Ceftazidime	41.9	52.9
Meropenem	44.2	52.8
Imipenem	45.1	52.0

表 15 对碳青霉烯类抗生素耐药的几种肠杆菌科细菌(耐药株数/总株数)

Table 15 Carbapenem resistant strains in several *Enterobacteriaceae* species (Number of resistant strains /total number of strains tested)

Year	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>Enterobacter</i> spp.	<i>Proteus</i> spp.
2005	79/3 758	103/2 136	82/749	20/321
2006	109/6 072	122/2 834	98/1 077	32/577
2007	87/6 527	107/3 037	77/1 231	36/548
2008	136/6 678	196/3 435	114/1 464	48/672
2009	198/7 992	298/4 556	131/1 684	57/907
2010	237/9 225	561/5 032	176/1 960	37/907
2011	227/11 860	683/6 390	211/2 519	138/1 271
2012	228/14 154	945/8 772	269/3 031	274/1 565

表 16 流感嗜血杆菌对抗菌药物的耐药率和敏感率(%)

Table 16 Resistance and susceptibility rates of *M. catarrhalis* and *H. influenzae* strains to antimicrobial agents (%)

Antimicrobial agent	<i>M. catarrhalis</i> (113)		<i>H. influenzae</i> from children(613)		<i>H. influenzae</i> from adults(347)	
	R	S	R	S	R	S
Ampicillin			40.8	48.1	25.7	68.4
Amoxicillin-clavulanic acid	0	100	9.4	90.6	6.0	94.0
Ampicillin-sulbactam			19.5	80.5	9.7	90.3
Cefuroxime	0	100	13.2	80.1	4.9	92.5
Ceftriaxone	0	100	13.1	86.9	8.0	92.0
Azithromycin	0	55.8	4.2	95.8	6.9	93.1
Chloramphenicol			17.1	65.6	12.8	79.2
Levofloxacin	0	98.2	0	98.8	0	95.7
Trimethoprim-sulfamethoxazole	1.8	95.6	72.3	26.5	51.4	46.2
Cefaclor	0	100				

Beta-lactamase was produced in 28.5% of the strains isolated from children.

Beta-lactamase was produced in 22.5% of the strains isolated from adult.

讨 论

2012 年 CHINET 细菌耐药性监测结果小结如下:①参加本次细菌耐药性监测的医院与 2011 年相比,退出 2 所,新增 2 所,总参加单位仍为 15 所。但 2012 年收集的总菌株数为 72 397 株,较 2011 年的 59 287 株增加 22.0%。在肠杆菌科细菌中克雷伯菌属、沙雷菌属有所增多,沙门菌属、志贺菌属减少。不发酵糖革兰阴性杆菌中不动杆菌属增多,产碱杆菌属减少。在革兰阳性球菌中肠球菌属和草绿色链球菌增多, β 溶血链球菌减少。②金葡菌中 MR 菌株检出率由 2011 年的 50.6%降低为 47.9%。金葡菌对甲氧苄啶-磺胺甲噁唑的耐药率有所降低(MSSA 由 16.6%降为 13.7%,MRSA 由 20.1%降为 11.5%)。③肠球菌属细菌中万古霉素耐药(VRE)粪肠球菌 8 株(2011 年为 2 株),其中 VanA 型 6 株, VanB 型 2 株;VRE 屎肠球菌 65 株,其中 VanA 型 37 株, VanB 型 27 株, VanM 型 1 株。发现少数利奈唑胺耐药粪肠球菌(9 株,0.3%)。④大肠埃希菌和奇异变形杆菌中产 ESBLs 株略有增多(分别为 55.3%对 50.7%, 20.7%对 13.8%)。⑤变形杆菌属、摩氏摩根菌和普罗威登菌对亚胺培南的耐药率均显著高于对美罗培南的耐药率。⑥历年肠杆菌科细菌中均出现少数碳青霉烯类耐药株,以肺炎克雷伯菌、大肠埃希菌、肠杆菌属、变形杆菌属中较多,尤其近二三年来在肺炎克雷伯菌和变形杆菌属中此种耐药菌株有显著增多。

肠杆菌科细菌是临床常见社区感染和医院感染的重要病原菌,近年来耐碳青霉烯类抗生素肠杆菌科细菌(CRE)出现并逐年增多,该类细菌常带有多种耐药基因,如 AmblerA、B、D 组 β 内酰胺酶中的碳青霉烯酶基因,某些 ESBLs(如 CTX-M 家族)、AmpC β 内酰胺酶等,外膜孔蛋白低表达或缺失及其他耐药基因,因而对多数或全部现有抗菌药物耐药。其所致感染罹患率和病死率高,有效治疗药物少。其中主要者如肺炎克雷伯菌、肠杆菌属、枸橼酸杆菌属等,成为临床治疗的难题^[3-5]。2010 年中国 CHINET 细菌耐药性监测中检出 CRE 菌株 670 株,包括克雷伯菌属细菌 430 株(64.2%)、大肠埃希菌 91 株(13.6%)、肠杆菌属 97 株(14.5%)、枸橼酸杆菌属 23 株(3.4%)、沙雷菌属 11 株(1.6%)等。其中分离自呼吸道标本者占 49.5%,科室中以重症

监护病房分离株最多,占 36.0%。CRE 菌株对多数临床常用抗菌药物高度耐药,除对阿米卡星和米诺环素的平均耐药率分别为 52.6%和 37.0%外,对其他抗菌药物的耐药率达 70.0%~100%,对厄他培南 100%耐药^[6]。国内报道 2004—2008 年 CRE 菌株 49 株,包括肺炎克雷伯菌 26 株、大肠埃希菌 8 株、阴沟肠杆菌 10 株等。其中 6 株产 KPC-2 或 IMP-4/8 碳青霉烯酶,28 株有外膜蛋白表达降低或缺失,部分菌株同时产生 ESBLs 或 AmpC 酶。此外 14 株带 *qnr* 基因,17 株带 *aac(6')-Ib*,9 株带 *aac(6')-Ib-Cr* 基因^[7]。另有报道 109 株肺炎克雷伯菌 CRE 菌株,其中 70.6%菌株产 KPC-2,59.6%菌株产 KPC-2 + CTX-M-14、CTX-M-15,10.9%菌株产 KPC-2 + CTX-M-14 + DHA-1,9.2%菌株产 MBL(GIM-1,或 VIM-1)或 OXA 型碳青霉烯酶^[8]。在肠杆菌科细菌中尤以肺炎克雷伯菌 CRE 菌株最多见^[9-12],并已出现对多黏菌素 B 和替加环素均耐药的泛耐药株^[13]。为此已有 WHO 等多个国际组织和学者呼吁针对上述细菌耐药性的新形势,全球应联手共同应对这一新挑战^[14-16]。

近年来,不少学者对 CRE 感染的治疗进行了探索,但有关的临床研究资料很少。药敏资料显示多黏菌素类(包括多黏菌素 B 和黏菌素)、替加环素、磷霉素和阿米卡星对 CRE 菌株有良好抗菌活性^[17]。根据现有临床研究资料上述抗菌药物联合应用的疗效均优于单药治疗,因此推荐联合疗法用于治疗 CRE 感染。可采用的给药方案有黏菌素或氨基糖苷类(主要为阿米卡星)联合碳青霉烯类,黏菌素联合替加环素,氨基糖苷类联合磷霉素,但不推荐多黏菌素类与氨基糖苷类联合^[18]。最近美国 FDA 发出警示,对严重感染采用替加环素治疗患者病死率增高,因此该药不宜用于严重感染患者,但仍有学者认为,该药与其他抗菌药物联合仍可作为治疗产碳青霉烯酶肠杆菌科细菌感染的最后选择^[19]。根据现有临床资料高度推荐磷霉素与其他抗菌药物联合用于产碳青霉烯酶肠杆菌科细菌感染。此外,有磷霉素成功治疗产 KPC 和 NDM β 内酰胺酶肺炎克雷伯菌尿路感染的报道^[20-21]。以上资料提示,将磷霉素列入今后细菌耐药性监测的常规测试药物很有必要。

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