## **Background**

Cumulative antibiograms summarise the collective susceptibility of bacterial isolates against various antibiotics. Prepared by Drs Jacklyn Joseph and John Ferguson, August 2019. Isolates were cultured from PMGH inpatients and outpatients served by the PMGH Laboratory. Outpatients came from clinic locations from around the National Capital District.

There is selection bias inherent in the samples included in hospital antibiograms and great care must be taken with its interpretation. Treatment guideline review and modification in the light of this antibiogram needs to take into account specific clinical data that assesses the response to treatment of both culture positive and negative infections across the different patient groups (paediatric, adult) and locations (intensive care, non intensive care, outpatient). Susceptibility rates at other institutions may differ significantly.

Where possible isolates derived from inadequate specimen types such as urinary catheter or endotracheal tube tips, have been excluded from analysis. However it is probable that many urine cultures may not have been collected for the correct reason or in the correct manner leading to the possibility of error due to contamination or sampling of patients with asymptomatic bacteriuria.

#### **Overall assessment**

High rates of methicillin-resistant *Staphylococcus aureus* (MRSA) across inpatient and outpatient paediatric and adult patients (Tables 2, 3, 5) were documented. MRSA is considered intrinsically resistant to nearly all beta-lactam antibiotics. *Staphylococcus aureus* is an important cause of sepsis in outpatient and inpatient populations. Intravenous vancomycin (a glycopeptide antibiotic) is considered the treatment of choice for MRSA bloodstream infection. Clindamycin is a reasonable second line option if susceptibility is proven. Bloodstream infection due to MSSA or MRSA (Table 3) has high mortality in adults if not managed effectively<sup>1</sup>. MSSA and MRSA susceptibility to tetracycline, erythromycin/clindamycin and cotrimoxazole remained above 75% across inpatient and outpatient settings (see below).

High rates of Gram negative resistance to ceftriaxone, gentamicin, chloramphenicol and ciprofloxacin, with predominance of multi-resistant *Klebsiella* species amongst inpatient isolates (Tables 1,2,3,4). This indicates probable hospital transmission of extended spectrum betalactamase-producing organisms. Meropenem and amikacin retain activity and meropenem is the preferred usual choice for directed treatment of significant ESBL infection.

**Emergence of meropenem-resistant isolates (Tables 2, 4)**, mostly *Klebsiella* species, likely due to carbapenemase production (89 isolates, 55 *Klebsiella* species, 15 *Acinetobacter* species) was documented<sup>2</sup>. Treatment options for these organisms are limited. Priority needed to confirm this finding and characterise these isolates further so that specific treatment guidelines can be developed. It is essential to store all future meropenem-resistant isolates (*Enterobacterales – E. coli, Klebsiella* species and *Acinetobacter* species) for later confirmatory testing.

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<sup>&</sup>lt;sup>1</sup> Essential clinical care steps of *Staphylococcus aureus* bloodstream infection are described here: https://aimed.net.au/2015/10/15/essential-clinical-care-of-staphylococcus-aureus-bloodstream-infection-sab/

<sup>&</sup>lt;sup>2</sup> Note that due to gaps in meropenem testing caused by unavailability of discs, it is likely that the number of meropenem resistant isolates detected represents an underestimate.

## Table 1 - Urinary isolate antibiogram (adults and children)

Orga	anism type	Isolates	% total	Ampicillin / Amoxycillin	Amoxycillint clavulanate	Cefaclor	Nitrofurantoin	Co-trimoxazole (Septrim)	Gentamicin (aminoglycoside)	Amikacin	Ceftriaxone	Ciprofloxacin / Norfloxacin
	All isolates	998	70 miscella	neous/cont	aminant spe	ecies exclud	ed.					
	Escherichia coli	402	40%	10%	28%	n/a	79%	21%	65%	<b>79</b> %	68%	70%
Gram negative isolates	Klebsiella species	327	33%	R	15%	n/a	40%	20%	36%	86% 228	32%	59%
gative	Enterobacter -like species*	53	5%	R	R	R	<b>42%</b> 31	<b>28%</b> 36	<b>60%</b> 35	82% 17	59% ** 37	<b>62%</b> 37
am ne	Proteus species	63	6%	20%	39%	n/a	R	19%	42%	<b>91</b> %	48%	52%
Ģ	Pseudomonas aeruginosa	36	4%	R	R	R	R	R	29%	<b>52%</b>	R	36%
ves	Staphylococcus saphrophyticus	16	2%	S	S	S	S	n/a	n/a	n/a	S	n/a
Gram positives	Streptococcus agalactiae (group B strep)	0	0%	S	S	S	S	n/a	R	R	S	n/a
Gran	Enterococcus species	31	3%	S	S	R	S	R	R	R	R	R

### Notes and key:

Twenty four percent of the urinary isolates were from children. Paediatric *E. coli* and *Klebsiella* species (n=67 and 101 respectively), showed similar levels of susceptibility to adult isolates. For other bacterial species, the number of paediatric isolates was insufficient for a comparison to be made. Inpatient isolates were less susceptible (see Table 4).

Where the result cell indicates that < 20 isolates were tested or where only a proportion of isolates were tested for an antibiotic (e.g. amikacin), the result may not be a true reflection on overall susceptibility. Isolates from urinary catheter tips were excluded. This is not a suitable specimen for testing.

n/a	not available - not routinely tested in this laboratory or no testing standard available
80%	Green percentage indicates susceptibility of greater than 75%
S	Susceptible by extrapolation or intrinsically susceptible
72%	Orange indicates susceptibility in the range of range 50-75%
45%	Red indicates susceptibility of less than 50%
R	Intrinsically resistant- the species is naturally resistant to this agent
*	Enterobacter, Serratia, Citrobacter, Providencia, Morganella species
**	Resistance may emerge during therapy and agent NOT recommended for these species.

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Table 2 - Non-urine sample cumulative antibiogram (adults and children)

		Isolates	% total	Fluctoxacillin/ dictoxacillin	Erythromycin/ clindamycin	Tetracycline	Amoxycillin + clavulanate	Trimethoprim+ S'methoxazole	Gentamicin (aminoglycoside)	Ceftriaxone	Chloramphenicol	Meropenem (carbapenem)	Ciprofloxacin
	All isolates	1,668	100%										
	Escherichia coli	166	10%	R	R	n/a	33%	25%	55%	52%	46%	<b>95</b> %	63%
ses	Klebsiella species	504	30%	R	R	n/a	<b>27%</b>	36%	41%	36%	31%	<b>88</b> %	67%
e isolat	Enterobacter -like species*	75	4%	R	R	R	<b>R</b> 59	39% 61	43%	** (38%)	36%	<b>92</b> %	67%
Gram negative isolates	Proteus species	88	5%	R	R	n/a	48%	100%	58%	59%	36%	88%	69%
Gram	Pseudomonas aeruginosa	217	13%	R	R	R	R	R	75%	R	0%	<b>38%</b>	79%
	Acinetobacter species	85	5%	R	R	n/a	<b>7%</b>	50%	64%	<b>15%</b>	<b>12%</b>	<b>48%</b>	83%
es	Staphylococcus aureus- ALL	493	30%	57%	78%	93%	57%	78%	n/a	57%	85%	57%	n/a
e isolat	Methicillin-susc. S. aureus	279	17%	100%	76%	97%	S	81%	n/a	S	90%	S	n/a
Gram positive isolates	Methicillin-resistant S. aureus	214	13%	R	81%	89%	R	73%	n/a	R	80%	R	n/a
Gram	Streptococcus species	19	1%	-	-	-	-	-	R	S	n/a	S	-
	Streptococcus pneumoniae	4	0%	-	-	-	-	-	R	S	n/a	S	-
	Enterococcus species	17	1%	R	R	R	-	n/a	R	R	60%	-	n/a

#### **Notes:**

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n/a	not available - not routinely tested in this laboratory or no testing standard available
80%	Green percentage indicates susceptibility of greater than 75%
S	Susceptible by extrapolation or intrinsically susceptible
72%	Orange indicates susceptibility in the range of range 50-75%
45%	Red indicates susceptibility of less than 50%
R	Intrinsically resistant- the species is naturally resistant to this agent.
*	Enterobacter, Serratia, Citrobacter, Providencia, Morganella Gram negatives (excludes C. diversus)
**	Resistance may emerge during therapy and agent NOT recommended for these species.
S. aureus	Staphylococcus aureus was isolated mainly from pus swabs. Also 18 blood events (Table 3 below).

## Cerebrospinal fluid isolates, 2018

Two infants had meningitis due to Streptococcus pneumoniae documented.

Twenty adults had CSF culture positive infection with *Cryptococcus* species. The HIV status of *Cryptococcus* patients and species designation (*C. gattii* or *C. neoformans*) was unknown.

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Table 3 - Significant blood isolates, 2018 by species and location

Organism type	Inpatient	outpatient	unknown	total
Fungi	1			1
Candida species	1			1
Gram Negatives	130	50	6	186
Acinetobacter species*	14	6		20
E. coli**	16	6		22
Enterobacter-like	17	1	1	19
GNR-other	27	17	2	46
Klebsiella species**	49	16	2	67
Proteus species**	1	2		3
Pseudomonas aeruginosa*	6	2	1	9
<b>Gram Positives</b>	24	11	2	37
Enterococcus	2			2
GPC other	4			4
Staph. aureus (MRSA)***	7	3	1	11
Staph. aureus (MSSA)***	11	7	1	19
Strep. pneumoniae		1		1
Total	155	61	8	224

<sup>\*</sup> Acinetobacter and Pseudomonas gentamicin susceptibility was 72% overall (n=29 isolates). Meropenem not tested for any isolates.

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<sup>\*\*</sup> Enterobacterales<sup>3</sup> ceftriaxone susceptibility: inpatient events- 27% and outpatient events- 54%. A majority of ceftriaxone-resistant isolates (ESBL) were resistant to ciprofloxacin, gentamicin, chloramphenicol and septrim (cotrimoxazole). A majority were susceptible to amikacin. Only 5 ESBL isolates were tested against meropenem and all were susceptible.

<sup>\*\*\*</sup> Overall macrolide (erythromycin, clindamycin) susceptibility was 90% and 72% for MRSA and MSSA respectively.

<sup>&</sup>lt;sup>3</sup> E. coli, Klebsiella, Proteus, Enterobacter and similar species

# Table 4 – Susceptibility of Gram negative bacteria (*Enterobacterales*<sup>4</sup>, *Pseudomonas* and *Acinetobacter* species) (all specimen types)

#### Percent susceptible

Location	N	Gentamicin	Amikacin*	Ciproflox.	Ceftriax.!	Meropenem*	Chloramp.*!
Adult inpat.	881	47%	82%	61%	37%	81%	29%
Outpatient**	360	74%	83%	79%	75%	87%	55%
Paed. inpat.	299	38%	82%	67%	31%	88%	38%
Outpatient**	69	68%	78%	87%	57%	92%	56%

Total 1,609

! *Pseudomonas aeruginosa* isolates (n=62) were not included only under the ceftriaxone and chloramphenicol results as it is intrinsically resistant to these agents.

Table 5 – Susceptibility of *Staphylococcus aureus* (all specimen types)

#### Percent susceptible

#### Erythromycin

Location	N	Methicillin	Tetracycline	Cotrimoxazole	/clindamycin	Chloramphen.
Adult inpt	110	47%	91%	78%	80%	83%
Outpatient*	31	42%	93%	83%	87%	94%
Paed. inpt	175	54%	90%	75%	<b>75</b> %	83%
Outpatient*	114	75%	96%	74%	80%	89%

Total 430\*\*

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<sup>\*</sup> The number of isolates tested against these antibiotics was only around 50% of the total and the susceptibility rates may represent underestimates (i.e. a more resistant subgroup of isolates had that antibiotic tested).

<sup>\*</sup> The trend to greater susceptibility of outpatient isolates was not significant.

<sup>\*\* 79</sup> isolates either had an unknown age or ward location and are not included in the analysis below.

<sup>&</sup>lt;sup>4</sup> E. coli, Klebsiella, Proteus, Enterobacter and similar species

#### **Notes**

- Due to lack of appropriate bacteriological media for isolation & susceptibility testing of *Streptococcus* pneumoniae, Neisseria gonorrhoeae and Haemophilus influenzae, no results are available for these species.
- Meropenem (carbapenem) disc susceptibility was not tested in 2016 and commenced in 2017. Testing disc availability has been variable and a significant number of Gram negative isolates were not tested.
- Testing at this location was performed according to the European Union Committee on Antimicrobial Susceptibility Testing (EUCAST) method over this period. During 2016 an internal daily quality control process for AST was established. AST of control organisms is usually performed weekly to assess whether testing is within the control limits defined by EUCAST. QC for 2018 was assessed as adequate.
- The methods employed to construct the antibiogram are based upon the Clinical and Laboratory Standards Institute M39-A3 document Analysis and presentation of cumulative antimicrobial susceptibility test data; approved guideline Third Edition. Whilst only the first isolate per patient per 365 day period should be included to avoid repeated sampling of multi-resistant isolates, this was not possible with the data set available as most isolates do not have a unique patient identifier recorded. It is unlikely that this created a significant bias.
- Where an antibiotic was not tested against every isolate (e.g. gentamicin), the number tested is shown below the % susceptible figure where there number tested was less than 90% of the total isolates. In this case susceptibility rates may over-estimate the level of resistance if only more resistant isolates were tested.
- Using an obsolete Clinical and Laboratory Standards Institute breakpoint, the laboratory detected 41 isolates of MSSA and MRSA with vancomycin resistance. As these isolates were not stored, it is not possible to confirm this unusual finding- until that time, these results should be disregarded.

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