

CONTAGIOUS COMMENTS

Department of Epidemiology

Hospital Antibiotic Guidelines

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Antibiotics are the most commonly prescribed drugs in the practice of pediatrics. Each year we publish the TCH Microbiology Lab's antimicrobial susceptibility tables to provide you with information on isolates that have been tested at The Children's Hospital. Antibigrams at TCH may not represent the general pediatric population and many bacteria isolates may have additional susceptibilities that are not reported on the lab computer requiring a call to the Microbiology Laboratory (303-861-6703) for additional information. The National Committee for Clinical Laboratory Standards (NCCLS), sets standards for testing as well as reporting recommendations.

Pharmaceutical Use Guidelines have been developed in conjunction with the Pharmacy & Therapeutics Committee to help guide you in antimicrobial prescribing best practices. The overarching principle is to use the best evidence available to guide your practice. Some of the key principles include: 1) focus on the diagnosis; 2) use therapeutically equivalent, lower cost drugs; 3) enteral (po) medications are usually less costly and safer than parenteral (IV); 4) report all adverse drug reactions; 5) minimize the practice of polypharmacy; and 6) minimize empirical treatment without diagnostic support.

Table 1 shows the susceptibility patterns for gram-negative organisms isolated at The Children's Hospital. Of note this year is decreased numbers of Shigella isolates with relatively resistant susceptibility profiles. Increasing third generation cephalosporin use is a factor in the development of inducible beta-lactamases (IB) as well as extended spectrum beta-lactamases (ESBL) by gram-negative organisms. Our automated susceptibility testing Microscan reports IB for species known to possess inducible beta-lactamase when the isolate meets a defined cutoff indicating that use of beta lactam drugs may promote development of resistance and subsequent therapeutic failure. Common bacteria producing inducible beta-lactamases can be remembered with the mnemonic SPICEA (*Serratia marcescens*, *Pseudomonas aeruginosa*, indole positive organisms, *Citrobacter*, *Acinetobacter*). The presence of ESBL is currently reported for *E. coli* and *Klebsiella* species, and indicates resistance to penicillins, cephalosporins and aztreonam. Nosocomial outbreaks have been reported with these difficult to treat organisms and patients require appropriate isolation measures.

TABLE 1. Antimicrobial Susceptibilities at The Children's Hospital -2004
Gram Negative Organisms (% susceptible)

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS							
		Ampicillin / Amoxicillin (IV / PO)	Cefazolin / cephalexin (IV / PO)	Cefuroxime/ efactor (IV / PO)	Cefotaxime/ ceftriaxone (IV)	Gentamicin (IV)	Tobramycin (IV)	Trimethoprim / sulfa (IV / PO)	Ciprofloxacin ² (IV / PO)
<i>Haemophilus species</i> ¹	35	29			100			69	
<i>Citro. amalonaticus</i>	16	19	12	19	94	100	100	94	100
<i>Citrobacter freundii</i>	24	29	4	50	62	92	92	96	100
<i>E. coli</i>	929	52	95	99	99	100	100	71	98
<i>Enterobacter aerogenes</i>	12	8	8	67	83	100	100	100	92
<i>Enterobacter cloacae</i>	61	11	3	41	66	100	100	92	98
<i>Klebsiella pneumoniae</i>	88	R	91	93	98	100	95	78	98
<i>Klebsiella oxytoca</i>	35	R	60	91	97	97	97	94	100
<i>M. morgani</i>	14	0	0	7	93	86	93	79	100
<i>Proteus mirabilis</i>	25	76	100	100	100	96	93	76	88
<i>Salmonella species</i>	27	96			96			93	N/A
<i>Serratia marcescens</i>	29	0	0	0	100	100	86	97	86
<i>Shigella sonnei</i>	6	67			100			17	100
<i>Shigella species</i>	7	86			100			57	100

Testing by Microscan panels (except *Haemophilus* by E-test)

¹ May include > 1 isolate / patient.

² The fluoroquinolone class is generally not FDA approved for use in children < 18 yrs. Three Isolates identified as ESBL. R = Resistant (Intrinsic)

Table 2 confirms the highly resistant patterns for most pseudomonas, especially in the cystic fibrosis patient population. Many patients that are highly antibiotic exposed will require carbapenems or quinolones for treatment of serious pseudomonas infections. Ciprofloxacin has been approved as a second-line drug for use in children older than 1 year for complicated urinary tract infections and pyelonephritis. (See Pharmacy guidelines for recommended uses for fluoroquinolones.)

TABLE 2. Antimicrobial Susceptibilities at The Children's Hospital - 2004
Non-Enterobacteriaceae (% susceptible)

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS									
		Ticarcillin/clav Timentin (IV)	Piperacillin (IV)	Ceftazidime (IV)	Cefipime (IV)	Aztreonam (IV)	Imipenem / Cilastatin (IV)	Ciprofloxacin ² (IV)	Gentamicin (IV)	Tobramycin (IV)	Meropenem
<i>Acinetobacter baumannii</i>	7	86	57	86		50	100	86	57	86	100
<i>Pseudomonas aeruginosa</i>	139	86	93	85	88	68	92	86	83	94	92
• CF-mucoid ¹	190	63		73		76	74	63		63	84
• CF-nonmucoid ¹	175	43		69		69	74	53		60	76
<i>A. xylosoxidans</i> ²	20	75					45	11			52

¹ Cystic fibrosis isolates by E-test. May include >1 isolate/patient.

² Not FDA approved for use in children < 18 yrs. Other testing by Microscan panels.

Acinetobacter and *Achromobacter xylosoxidans* reflect the highly resistant nature

of these organisms and the continued need to utilize broader spectrum antimicrobials for treatment.

Table 3 shows the results for gram-positive organisms (except for *Streptococcus*, which is shown in Table 4). We are seeing increased numbers of MRSA, particularly community acquired MRSA (CA-MRSA). (See Contagious Comments November 2004 issue, "Community Acquired MRSA in Children.") The majority of CA-MRSA is associated with skin and soft-tissue infections and may be susceptible to clindamycin or TMP/SMZ. Now more than ever, it is important to get a good microbiologic sample for culture because of the increased incidence of CA-MRSA. Additionally, clindamycin may not be adequate treatment because the national average for clindamycin inducible enzyme is approximately 50% (positive D-test). Life threatening infections necessitates the use of vancomycin until susceptibilities are known. Increased use of antibiotics, especially fluoroquinolones, vancomycin, third generation cephalosporins, and antibiotics with potent anti-anaerobic activity, have been associated with increased rates of MRSA and VRE colonization within hospitals. Most enterococcus is still susceptible to ampicillin. TCH has had one vancomycin resistant enterococcus (VRE) isolate from a serious deep skin infection.

TABLE 3. Antimicrobial Susceptibilities at The Children's Hospital - 2004
Staphylococcus (% susceptible)

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS						
		Penicillin (IV / PO)	Oxa-/ Naf-/ Dicloxacillin (IV / PO)	Cefazolin / Cephalixin (IV / PO)	Trimethoprim / Sulfa (IV / PO)	Erythromycin (IV / PO)	Clindamycin (IV / PO)	Vancomycin (IV)
Staph aureus								
• <i>Staph aureus</i> (MSSA) ¹	207	8	100	100	100	79	82	100
• <i>Staph aureus</i> (MRSA) ¹	121	0	R	R	100	7	55	100
Coag negative staph ¹								
• <i>Staph hominis/hominis</i>	25	4	40	40	67	40	72	100
• <i>Staph epidermidis</i>	148	4	21	21	59	26	52	100
• <i>Staph warneri</i>	11	36	73	73	100	40	70	100

¹ May include > 1 isolate / patient.
 Testing by Microscan panels – Confirmation of MRSA by PbP2a¹ testing.

TABLE 4. Antimicrobial Susceptibilities at The Children's Hospital– 2004
Streptococcus (% susceptible)

Organisms	# of Isolates	Penicillin			Cefotaxime			Erythromycin	Clindamycin	Trimethoprim/ Sulfa	Cefotaxime	Ampicillin/ Amoxicillin (IV / PO)	Vancomycin (IV)
		S ≤ 0.06	I = 0.12-1	R ≥ 2	S ≤ 0.5	I = 1	R ≥ 2						
S. pneumoniae Invasive (systemic)	19	68	16	16	84	11	5	84	42	58			
		S ≤ 0.06	I = 0.12-1	R ≥ 2	S ≤ 1.0	I = 2	R ≥ 4						
S. pneumoniae Localized (respiratory)	80	51	43	6	96	3	1	64	36	64			
		S ≤ 0.05-12	I = 0.25-2	R ≥ 4									
Viridans Strep (Invasive only)	29	52	41	7				48	90		93		
Testing by E-test.													
<i>Enterococcus faecalis</i>	78											100	100
<i>Enterococcus faecium</i>	19											74	*
Testing by Microscan panel. Gentamicin Synergy Screen – <i>E. faecalis</i> = 82 Gentamicin Synergy Screen – <i>E. faecium</i> = 84 * 1 patient identified.													

Table 4 shows the susceptibilities for *Streptococcus pneumoniae*. We continue to see decreased numbers of invasive isolates with the usage of conjugate pneumococcal vaccine. Only 68% of isolates for invasive disease, bacteremia or meningitis, are susceptible to penicillin. Penicillin resistance is conferred by an alteration of penicillin-binding proteins, which also affects the susceptibilities for cephalosporins.

We recommend vancomycin and a third generation cephalosporin plus / minus rifampin as the drug of choice for children with *S. pneumoniae* meningitis or severe sepsis until you have the results of susceptibilities. Six percent of localized respiratory isolates from nasopharynx, sinus and ear taps are highly resistant to penicillin with an MIC greater than 2. This year, we have seen an increase in resistance to clindamycin for the treatment of *S. pneumoniae* in respiratory specimens.

Increasing numbers and varieties of yeast and fungal infections continue to infect our ever-increasing immune compromised populations at TCH. This year we have a comprehensive antifungal ordering form that complements the antimicrobial ordering form for pediatric and neonatal patients. Standardized antifungal susceptibility testing is available only for yeasts with development of methods and standards for filamentous fungi (i.e., *Aspergillus*) underway. Currently, our antifungal susceptibility testing is done in Dr. Mike Rinaldi's laboratory at the University of Texas, San Antonio. Twelve *Candida albicans* isolates were sent for testing with fluconazole, intraconazole and flucytosine (5-FC) susceptibilities reported in **Table 5**. *Candida albicans* has been uniformly susceptible to amphotericin B. Breakpoints for fluconazole are based on experience with mucosal infections, but are consistent with limited information available for invasive infections due to *Candida* spp. Isolates of *C. krusei* are assumed to be intrinsically resistant to fluconazole. Intraconazole breakpoints are based entirely on experience with mucosal infections and data supporting breakpoints for invasive infections due to *Candida* spp. are not available.

In the community and within the hospital, we continue to see more resistant and more difficult to treat infections. Judicious use of appropriate antibiotics for infections that we have identified and cultured will help to preserve our ability to treat these infections. The decision to prescribe antibiotics in patients likely to benefit, is only made more difficult when we have a difficult time deciding when to start them and knowing when to stop. Obtaining appropriate specimens for microbiologic diagnosis, limiting use of antimicrobial prophylaxis, and narrowing

Antimicrobial coverage when susceptibilities are known, are principles that will help keep antibiotics in our armamentarium fighting infection.

TABLE 5. Antimicrobial Susceptibilities at The Children's Hospital – 2004 Candida albicans (# of isolates susceptible)						
ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS				
		Fluconazole		Flucy to sine		
		S ≤ 8	I = 16 - 32	R ≥ 64	S ≤ 4.0	I = 8 – 16
Candida albicans	12	12			9 ¹	

Testing by UTHSC (at San Antonio).
¹ Only 9 isolates tested.





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