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Children's Hospital Colorado

CONTAGIOUS COMMENTS

Department of Epidemiology

Bugs and Drugs

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UPDATES TO THE 2023 BUGS AND DRUGS HANDBOOK

- MALDI-TOF MS (mass spectrometry) technology has been used for organism identification at CHCO for 10 years and with the addition of a second analyzer, we have essentially eliminated the use of biochemical methods for organism identification in the Microbiology Lab, forever changing the way that we identify bacteria and yeast. For providers, this may result in some microorganism names or groupings that are unfamiliar.
  - This technological breakthrough has affected taxonomy in a way that has shifted organism groupings, particularly within the streptococci. Going forward, we will use the groupings reflected in table 2A, which separates *S. anginosus* from the other viridans (*Strep. mitis-sanguinis-oralis*) group streptococci.
  - These taxonomical shifts have affected the total isolate numbers in each group within our antibiogram tables in Bugs and Drugs, making past antibiogram tables difficult to compare with current antibiogram tables. Moving forward, we plan to continue using these current taxonomic groupings so that future tables can be comparable year-to-year.
- In the Bugs and Drugs antibiogram tables, drug-bug combination data represented by very low numbers of organisms is identified by enclosing the number of isolates in parentheses. In some cases, we have combined isolates from multiple years to obtain at least 30 isolates, which is the minimum necessary for statistical relevance.

UPCOMING CHANGES FOR LATE 2023 AND BEYOND

MIC (minimum inhibitory concentration) susceptibility breakpoint changes were implemented in December 2023. These changes affect susceptibility interpretations in the following ways that may impact providers:

- For *Enterobacterales,* breakpoints are changed for cefazolin, cefotaxime, ceftazidime, cefepime, piperacillin-tazobactam, meropenem, aminoglycosides and fluoroquinolones. As a result of these changes, *Enterobacterales* will be less susceptible going forward.
- For *P. aeruginosa,* breakpoint changes include meropenem, fluoroquinolones and aminoglycosides; this includes removing gentamicin susceptibility criteria, so going forward *P. aeruginosa* is considered inherently resistant to gentamicin, and amikacin is to be used for urinary tract infections only.
- One exciting change to breakpoints is the availability of urine-specific criteria for cefazolin. For lower urinary tract infections, a cefazolin MIC ≤ 16mcg/mL for *E. coli, K. pneumonia,* or *P.* mirabilis predicts susceptibility to cefazolin as well as many oral cephalosporins (e.g. cephalexin). For urine isolates, more will be considered susceptible and thus treatable if infection is isolated to the lower urinary tract.

These changes will not be represented in the annual antibiogram until the 2025 edition of the Bugs and Drugs Handbook. We expect to see a small increase in the frequency of non-susceptible isolates because most of these changes have resulted in a decreased MIC breakpoint. These changes are in accordance with current CLSI standards and are required by our accrediting organization, the College of American Pathologists. Antimicrobials with updated breakpoints are asterisked in the tables below and reflected in patient reports beginning December 7, 2023.

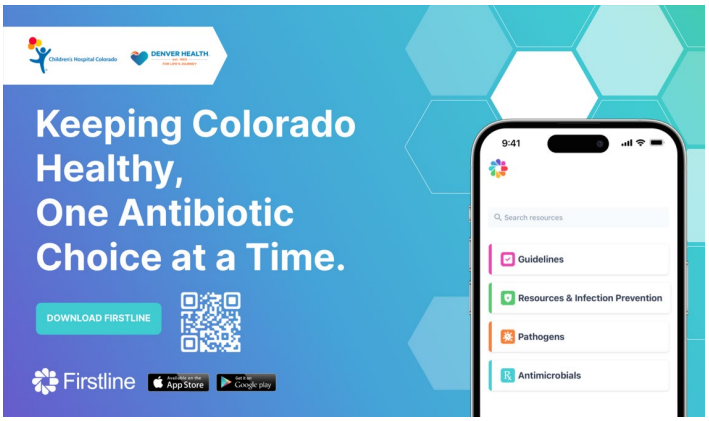
An update to current reporting rules was also implemented. Cascading reporting logic is based on the organism, resistance profile, patient age, and specimen type, meaning certain drug susceptibilities won't be released unless there is resistance detected. Selective antibiotic reporting is a helpful stewardship tool used to nudge towards de-escalation to the narrowest effective antimicrobial option. The full panel of antibiotics tested are available in the background, and if questions arise, please contact Infectious Diseases or Antimicrobial Stewardship. See following table for example of *E. coli* from a non-urine specimen.

<table>
<tr><th>Tier 1</th><th>Tier 2 (resistant to tier 1)</th><th>Tier 3</th><th>Tier 4</th></tr>
<tr><td>Ampicillin</td><td>Ampicillin-sulbactam[1]
Amoxicillin-clavulanate[1]</td><td colspan="2">No additional cascading off these</td></tr>
<tr><td>Cefazolin[1]</td><td>Ceftriaxone (replaces cefotaxime)</td><td>Ertapenem[1]
Meropenem
Ceftazidime[2]
Cefepime[2]
Pip-tazo[1,2]</td><td>Ceftazidime-avibactam
Meropenem-vaborbactam
Aztreonam</td></tr>
<tr><td>Trim-Sulfa</td><td>Ciprofloxacin[1]
Levofloxacin[1]</td><td colspan="2">No additional cascading off these</td></tr>
<tr><td>Tobramycin[1]
Gentamicin[1]</td><td colspan="3">No additional cascading off these. Amikacin not reported due to updated breakpoint now ≤ 4mcg/mL, which is below the lowest well of 16mcg/mL on new panel.</td></tr>
<tr><td>Conditional
• PNA < 28 days:
  • Ceftazidime
• CSF isolate:
  • Ceftriaxone
  • Ceftazidime</td><td colspan="3">Cascades as above</td></tr>
</table>

[1] Not routinely reported on CSF isolates
[2]Ceftriaxone non-susceptibility suggests the presence of Extended-Spectrum Beta-Lactamase (ESBL) production. Other non-carbapenem beta-lactams (e.g. piperacillin-tazobactam, cefepime) may appear susceptible, but should be avoided for complicated, deep-seated infections. They may be appropriate for uncomplicated sources (e.g. urinary tract).

Antimicrobial Stewardship Update – Firstline Mobile App

Recently, the CHCO Antimicrobial Stewardship team in collaboration with Denver Health and the Colorado Department of Public Health launched a mobile app resource. Our app allows users to access the Children's Colorado evidence based clinical pathways, antimicrobial dosing information, pathogen information, infection prevention information, and more. It can be used in all clinical settings and points of care. The app is free to download (iOS and Android as well as via the web) and includes both adult (Denver Health) and pediatric (CHCO) guidance. It is updated regularly and based on the latest evidence. **No matter your specialty or practice, we are all stewards.** Please use the QR code in the graphic below, or search for Firstline wherever you download your apps! After downloading, search for Childrens Hospital Colorado and login. Hint: say yes to push notifications, that is us telling you about shortages, not advertising. Then do the same for Denver Health! It is free, and you don't even have to give your email!



Antimicrobial tables:
Antimicrobial tables have been color coded to indicate which drug/bug combinations are most desirable from a treatment perspective. Color coding is used to designate appropriate empiric treatment selections for each bug-drug combination similar to the "Sanford Guide for Antimicrobial Therapy".

Blue shaded boxes indicate first-line therapy, with susceptibility between 75-100%. This medication has good penetration, limited side-effects and overall strong susceptibilities.

Green shaded box indicates second-line choice with susceptibility between 75-100%, but not first choice due to overly broad-spectrum, toxicities, or both. May be appropriate as initial therapy before specific bacteria has been identified.

Yellow shaded box indicates susceptibility between 50-74%. Not initial treatment of choice but can be used if other medications are not available, patient has significant allergies, or susceptibility known.

Pink shaded box indicates susceptibility for these medications is less than 50%. Consult ID prior to using these medications and/or use only if known susceptible.

\- Colorless box with a dash is a drug-bug combination that is not tested per policy.

R Pink box with an R indicates this organism is known to have intrinsic resistance to this antibiotic.

S Green box with an S indicates that this organism is known to be susceptible to this antibiotic.

( ) Colorless box with parentheses around the number indicates that a smaller number of organisms were used for the antibiogram data collection.

TABLE 1. Gram-Positive Organisms: *Staphylococcus* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS			
		Vancomycin	Clindamycin	Trimethoprim / Sulfa	Oxacillin[A]
***Staph aureus* (MSSA)**	**554**	**100**	**81**	**99**	**100**
***Staph aureus* (MRSA)**	**156**	**100**	**78**	**99**	**R**
Staph epidermidis	**137**	**100**	**-**	**67**	**44**
Staph hominis	**36**	**100**	**-**	**92**	**47**

Tested by Microscan Microtiter Panel.

[A]Includes agents: Nafcillin/Dicloxacillin/Methicillin. **If susceptible, isolate is also susceptible to cefazolin/cephalexin and beta-lactam + beta-lactamase combinations. Does not infer susceptibility to clindamycin; see specific clindamycin results.**

Oxacillin resistance in *Staphylococcus* sp. predicts resistance to ALL beta-lactams including penicillins, carbapenems, β-lactam/β-lactamase inhibitor combinations, cephems (except for cephalosporins with anti-MRSA activity, namely ceftaroline).

Confirmation of MRSA is performed by PBP2, Cefoxitin Screen, or Microscan Panel. Cefoxitin is tested as a surrogate for oxacillin. Oxacillin susceptibility is based on the Cefoxitin Screen result.

The Inducible Clindamycin Test detects inducible clindamycin resistance, due to the *erm* genes. The isolate is presumed resistant to clindamycin when the Inducible Clindamycin Test is positive. Clindamycin susceptibility is not determined by Cefoxitin Screen or oxacillin resistance.

In *S. aureus* recovered from blood cultures, 15% were MRSA (11 of 71 total, table on pg. 19).

Please also note that comments in the footnotes of the tables are updated annually with important interpretive information.

TABLE 2A. Gram-Positive Organisms - Streptococcus and Enterococcus (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS				
		Penicillin[A]	Ampicillin/ Amoxicillin	Vancomycin	Clindamycin[B]	Ceftriaxone
***Strep. anginosus* Group**[1,4,5]	41	98	-	100	93	100
***Strep. mitis-sanguinis-oralis* Group - Invasive**[1,4,6]	(19)	53	-	100	94	95
Beta Strep Group A[1] – Invasive[3,7]	(25)	S	S	S	88	S
Beta Strep Group B[1,4]	(10)	S	S	S	40	S
Beta Strep Group B[1] (prenatal screens)	99	S	S	100	51	S
Enterococcus faecalis[2]	111	-	100	100	R	R
Enterococcus faecium[2,3]	(17)	-	82	100	R	R

[1]Tested by Sensititre Microtiter Panel.
[2]Tested by Microscan Microtiter Panel.
[3]Isolates were recovered in 2020, 2021 and 2022.

***Streptococcus*:**
[4]Most penicillin non-susceptible streptococci that fall into the intermediate MIC range (0.25 to 2 µg/mL) can be treated with high dose ampicillin/amoxicillin.
[5]Of penicillin non-susceptible *S. anginosus* isolates, 2% were intermediate and 0% were resistant.
[6]Of penicillin non-susceptible *S. mitis* group isolates, 36% were intermediate and 8% were resistant.
[7]Invasive isolates include those recovered from blood, tissue and aspirate sources.

[A]Streptococci susceptible to penicillin are also susceptible to ampicillin/amoxicillin.
[B]The Inducible Clindamycin Test (D-test) detects inducible clindamycin resistance due to the *erm* gene. For streptococci, resistance to clindamycin is presumed when the D-Test is positive.

Enterococcus
Combination therapy should be used in endocarditis due to *Enterococcus* sp.; ampicillin plus ceftriaxone is the preferred combination due to lower nephrotoxic risks.
Gentamicin Synergy Screen – *E. faecalis* = 88% susceptible
Gentamicin Synergy Screen – *E. faecium* = 82% susceptible
Isolates that are susceptible to ampicillin cannot be assumed to be susceptible to penicillin.
One new VRE patient was identified in 2019, no new VRE in 2020, 2021 or 2022. For therapy choices, ID consultation is recommended.

TABLE 2B. Gram-Positive Organisms: *Streptococcus pneumoniae* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

Source	NUMBER OF ISOLATES	ANTIMICROBIALS						
		Penicillin[A] (Non-meningitis breakpoint)	Penicillin[A] (Meningitis breakpoint)	Ceftriaxone (Non-meningitis breakpoint)	Ceftriaxone (Meningitis breakpoint)	Clindamycin	Trimethoprim/Sulfa	Vancomycin
CSF[1,2]	**(5)**	**NA**	**60**	**NA**	**80**	**-**	**-**	**100**
Blood or Sterile Aspirate	**40**	**100**	**78**	**100**	**90**	**98**	**88**	**100**
Respiratory and Other	**99**	**98**	**61**	**98**	**83**	**91**	**73**	**100**

Tested by Sensititre Microtiter Panel.

[1]Isolates recovered from 2020, 2021 and 2022.

[2]**Patients with pneumococcal meningitis should be started on vancomycin and ceftriaxone until susceptibilities are resulted.**

[A]Refer to organism-specific susceptibility pattern. Isolates in the intermediate category to penicillin may be treated with high dose ampicillin/amoxicillin unless in the CNS.

S. pneumoniae isolates that are susceptible to penicillin are also susceptible to ampicillin (and amoxicillin if oral choice is appropriate).

Ceftriaxone susceptibility does not imply susceptibility to oral cephalosporins.

TABLE 3. Gram-Negative Organisms, Non-Urine (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS					
		Ampicillin / Amoxicillin	Cefazolin	Cefotaxime [A]	Gentamicin	Trimethoprim / Sulfa	Ciprofloxacin
***Haemophilus influenzae*[1] Beta-lactamase testing (isolates recovered in 2022)**	**No further susceptibility testing is routinely performed for beta-lactamase <u>negative</u> isolates (57/87, 66%). These isolates are considered ampicillin susceptible.**						
***Haemophilus influenzae*[1,4]**	**(22)[6]**	**-**	**-**	**100**	**-**	**-**	**-**
***Escherichia coli*[2]**	**96**	**43**	**79[8]**	**84[8]**	**83[8]**	**69**	**81[8]**
***Enterobacter cloacae* complex[2,7]**	**44**	**R**	**R**	**IB[B]**	**98[8]**	**91**	**98[8]**
***Klebsiella pneumoniae*[2]**	**31**	**R**	**94[8]**	**97[8]**	**97[8]**	**84**	**94[8]**
***Klebsiella oxytoca*[2]**	**(27)**	**R**	**78[8]**	**93[8]**	**93[8]**	**93**	**96[8]**
***Klebsiella aerogenes*[4,5,7]**	**(23)**	**R**	**R**	**IB[B]**	**100[8]**	**100**	**100[8]**
***Serratia marcescens*[2,4]**	**39**	**R**	**R**	**92[8]**	**95[8]**	**97**	**95[8]**
***Salmonella* species[2]**	**62**	**90**	**-**	**98[8]**	**-**	**95**	**-**
***Shigella* species[2,3,5]**	**(25)**	**52**	**-**	**100[8]**	**-**	**24**	**-**

[1]Tested by Sensititre Microtiter Panel.
[2]Tested by Microscan Microtiter Panel.
[3]Tested by disk diffusion.
[4]Isolates were recovered from 2021 and 2022.
[5]Isolates were recovered from 2020, 2021 and 2022.
[6]*Haemophilus influenzae* isolates indicated had full susceptibilities performed based on source and clinician request. *Haemophilus influenzae* isolates that test positive for beta-lactamase production are still considered susceptible to ampicillin-sulbactam or amoxicillin-clavulanic acid.
[7]Cefepime is the empiric treatment of choice for *E. cloacae* complex and *Klebsiella aerogenes* isolates due to inducible AmpC resistance. Rate of susceptibility in our patient population for *E. cloacae* complex against cefepime is 93% and for *K. aerogenes* against cefepime is 100%. These data do not reflect current CLSI breakpoints and may underreport resistance.
[8] These data do not reflect current CLSI breakpoints and may underreport resistance.

[A]Cefotaxime susceptible isolates are also ceftriaxone susceptible.
[B]When IB is indicated, the organism may have an inducible beta-lactamase. Organisms with the inducible beta-lactamase (IBL) designation are at risk for failure with ceftriaxone, ceftazidime, and piperacillin-tazobactam. However, not all infections due to IBL organisms warrant cefepime or carbapenem, and ceftriaxone is a safe option in certain contexts (e.g. UTI and other uncomplicated infections). Organisms at moderate-to-high risk of failure include *Hafnia alvei, Enterobacter cloacae* complex, *Citrobacter freundii* complex, *Klebsiella aerogenes*, and *Yersinia enterocolitica*.

TABLE 4. Gram-Negative Organisms Isolated from Urine (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS										
		Ampicillin / Amoxicillin	Ampicillin/Sulbactam	Cefazolin[A]	Cefuroxime	Cefotaxime[B]	Gentamicin	Nitrofurantoin	Trimethoprim / sulfa	Ciprofloxacin	Cefepime	Ceftazidime
E. coli	1171	55	64	91[1]	94	94[2]	91[2]	99	73	90[2]	-	-
***Enterobacter cloacae* complex**	30	R	R	R	R	IB[C]	100[2]	34	93	100	100[2]	-
***Klebsiella pneumoniae* complex**	88	R	80	87[1]	85	90[2]	93[2]	60	79	93	91[2]	-
Klebsiella oxytoca	43	R	74	67[1]	91	98[2]	93[2]	95	88	95	98[2]	-
Proteus mirabilis	75	83	92	91[1]	96	97[2]	92[2]	R	84	95	97[2]	-
***Citrobacter freundii* complex**	(18)	R	R	R	R	IB[C]	100[2]	94	72	100	100[2]	-
Pseudomonas aeruginosa	33	R	R	R	R	R	R[2]	R	R	91	97	94

Tested by Microscan Microtiter Panel
Breakpoints used for interpretations have been established by the FDA for the specific Microscan Microtiter Panel used in the Micro Lab and may not be consistent with current CLSI guidelines. Isolates that test resistant may respond to high levels of antimicrobials present in urine.

[1]**These data do not reflect current CLSI breakpoints and may overreport resistance.**
[2]**These data do not reflect current CLSI breakpoints and may underreport resistance.**

[A]Cefazolin results are a surrogate to predict susceptibility to oral cephalosporin agents: cephalexin, cefuroxime, cefpodoxime, and cefdinir. Notably for lower tract infection, low level resistance can be overcome by high-end dosages due to high concentrations of these agents in the urine.

[B]Isolates that are susceptible to cefotaxime are also susceptible to ceftriaxone.

[C]When IB is indicated, the organism may have an inducible beta-lactamase. Organisms with the inducible beta-lactamase (IBL) designation are at risk for failure with ceftriaxone, ceftazidime, and piperacillin-tazobactam. However, not all infections due to IBL organisms warrant cefepime or carbapenem, and ceftriaxone is a safe option in certain contexts (e.g. UTI and other uncomplicated infections). Organisms at moderate-to-high risk of failure include *Hafnia alvei, Enterobacter cloacae* complex, *Citrobacter freundii* complex, *Klebsiella aerogenes*, and *Yersinia enterocolitica*.

TABLE 5. Non-*Enterobacterales* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS										
		Ceftazidime	Aztreonam	Tobramycin	Minocycline	Trimethoprim / Sulfa	Ciprofloxacin	Gentamicin	Cefepime	Pip/Tazobactam	Levofloxacin	Meropenem
Pseudomonas aeruginosa												
• **Non CF[1]**	**48**	**98**	**92**	**-**	**-**	**-**	**90[5]**	**R**	**94**	**100**	**-**	**-**
• **CF-mucoid[2,3]**	**(21)**	**86**	**81**	**86[5]**	**-**	**-**	**86[5]**	**R**	**-**	**-**	**-**	**95[5]**
• **CF-nonmucoid[2,3]**	**27**	**92**	**85**	**81[5]**	**-**	**-**	**81[5]**	**R**	**-**	**-**	**-**	**96[5]**
Stenotrophomonas maltophilia[2,4]	**60**	**R**	**R**	**R**	**100**	**98**	**-**	**R**	**R**	**R**	**88**	**R**

[1] Non-CF testing performed by Microscan Microtiter Panel.

[2] Cystic fibrosis (CF) *Pseudomonas* sp. isolates and *S. maltophilia* isolates tested by E-test.

[3] Isolates from 2020, 2021 and 2022 were included in this data.

[4] Isolates from 2021 and 2022 were included in this data.

[5] **These data do not reflect current CLSI breakpoints and may underreport resistance.**

TABLE 6. *Candida* species (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2022

ORGANISMS	NUMBER OF ISOLATES	ANTIFUNGALS						
		5-Flucytosine	Amphotericin	Fluconazole	Itraconazole	Micafungin	Posaconazole	Voriconazole
Candida albicans	**(22)[1]**	**NI**	**NI**	**100**	**NI**	**100**	**NI**	**100**
Candida parapsilosis	**(16)[1]**	**NI**	**NI**	**100**	**NI**	**94**	**NI**	**100**
Candida glabrata (Nakaseomyces glabrata)	**(8)[1]**	**NI**	**NI**	**86[2]**	**NI**	**75**	**NI**	**NI**
Candida lusitaniae (Clavispora lusitaniae)	**4**	**NI**	**NI**	**NI**	**NI**	**NI**	**NI**	**NI**
Candida tropicalis	**(5)[1]**	**NI**	**NI**	**100**	**NI**	**100**	**NI**	**100**

Testing performed at Mayo Medical Laboratories by microbroth dilution

[1]Isolates from 2020, 2021 and 2022 were included in this table.

NI – No interpretative criteria available

[2]SDD - Susceptible Dose Dependent
The susceptible dose dependent category indicates the need for higher doses in the context of infection site, alternative antifungals, and patient characteristics. For bloodstream and other complicated infections due to *C. glabrata*, consultation with Infectious Diseases is encouraged.

Please Note:
C. krusei (*Pichia kudriavzevii*) is intrinsically resistant to fluconazole (isolates not tested).
C. auris is often multi-drug resistant, ID consultation is recommended.

In this table, susceptibilities were performed from the following sources:
- CSF/Shunt/Blood – 26
- Sterile Aspirate/Tissue - 8
- Stool – 1
- Miscellaneous/Wound – 7
- Urine – 5
- Respiratory –8

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