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Children's Hospital Colorado

CONTAGIOUS COMMENTS

Department of Epidemiology

Bugs and Drugs

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Updates to the 2025 Bugs and Drugs handbook

Susceptibility changes were implemented in December 2023 which affected the reporting of Minimum Inhibitory Concentration (MIC) breakpoints. These changes were required by the College of American Pathologists (CAP), which is our accrediting organization, and the detailed breakpoints that we are required to adhere to are defined by the Clinical and Laboratory Standards Institute (CLSI). CLSI establishes methods and interpretive standards for susceptibility testing and defines the ranges for MIC interpretations for susceptible, intermediate, resistant and susceptible-dose-dependent reporting. The 2025 CHCO issue of the Bugs and Drugs Handbook and the data tables contained in this document reflect data collected from isolates recovered from cultures collected in 2024, after changes were implemented. These changes have shifted organism susceptibility interpretations with the following bug-drug combinations.

- For *Enterobacterales,* breakpoints changed for cefazolin, ceftriaxone, ceftazidime, cefepime, piperacillin-tazobactam, meropenem, aminoglycosides and fluoroquinolones and these changes were initially expected to shift interpretations to reflect more resistance. Although we expected to see a small increase in the frequency of non-susceptible isolates, susceptibility patterns have remained relatively stable across this change.
- An 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. pneumoniae,* or *P. mirabilis* predicts susceptibility to cefazolin as well as many oral cephalosporins (e.g. cephalexin). Cefazolin is represented in the urine table twice, once for uncomplicated UTI and once for systemic infection. While the resistance rate for uncomplicated UTI has not changed significantly between 2023 and 2024 data, systemic infection susceptibility rate appears lower.
- For *P. aeruginosa,* breakpoint changes include meropenem, fluoroquinolones and aminoglycosides; *P. aeruginosa* is considered inherently resistant to gentamicin and is not reported while amikacin is to be used for urinary tract infections.
- Separation of **HECK-Yes** and **Non-HECK Yes** organisms to different tables based on similarities in antimicrobial usage and cascades.
- Of note, susceptibility testing is performed on significant isolates from the first two positive CSF or blood cultures and the first positive culture from tissues, aspirates and other significant sources. Additional positive cultures are referred to the first culture(s) collected from the same or similar source for three days. Organisms recovered four or more days later will be retested.

Upcoming changes for 2025 and beyond

- In the Bugs and Drugs antibiogram tables, drug-bug combination data with less than 30 isolates is not statistically significant and will no longer be reported. As a result, some organisms have been left out of the tables while we collect enough data to report their antimicrobial susceptibility patterns because CLSI will allow for us to report an antibiogram by combining up to three years of data.

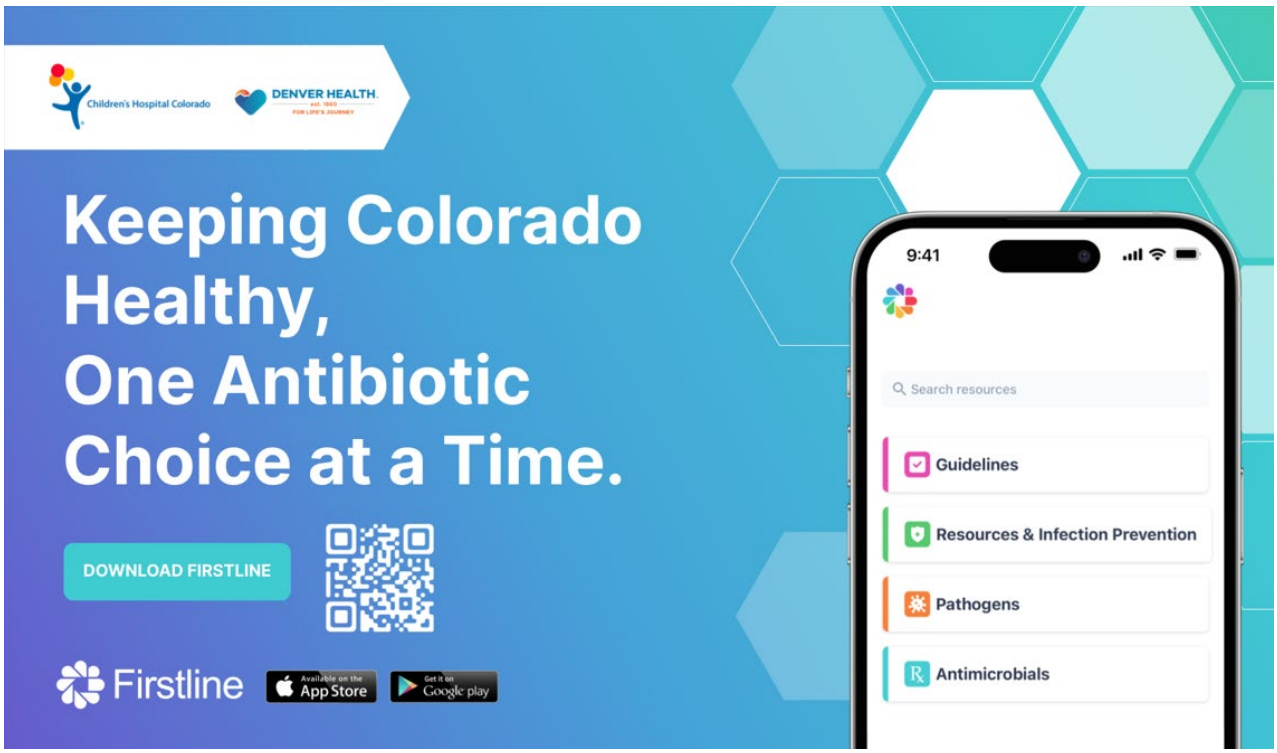
- Several changes are in the planning stages for our result reporting, and you will begin to see them in the coming months:
  - Ceftriaxone will be added to Non-HECK Yes, Non-Urine Enterobacterales organism reports.
  - Nitrofurantoin will be added to Non-HECK-Yes, Urine Enterobacterales reports.
  - Tetracycline will be added as a predictor of doxycycline susceptibility for MRSA and MSSA.
  - Ceftazidime and ceftriaxone will be removed from HECK-Yes, Non-Urine reports on Enterobacterales organisms.

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>
<tr><td colspan="4">[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).</td></tr>
</table>

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 Children's 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.

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Grey 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.

TABLE 1. Gram-Positive Organisms: *Staphylococcus* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS			
		Vancomycin	Clindamycin	Trimethoprim / Sulfa	Oxacillin[A] (Surrogate for drugs listed below)
***Staph aureus* (MSSA)**	**579**	**100**	**79**	**99**	**100**
***Staph aureus* (MRSA)**	**164**	**100**	**77**	**100**	**R**
Staph epidermidis	**134**	**100**	**80**	**67**	**34**
Staph hominis	**34**	**100**	**50**	**64**	**52**

Tested by Microscan Microtiter Panel.

[A]Oxacillin susceptibility infers susceptibility to these agents: cefazolin (IV agent of choice), nafcillin/dicloxacillin/methicillin, cephalexin, cefepime, ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam. Note, MSSA is almost always resistant to penicillin, ampicillin and amoxicillin due to penicillinase production. **Does not infer susceptibility to clindamycin; see specific clindamycin results reported.**

Staphylococcus aureus is identified in the lab as MRSA using several different test methods. When *mecA/C* and MREJ genes are both detected in our BCID-2 assay performed from a blood culture bottle, the organism identified is a MRSA. When grown in culture, a *S. aureus* may be identified as a MRSA by growth on a CHROMAgar or by testing with a PBP2 latex test or we may perform susceptibility testing using the oxacillin microtiter MIC method on the Microscan or detection of cefoxitin resistance on media with an antibiotic impregnated disk. Regardless of the identification method, when we report MRSA, this predicts resistance to ALL beta-lactams including penicillins, cephalosporins (except for cephalosporins with anti-MRSA activity, namely ceftaroline), carbapenems, and β-lactam/β-lactamase inhibitor combinations.

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

TABLE 2. Gram-Positive Organisms - Streptococcus and Enterococcus (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS						
		Penicillin[A]	Ampicillin/ Amoxicillin	Vancomycin	Clindamycin	Ceftriaxone	Linezolid	Nitrofurantoin[B]
***Strep. anginosus* Group**[1,2,4]	97	93	A	100	89	97	-	-
***Strep. mitis-sanguinis-oralis* Group**[1,2,4]	96	54	A	100	88	90	-	-
Beta Strep Group A[1]	50	S	S	S	95	S	-	-
Beta Strep Group B[1,3]	33	S	S	S	54	S	-	-
Enterococcus faecalis[2]	99	-	100	100	R	R	100	100
Enterococcus faecium[2,4]	35	-	68	100	R	R	100	100

[1]Tested by Sensititre Microtiter MIC Panel.
[2]Tested by Microscan Microtiter MIC Panel.
[3]Isolates were recovered from 2023 and 2024
[4]Isolates were recovered from 2022, 2023 and 2024.

***Streptococcus*:**

[A] **Streptococci susceptible to penicillin are also susceptible to ampicillin/amoxicillin.**
Most penicillin non-susceptible streptococci that fall into the intermediate MIC range (0.25 to 2 µg/mL) can be treated with high dose amoxicillin (e.g. 90mg/kg/day in 3 divided doses).

Enterococcus

Combination therapy should be used in endocarditis due to *Enterococcus* sp.; ampicillin plus ceftriaxone (synergistic with ampicillin) is the preferred combination due to lower nephrotoxic risks. Isolates that are susceptible to ampicillin cannot be assumed to be susceptible to penicillin.

[B] Nitrofurantoin does not penetrate the kidneys, do not use for pyelonephritis or systemic infection; use for cystitis only.

TABLE 3. Gram-Positive Organisms: *Streptococcus pneumoniae* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

Source	NUMBER OF ISOLATES	ANTIMICROBIALS					
		Penicillin[A] (Non-meningitis breakpoint)	Penicillin[A] (Meningitis breakpoint)	Ceftriaxone[B] (Non-meningitis breakpoint)	Ceftriaxone[B] (Meningitis breakpoint)	Clindamycin[C]	Vancomycin
***S. pneumoniae* All sources[1]**	**31**	**99**	**71**	**99**	**88**	**91**	**100**

Tested by Sensititre Microtiter MIC Panel.

[1]Patients with pneumococcal meningitis should be started on vancomycin and ceftriaxone until susceptibility results are available.

[A]Refer to organism-specific susceptibility patterns. 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).

[B]Ceftriaxone susceptibility does not imply susceptibility to oral cephalosporins.

[C] Clindamycin should not be used for CNS infections due to limited penetration to this site.

TABLE 4. Gram-Negative Organisms Non-Urine (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS					
		Ampicillin	Cefazolin	Ceftriaxone[A]	Gentamicin	Tobramycin	Trimeth/Sulfa
Escherichia coli	102	45	77	86	86	85	72
Klebsiella pneumoniae	41	R	82	85	97	92	80
Klebsiella oxytoca	35	11	29	91	97	97	88
Serratia marcescens	34	R	R	97	100	76	100

Performed by Microscan Microtiter MIC Panel

[A]Resistance to ceftriaxone suggests extended spectrum beta-lactamase production (ESBL). Carbapenems are the drugs of choice for these infections.

TABLE 5. Gram-Negative Organisms Urine (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS							
		Ampicillin	Cefazolin[1] uncomplicated	Cefazolin systemic infection	Ceftriaxone[2]	Gentamicin	Tobramycin	Trimeth/Sulfa	Nitrofurantoin[3]
Escherichia coli	1337	52	91	80	92	90	89	72	99
Klebsiella pneumoniae	111	R	79	70	81	92	92	70	63
Klebsiella oxytoca	36	8	-	22	91	97	94	86	97
Proteus mirabilis	82	91	93	78	96	97	92	91	R

Performed by Microscan Microtiter MIC Panel

[1] Urine interpretations are now available for these organisms only. Refer to systemic interpretation for patients that have pyelonephritis or other systemic infection. Cefazolin may be used as a surrogate to predict susceptibility for the oral agents cephalexin and cefpodoxime when used for therapy of uncomplicated UTIs due *to E. coli, K, pneumoniae and P. mirabilis*.

[2] Resistance to ceftriaxone suggests extended spectrum beta-lactamase production (ESBL). Carbapenems are the drugs of choice for these infections.

[3] Nitrofurantoin does not penetrate the kidneys, do not use for pyelonephritis or systemic infection; use for cystitis only.

TABLE 6. Gram-Negative Organisms – HECK-Yes Organisms* Non-Urine (% Susceptible)

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS							
		Ampicillin	Amp/Sulbactam	Amox/Clav	Cefazolin	Cefepime	Gentamicin	Pip/Tazo	Trimeth/Sulfa
***Enterobacter cloacae* complex**	**57**	**R**	**R**	**R**	**R**	**92**	**96**	**78**	**89**

Performed by Microscan Microtiter MIC Panel

***HECK-Yes Organisms** are AmpC producing and potentially resistant to beta-lactam drugs. This group of organisms includes: *Hafnia alvei*, *Enterobacter cloacae* complex, *Citrobacter freundii* complex, *Klebsiella aerogenes* and *Yersinia enterocolitica*.

TABLE 7. Gram-Negative Organisms – HECK-Yes Organisms* in Urine (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS							
		Ampicillin	Amp/Sulbactam	Amox/Clav	Cefazolin	Ceftriaxone	Gentamicin	Tobramycin	Trimeth/Sulfa
***Enterobacter cloacae* complex**	**51**	**R**	**R**	**R**	**R**	**64**	**96**	**87**	**89**

Performed by Microscan Microtiter MIC Panel

***HECK-Yes Organisms** are AmpC producing and potentially resistant to beta-lactam drugs. This group of organisms includes *Hafnia alvei*, *Enterobacter cloacae* complex, *Citrobacter freundii* complex, *Klebsiella aerogenes* and *Yersinia enterocolitica*. Only organisms with more than 30 isolates are presented in the antibiogram.

TABLE 8. *Haemophilus* and *Salmonella* (% Susceptible)
Antimicrobial Susceptibilities at Children's Hospital Colorado – 2024 isolate data

ORGANISMS	NUMBER OF ISOLATES	ANTIMICROBIALS				
		Ampicillin	Ceftriaxone	Levofloxacin	Trimethoprim Sulfamethoxazole	Ciprofloxacin
Haemophilus influenzae*[4] *Beta-lactamase testing	Beta-lactamase is performed on all isolates. If beta-lactamase negative [99/121 (82%)], no further susceptibility testing is routinely performed unless it is an invasive isolate (blood/CSF) or is specifically requested. **Beta-lactamase negative isolates (82%) are generally considered ampicillin (and ceftriaxone) susceptible. Beta-lactamase positive isolates (18%) are considered ampicillin-sulbactam/amoxicillin-clavulanic acid and ceftriaxone susceptible.**					
Haemophilus influenzae *2,3,5* *Only includes beta-lactamase positive isolates and formal susceptibility requests.*	**65**	**15**	**S**	**S**	**-**	**S**
***Salmonella spp.*[1,6]**	**68**	**89**	**97**	**81**	**95**	**81**

[1] Performed by Microscan Microtiter MIC Panel.
[2] Performed by Sensititre MIC

[3] Isolates were recovered from 2022, 2023 and 2024.

[4] *Haemophilus influenzae* isolates are first tested for beta-lactamase, which confers resistance to ampicillin. In 2024, 99/121 (82%) isolates tested were negative for beta-lactamase.

[5] Susceptibilities were routinely performed on beta-lactamase positive isolates and isolates for which susceptibility testing was formally requested.

[6] Levofloxacin and Ciprofloxacin susceptibilities were only reported for blood isolates. Azithromycin is a first line therapy for Salmonella infection with the exclusion of CNS infection, although testing was not available for this agent in the lab at CHCO.

If you wish to receive the Contagious Comments publication, please send your e-mail address to Maggie Bay–maggie.bay@childrenscolorado.org

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https://www.childrenscolorado.org/health-professionals/publications/

Thank you for your interest in our publication.