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ANTIMICROBIAL AND CLINICAL MICROBIOLOGY GUIDEBOOK

INTRODUCTION

This is the Second Edition of the Antimicrobial and Clinical Microbiology Guidebook at The Nebraska Medical Center. The development of this guidebook has been a joint effort of the Antimicrobial Stewardship Program (ASP), the Microbiology Department, the Infectious Disease section, and the Department of Healthcare Epidemiology. The purpose of the booklet is to optimize antimicrobial usage and patient outcomes for infectious disease-related issues. We hope that the information in this booklet will be useful in the provision of best practices to patients at The Nebraska Medical Center. .

Every effort has been made to ensure that the information included is complete, accurate, and up to date; however this booklet does not serve as a substitute for clinical judgement or consultation with experts in Infectious Diseases. Application of the information contained herein to each clinical situation is the responsibility of the practitioner.

The content in the booklet can be found online at http://www.nebraskamed.com/asp.

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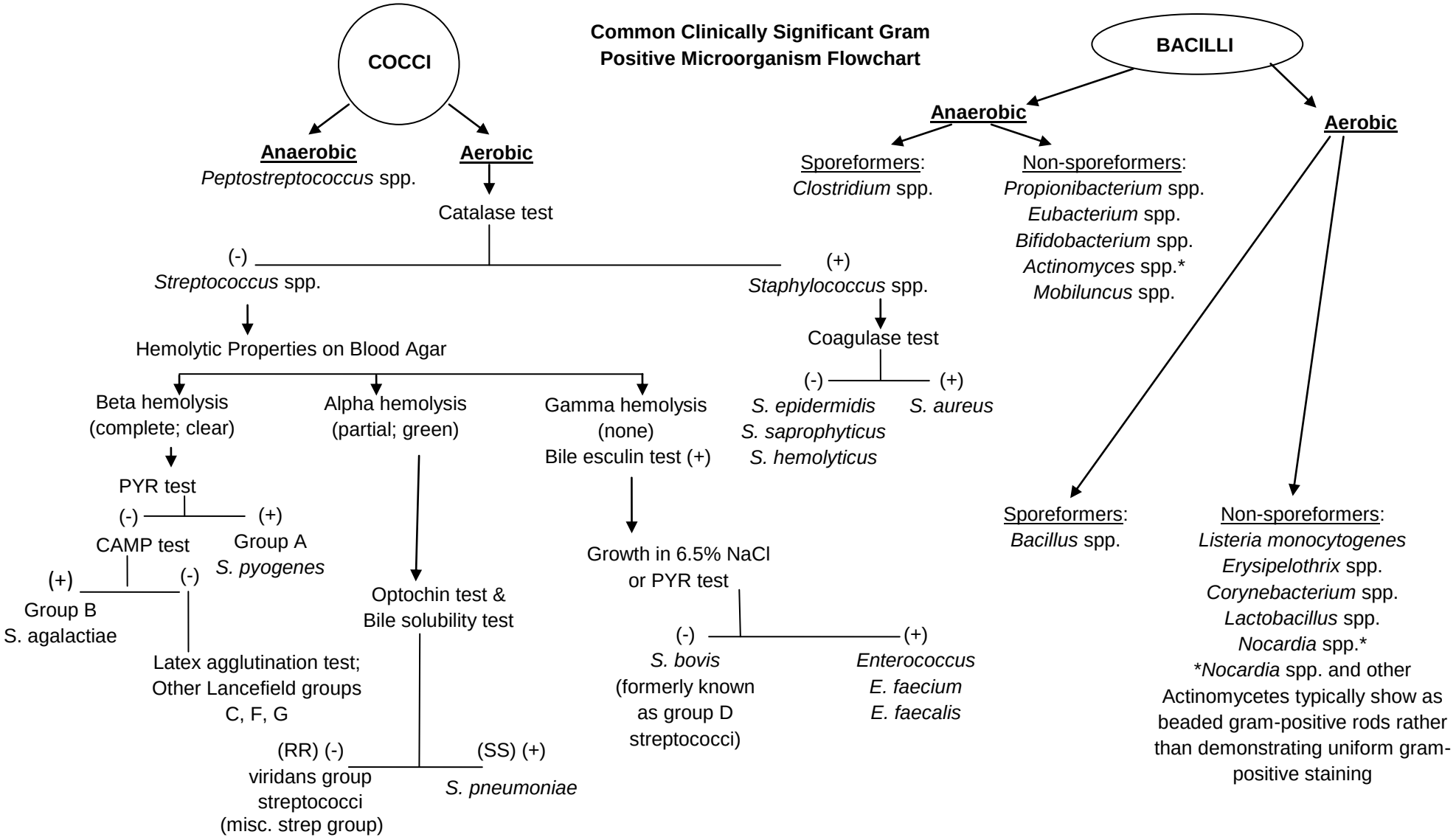
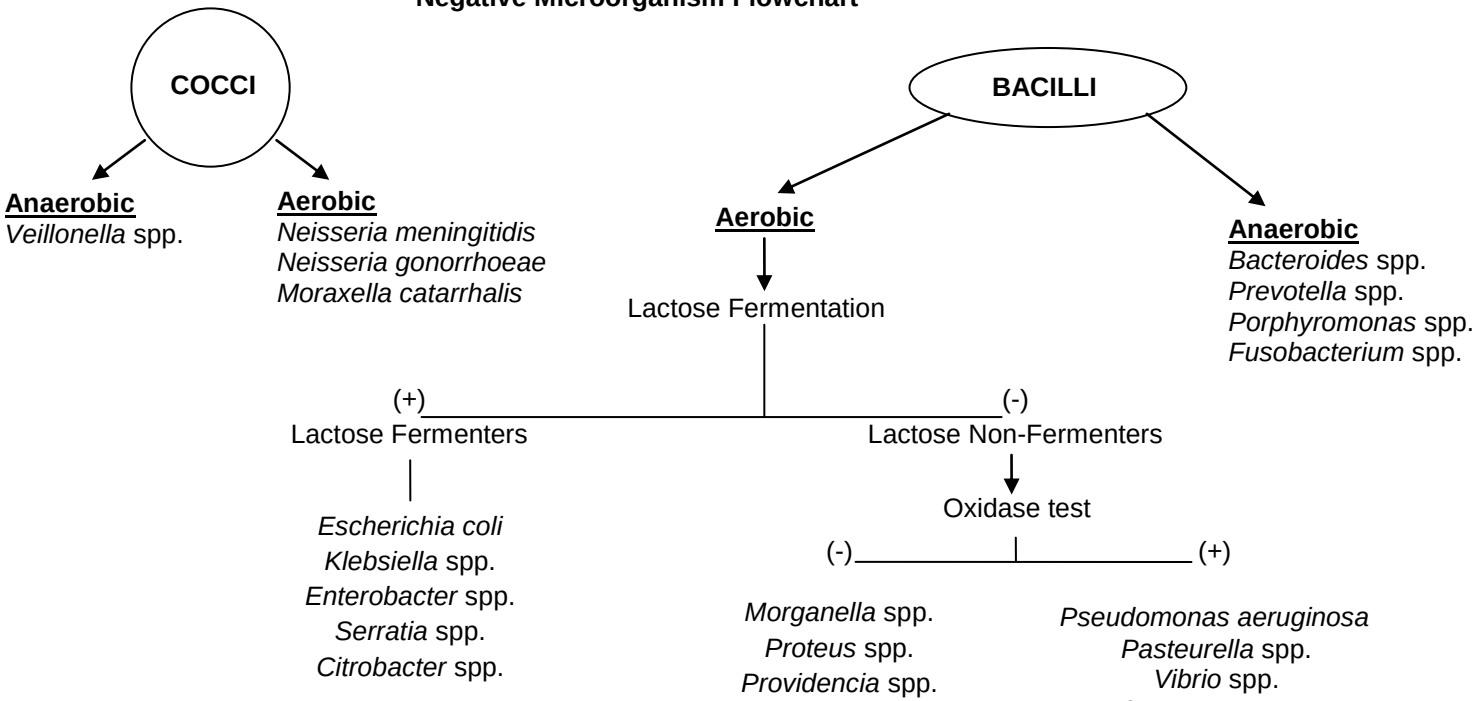
Infectious Diseases 559-8650
(This number can be called for infectious disease consult services, or the person on call may be paged.)

Organism Identification Flowcharts



Common Clinically Significant Gram Negative Microorganism Flowchart



OTHER GRAM (-) BACILLI
(special growth requirements)
Haemophilus spp.
Campylobacter spp.
Legionella pneumophila
Bordetella pertussis
Brucella spp.
Francisella tularensis
Helicobacter pylori

Key phrases from the Microbiology Laboratory

“Gram positive cocci in clusters” may suggest *Staphyloccocus* species.

"Gram positive cocci in pairs and chains" may suggest *Streptococcus* species or *Enterococcus* species.

“Gram positive diplococci” may suggest *Streptococcus pneumoniae.*

“Gram negative coccobacilli” may suggest *Haemophilus* species.

“Lactose fermenting Gram negative rods” may suggest *Enterobacteriaceae*.

“Non-lactose fermenting Gram negative rods” may suggest non-*Enterobacteriaceae*.

“Non-lactose fermenting Gram negative rods, oxidase positive” may suggest *Pseudomonas* species.

“Branching Gram positive rods, modified acid fast stain positive” may suggest *Actinomyces* or *Nocardia* species.

“Acid fast bacilli” may suggest *Mycobacterium* species.

“Budding yeast” suggests yeast.

"Germ-tube negative yeast" suggests non-*albicans Candida* yeast (and rules out *C. albicans*).

“Germ-tube positive yeast” is identified as *Candida albicans*.

“Fungal elements or hyphal elements” suggests mold.

BACTERIOLOGY

Susceptibility Testing

Susceptibility testing is an *in vitro* assay that allows us to predict the likelihood of successfully treating an infection with a particular antimicrobial agent. However, clinical outcome may depend on a variety of factors, such as host immunity or surgical treatment, which are not reflected in laboratory tests. All methods of susceptibility testing are based on diffusion or dilution.

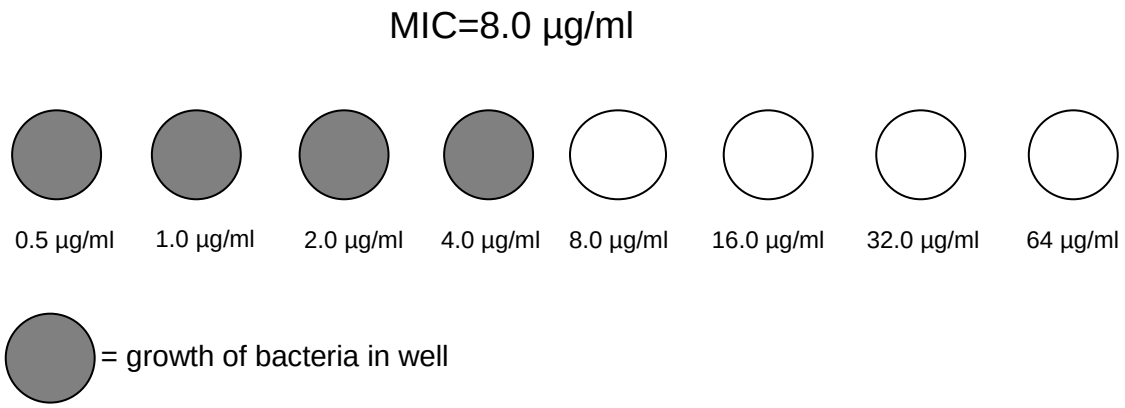
A. Semi-Automated Susceptibility Testing

Semi-automated antimicrobial susceptibility testing is performed using the Microscan system, which is based on broth microdilution. This system allows the laboratory to rapidly perform identification and susceptibility testing on most common pathogens (e.g. *Enterobacteriaceae,* Staphylococci, Enterococci, and *Pseudomonas aeruginosa*). The antibiotics tested vary based upon the Microscan panel used and the antibiotics that are currently on The Nebraska Medical Center hospital formulary. However, the microbiology laboratory reports antibiotics (that are on formulary) from most antibiotic classes that are appropriate for the specific organism tested. For instance, if the laboratory recovers an *Escherichia coli* isolate from urine, the following results are reported: penicillin, penicillin/β-lactamase inhibitor combination(s), first generation cephalosporin, a cephamycin, multiple expanded-spectrum cephalosporins (including cefepime), a carbapenem, one or two fluoroquinolones, at least two aminoglycosides, trimethoprim-sulfamethoxazole, and nitrofurantoin.

The results obtained from the Microscan system are based on the minimum inhibitory concentration (MIC). The MIC is defined as the lowest concentration of antibiotic that completely inhibits growth of the specific organism being tested. For instance, in figure 1, the

organism being tested grew in wells containing 0.5, 1.0, 2.0 and 4.0 μg/ml of antibiotic. The lowest concentration of antibiotic (MIC) that completely inhibits growth was 8.0 μg/ml.

Figure 1



The MIC is then interpreted (S=susceptible, I=Intermediate, or R=resistant) using CLSI (formerly NCCLS) standards, which are published each year in January. For example, the MIC interpretive standards for ampicillin against *E. coli* are ≤8μg/ml=susceptible, 16 μg/ml=intermediate, and ≥32 μg/ml=resistant. These interpretive standards are based on many studies, including clinical, pharmacokinetic/pharmacodynamic, and microbiological studies. It is important to be aware that, although there are many examples of bacteria and antibiotics for which we have CLSI interpretive standards (particularly for the most common pathogens), there are some bacteria for which there are no interpretive standards. Additionally, there are some antibiotics for which there are no interpretive standards. Consultation with the Microbiology laboratory (552-2090) is encouraged when seeking MIC data in these circumstances.

B. Disk Diffusion

The Nebraska Medical Center Microbiology laboratory does not routinely perform disk diffusion (commonly referred to as Kirby-Bauer testing) antimicrobial susceptibility testing except for *Pseudomonas aeruginosa* isolates obtained from cystic fibrosis (CF) patients. The Microscan system is not FDA approved to perform susceptibility testing on CF *P. aeruginosa* isolates due to the large amount of extracellular material typically produced by these isolates. Disk diffusion allows for measurement of the zone of growth inhibition (Figure 2).

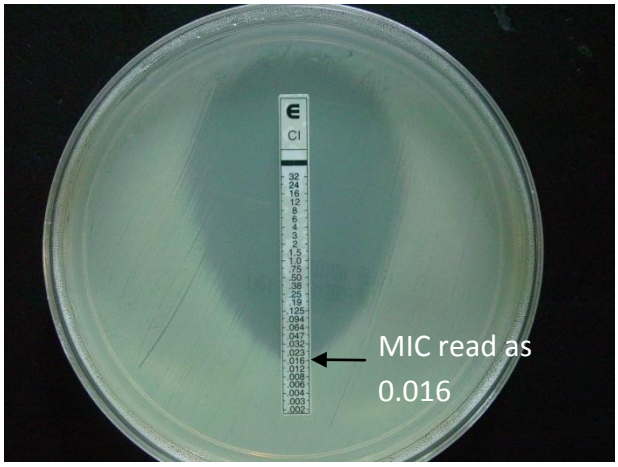
Figure 2

The CLSI provides interpretive standards for reporting an organism as S, I, or R based on the zone of inhibition. The main difference between disk diffusion testing and MIC testing is that disk diffusion gives clinicians qualitative results, whereas MIC testing gives quantitative results. Knowing the MIC can help clinicians incorporate pharmacodynamic/pharmacokinetic principles into the design of the treatment regimen. For instance, if we want to use ceftriaxone to treat meningitis due to *Streptococcus pneumoniae*, we need to achieve a concentration in the cerebrospinal fluid (CSF) of approximately four times the MIC for about 40% of the dosing interval due to the time-dependent/concentration-independent nature of the drug. Therefore, if the MIC of the *S. pneumoniae* isolate to ceftriaxone is 0.25 µg/ml, we want a concentration of at least 1 µg/ml in the CSF for 40% of the dosing interval. The size of the zone of inhibition does not tell us the MIC, so in this case, disk diffusion methodology is unhelpful. One other note, zone sizes cannot be compared between drugs. Just because drug A has a larger zone size than drug B, does not mean that drug A will work better. Zone sizes must be correlated back to the CLSI interpretive standards in order to determine susceptibility or resistance.

C. E-test

The CLSI only interprets MIC results for common pathogens (*Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter* spp., *Stenotrophomonas maltophilia, Burkholderia cepacia, Staphylococcus* sp., *Enterococcus* sp., *Haemophilus* sp., *Neisseria gonorrhoeae, Streptococcus pneumoniae, Streptococcus* sp., and *Vibrio cholerae*). However, in many cases, bacterial species are isolated that do not have CLSI standards (i.e. *Corynebacterium* sp. or certain gram-negative glucose non-fermenting organisms, such as *Flavobacterium* sp. or *Alcaligenes* sp.) that need antibacterial susceptibility testing. Many of these bacterial species are also not FDA approved to use with the Microscan system or do not grow well under these conditions. Therefore, the E-test methodology is typically used under these conditions. The E-test is an agar based method that uses a plastic strip with with antibiotic concentrations in variable size plastic disks on its backside. When placed on an agar surface preinoculated with the bacterial isolate of interest, the diffusing antibiotic creates a concentration gradient in the agar. Decreasing concentrations of antibiotic from the top of the strip to the bottom create an ellipsoid diffusion pattern around the strip. The resultant elliptical zone of inhibition allows the MIC to be read at the point where the zone crosses the E-test strip (Figure 3). If susceptibility testing is needed for an organism that does not have CLSI standards, please call the microbiology laboratory to discuss the antibiotic regimen to be tested.

Figure 3



Interpretation of these MIC results is based upon clinical, pharmacokinetic and pharmacodynamic experience as well as published reports of clinical success/failure. For example, if the isolate MIC =2 µg/ml, and one can achieve trough levels of 16µg/ml of that particular antibiotic at the site of infection, use would be reasonable. If susceptibility testing is performed in these situations, the following statement will be added to the final report

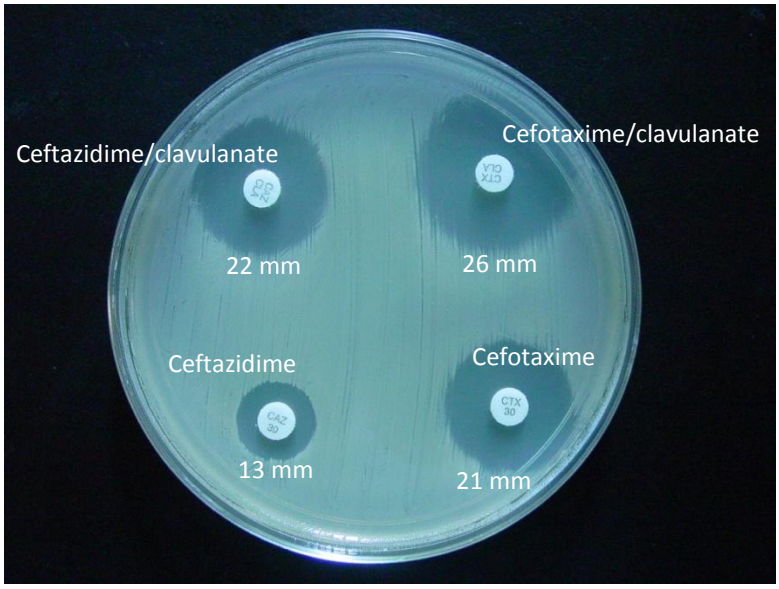
"National Standards for antimicrobial susceptibility testing for this isolate have not been established and results may not predict clinical response. The Infectious Disease Service may be contacted for specific treatment and recommendations."

D. Special susceptibility testing issues

Extended-spectrum ß -lactamases (ESBLs)

ESBLs are ß-lactamases that are capable of hydrolyzing expanded-spectrum cephalosporins (ceftriaxone, cefotaxime, and ceftazidime) as well as cefepime and aztreonam. ESBLs can be isolated from many different *Enterobacteriaceae* species, but are most commonly isolated from *Klebsiella pneumoniae, K. oxytoca, E. coli,* or *Proteus mirabilis.* Using *in vitro* testing systems such as Microscan, isolates that carry ESBLs can initially be intermediate or resistant to one or all of the expanded-spectrum cephalosporins, cefepime or aztreonam. This is due to the fact that there are many different ESBLs with different substrate specificities. If a particular *Klebsiella pneumoniae, K. oxytoca, E. coli,* or *Proteus mirabilis* isolate is resistant or intermediate to any of the expanded-spectrum cephalosporins, cefepime or aztreonam, the following statement will be included in the preliminary report: "Suspected Extended Spectrum β-Lactamase (ESBL), confirmation to follow." An ESBL test will then be performed which is based upon the fact that clavulanic acid will inhibit ESBLs (Figure 4) The test is performed using disk diffusion disks that contain either cefotaxime or ceftazidime and corresponding disks containing cefotaxime/clavulanic acid or ceftazidime/clavulanic acid (a β-lactamase inhibitor). If the disk containing cefotaxime (or ceftazidime)/clavulanic

Figure 4



acid is 5mm in diameter greater than either cefotaxime (or ceftazidime) alone, it is considered a positive test. Note that in figure 4, the zones of inhibition surrounding ceftazidime/clavulanate (22 mm) and cefotaxime/clavulanate (26 mm) are at least 5 mm greater than the zones of inhibition surrounding ceftazidime (13 mm) of cefotaxime (21 mm) alone, demonstrating that this isolate is producing an ESBL. If the isolate is positive for an ESBL, the following statement is added to the final report "Positive for Extended-Spectrum β-lactamase (ESBL). This is an extended-spectrum β-lactamase producing strain which is clinically resistant to all cephalosporins and aztreonam.**"** In addition, all β-lactams excluding the cephamycins, piperacillin/tazobactam and the carbapenems, are changed to resistant (if they were initially reported as susceptible or intermediate).

Carbapenemases

Carbapenemases are ß-lactamases that are capable of hydrolyzing all ß-lactams, including the carbapenems. Carbapenemases can be isolated from many different *Enterobacteriaceae* species. Thus, among *Enterobacteriaceae,* if the microscan susceptibility profile suggests a carbapenemase, the Microbiology department will perform a Modified Hodge Test (MHT) to confirm the isolate as a carbapenemase producer. The criteria for this initial screen are (need 1 AND 2 OR 3): 1 - ertapenem MIC of 2 mg/L or imipenem/meropenem MIC of 2 – 4 mg/L; AND 2 - resistant/intermediate to any of the 3rd or 4th generation cephalosporins; OR 3 - resistant/intermediate to any of the carbapenems. If the MHT is negative, no changes are made to the susceptibility report; if the MHT is positive, the isolate is reported as such, with the comment "This isolate produces a carbapenemase and may be clinically resistant to all beta-lactam antibiotics. The Infectious Disease Service may be consulted regarding treatment options." In the event of a positive MHT, all beta-lactams and carbapenems are changed to resistant.

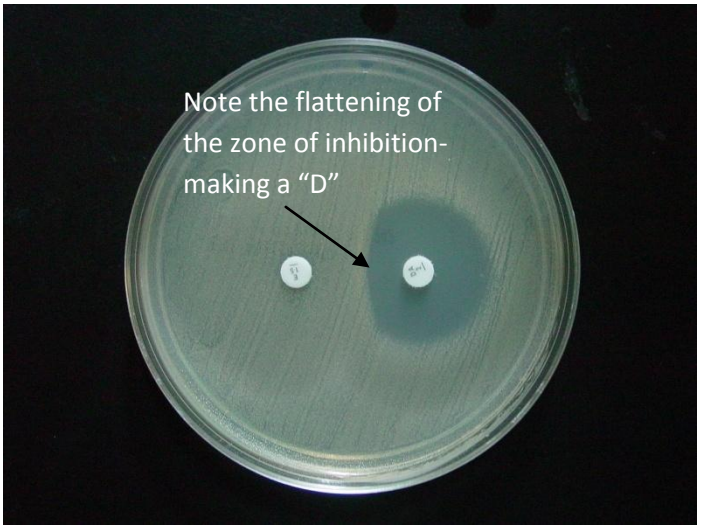
Inducible β-lactamase in staphylococci

The prevalence of penicillin-susceptible *Staphylococcus* spp. isolates is low at The Nebraska Medical Center. Staphylococcal isolates appearing phenotypically susceptible to pencillin may harbor an inducible β-lactamase and must undergo further testing to confirm susceptibility if penicillin is to be used. Thus, for staphylococcal isolates that show a penicillin MIC of <= 0.12, a comment will be added to the report stating, “This isolate is susceptible to oxacillin but only phenotypically susceptible to penicillin. A confirmatory induction test is required to rule out inducible resistance and ensure susceptibility to penicillin. Please contact the laboratory for further testing if penicillin therapy is anticipated.” The laboratory can then perform an inducible β-lactamase test to determine penicillin susceptibility or resistance.

Inducible clindamycin-resistance in *Staphylococcus aureus*

Erythromycin resistance within staphylococci is typically mediated through two distinct mechanisms. The first mechanism entails protection of the ribosome from erythromycin (and clindamycin) through methylation (referred to as MLS_B resistance). This mechanism may be constitutive (conferring resistance to both erythromycin and clindamycin) or inducible (conferring resistance only to erythromycin). Published clinical reports have demonstrated that *S. aureus* isolates carrying an inducible MLS_B resistance gene should be considered resistant to clindamycin even if the *in vitro* result considers the isolate susceptible to clindamycin. The second resistance mechanism is conferred through efflux of erythromycin out of the cell through specific pumps (encoded by the *msrA* gene). Staphylococcal isolates carrying the MsrA efflux pump are resistant only to erythromycin and not clindamycin. If a *S. aureus* isolate is resistant to erythromycin and susceptible to clindamycin and the clinician would like to use clindamycin for therapy, a D-test should be performed to determine the presence of MLS_B resistance. The D-test has traditionally been performed by placing an erythromycin disk 15 mm away from a clindamycin disk. Organisms that demonstrate flattening of the clindamycin zone adjacent to the erythromycin disk are considered positive for inducible MLS_B resistance and clindamycin should not be used during therapy (Figure 5). Recently, the Microbiology laboratory started performing the D-Test using a new methodology. The D-test is now done directly in the Microscan panels for Gram-positive organisms, and clindamycin susceptibility is automatically reported. In cases of vaginal specimens that grow *Streptococcus agalactiae* (Group B Strep), where the patient is allergic to penicillin, the manual D-test will automatically be performed as these isolates may also harbor MLS_B resistance. Clindamycin resistance will be reported with the comment, “This isolate is presumed to be clindamycin resistant based on detection of inducible clindamycin resistance. Clindamycin may still be effective in some patients.”

Figure 5



Interpretation of Micro Reports

Cut-off values (rare/few/moderate/etc) depend on a number of factors including: source of the culture, Gram stain results, organism, likelihood that the culture was contaminated based on the organisms that are isolated, number of organisms that grow, patient gender, patient age, and type of patient (OB, CF, Immunocompromised, etc). Of note, when a report says, "rare gram-negative rod", it does not mean rare as in unusual, it means rare as in very few.

Contaminant vs. pathogen

Blood – normally sterile

Pathogens – any organism isolated

Likely Contaminants
Coagulase-negative staphylococci
Alpha-hemolytic streptococci
Bacillus spp.
Corynebacterium spp. (except *C. jeikeium*)
Propionibacterium acnes
NOTE: must take into consideration how many cultures were drawn versus how many are positive and what the organism is

Tissue and Body Fluids – should be sterile
Pathogens – any organism isolated; use judgment to evaluate the possibility of normal flora being present in relation to the source of the specimen

Normal Flora
Eye/Ear
Coagulase-negative- staphylococci
non-hemolytic streptococci
alpha-hemolytic streptococci
Diphtheroids
Skin
Coagulase-negative staphylococci
Propionibacterium acnes
diphtheroids
alpha-hemolytic- streptococci
Bacillus spp.

Genital
Pathogens
Neisseria gonorrhoeae
ß-hemolytic streptococci
Listeria spp.
Gardnerella vaginalis
Predominant numbers of *S. aureus*
Predominant numbers of yeast

Normal flora
Staphylococcus spp.
Lactobacillus spp.
Diphtheroids
Enterococcus spp.
Streptococcus spp.
Gram-negative rods
Anaerobes
Yeast

Urine – should be sterile

Pathogens
Enterobacteriaceae
Enterococcus spp.
Pseudomonas spp. and other non-fermenters
group B *Streptococcus* (*Streptococcus agalactiae*)
S. aureus and S.saprophyticus
Yeast

Likely Contaminants
Diphtheroids
coagulase-negative staphylococci
alpha-hemolytic streptococci
Lactobacillus spp.
Gram-negative rods
Bacillus spp.
NOTE: significance of organism is determined by colony count

Gastrointestinal tract

Pathogens
Salmonella spp.
Shigella spp.
Campylobacter jejuni
E. coli O157:H7
Aeromonas/Plesiomonas spp.
Yersinia enterocolitica
Vibrio spp.
Clostridium difficile (toxin)
S. aureus (in the context of enterotoxin food poisoning)
Helicobacter pylori (antigen)

Normal Flora
Enterobacteriaceae
Staphylococcus spp.
Streptococcus spp.
Enterococcus spp.
Pseudomonas spp.
Anaerobes
Yeast

Respiratory tract

Pathogens
Group A *Streptococcus*-(*Streptococcus pyogenes*)
Streptococcus pneumoniae
Predominant *S. aureus*
H. influenzae
Neisseria meningitidis/gonorrhoeae
Predominant *Enterobacteriaceae*
Predominant *Pseudomonas* spp. and other non-fermenters
Corynebacterium diphtheriae
Bordetella pertussis
Legionella pneumophila
Mycobacterium spp.
Nocardia spp.
Predominant *Moraxella catarrhalis*
Predominant yeast

Normal Flora
Staphylococcus spp.
alpha-hemolytic streptococci
Gram-negative rods
β-hemolytic streptococci other than group A
Neisseria spp.
Enterococcus spp.
Corynebacterium spp.
Bacillus spp.
Yeast
Anaerobes
Haemophilus spp.
Micrococcus spp.
Stomatococcus spp.
NOTE: amount of organism present, source of culture, and patient age may determine significance as a pathogen

Specimen requirements (online)

www.preceptor.com – Laboratory Services – Specimen Collection Guidelines
intranet.nebraskamed.com/index.cfm – Nursing – Manuals – Laboratory Services – Specimen Collection Guidelines

Target Timing of reports

Gram Stain
Stat – within one hour of receipt in lab
Routine – within 4 hours of receipt in lab
Stat and Routine Gram stains are performed/reported on all shifts, including Shift III (overnight).

Organism identification
a. The organism will be identified within 24 hours of isolation of an organism unless it is an unusual or fastidious organism and/or requires further work-up to confirm.

b. **Antibiogram** – The hospital-wide and unit-specific antibiograms can be found on the intranet.

1. intranet.nebraskamed.com/index.cfm – Departments – Infection Control/Healthcare Epidemiology – Unit-specific Antibiograms
2. www.nebraskamed.com/asp -- Antibiograms

Susceptibility results

a. The susceptibility results will be reported within 24-48 hours of isolation of an organism unless it is an unusual or fastidious organism and/or requires further work-up to confirm identification
b. See Appendix A for commonly used antibiotic abbreviations.

Urinalysis and Urine Culture

Indicators of infection from a urinalysis

- Turbid/cloudy urine
- Positive leukocyte esterase, which indicates the presence of WBCs in the urine.
- Presence of > 10 WBCs
- The presence of 10 WBCs per high-power field, upon microscopy, is equivalent to 100 cells/mm^3 of urine, which is considered the upper limit of normal.
- Positive nitrite test, which indicates the presence of a nitrate-reducing microorganism, such as *Escherichia coli* or any other member of the *Enterobacteriaceae* family.
- Elevated pH (6.5 – 8)

  This is caused by organisms that produce the enzyme urease, which catalyzes the hydrolysis of urea into ammonia and carbon dioxide. Some of these organisms include *Staphylococcus saprophyticus, Klebsiella pneumoniae,* and *Proteus* spp.
- Presence of ≥ 10^5 colony forming units (CFU) of bacteria per milliliter of urine.

  Approximately one-third to one-half of young women with symptomatic lower urinary tract infections have less than 10^5 CFU/ml of urine. Thus, the presence of ≥ 10^2 CFU/ml should be considered in the context of the patient characteristics and signs and symptoms.

Urine Culture

A urine culture must ALWAYS be interpreted in the context of a urinalysis and patient symptoms. Ideally, a urine culture would not be performed unless a urinalysis indicated a possible infection. If a patient has no signs of infection on urinalysis, no symptoms of infection, but a positive urine culture, the patient by definition has asymptomatic bacteriuria, or the specimen was contaminated at the time of collection with organisms present on the skin/mucous membranes. Typically, catheterized patients will become colonized within 48 hours of catheterization. The only patient populations for which it is recommended to screen for and treat asymptomatic bacteriuria are pregnant women and patients scheduled for a genitourinary surgical procedure.

Stool cultures

Stool for WBC – The presence of stool WBCs, indicated by detection of lactoferrin released from fecal WBCs using a latex agglutination test, suggests inflammation of the bowel. This should lead the physician evaluate for the cause of inflammation and consider selective cultures for the most common invasive pathogens, *Campylobacter jejuni, Salmonella* spp., *Shigella* spp., and enterohemorrhagic *E. coli*.

Stool culture for bacterial pathogens – If a stool culture is ordered, the laboratory will screen for *Campylobacter* spp., *Salmonella* serogroups, *Shigella* spp., *Plesiomonas shigelloides, Aeromonas* spp, and enterohemorrhagic *E. coli* (*E. coli* O157:H7). The most common pathogen causing bacterial gastroenteritis in Nebraska is *Campylobacter jejuni.* However, if *Yersinia enterocolitica* or *Vibrio* spp. are suspected, separate orders are required as different media are needed to isolate these pathogens. It is pertinent to note that 30-50% of all EHEC in Nebraska are not *E. coli* O157:H7 but other serotypes (e.g. O111:NM, O26:H11, O103:NM, etc.). An EIA-based screening test is performed routinely on all stool

culture specimens to look for the presence of shiga-toxin or shiga-like toxin-producing organisms. Secondary testing is performed on all positive EIA isolates to determine if the organism is E. coli O157:H7. If the isolate is determined to be non-O157:H7, it gets sent to the Nebraska Public Health Laboratory for serotyping. It is inappropriate to order a stool culture on patients who have been in the hospital for more than 3 days and then develop diarrhea; in these situations, studies have shown that the most common pathogen is *C. difficile*, and a toxin assay should be ordered.

***Clostridium difficile* toxin assay**

a. Cultures for *C. difficile* are technically demanding, require two to three days for growth, and are not specific for distinguishing between toxin-negative or toxin-positive strains or asymptomatic carriage.

b. The *C. difficile* GDH antigen/toxin A/B assay is the test currently used for diagnosing *C. difficile* infection (CDI) at The Nebraska Medical Center. This is a dual enzyme immunoassay that detects the glutamate dehydrogenase (GDH) enzyme, common to all *C. difficile*, and the toxins (A and B) produced by some *C. difficile* strains. This assay was validated by the Microbiology laboratory to be 94% sensitive and >99% specific. However, there is some confusion related to test results that are GDH-positive/toxin-negative. In these cases, the laboratory will automatically reflex to a PCR test to determine the presence or absence of the toxin gene. It is not recommended to order multiple tests, as studies have shown no significant improvement in sensitivity or specificity with repeated stool specimens. Appropriate specimens from patients suspected of having CDI are diarrheal/loose stools that take the shape of the container.

c. The *C. difficile* toxin assay should not be used to assess response to therapy because many patients will continue to carry the toxin without any clinical manifestations of colitis.

Blood cultures

A minimum of two sets (four bottles; one set = one aerobic bottle, one anaerobic bottle) should always be obtained (maximum = three sets/24 hours). The minimum volume of blood needed per bottle for adults is 10 ml. Thus, the minimum volume of blood per set is 20 ml. The minimum volume necessary for one pediatric bottle is 1 ml.

Ordering one set may lead to confusion if the culture is positive for an organism that is commonly a contaminant. For example, if one set is ordered and is positive for coagulase-negative staphylococci (CoNS), a common contaminant, it is impossible to determine if this represents contamination or infection. However, if two sets are ordered, and only one is positive for CoNS, this most likely represents contamination.

Please specify the desired sites of the blood draw (e.g., one from line, one peripherally).
Ideally, blood cultures should be drawn before the first dose of antibiotics, but antibiotics should not be withheld because of a delay in getting cultures drawn. Although it is common practice to wait 30-60 minutes between blood cultures, there is little data to support this practice, and we do not recommend it.

If the patient is persistently febrile, obtain two sets of cultures per day for 48-72 hours. Do not continue drawing daily blood cultures beyond 72 hours.

If a vascular catheter is thought to be a potential site of infection, blood should be drawn from the catheter and the periphery. Site and time of phlebotomy should be noted. The differential time to positivity can help in assessing whether the catheter is the likely source.

Differential Time to Positivity (DTP)

a. A positive line culture result is obtained at least 2 hours earlier than a positive peripheral blood culture result.

b. Typically, the diagnosis of a line-associated infection can be made according to the following criteria: presence of an intravascular device, at least one positive blood culture obtained from a peripheral site, clinical manifestations of infection, and no other apparent source for bloodstream infection

PLUS:
positive semiquantitative catheter culture with the same organism as that isolated peripherally from the blood or differential time to positivity.

Respiratory cultures

Lower respiratory tract: Appropriate specimens to identify pathogens causing disease of the lower respiratory tract (tracheitis, bronchitis, pneumonia, lung abscess, and empyema) include expectorated and induced sputum, endotracheal tube aspirations, bronchial brushings, washes, or alveolar lavages collected during bronchoscopy and pleural fluid.

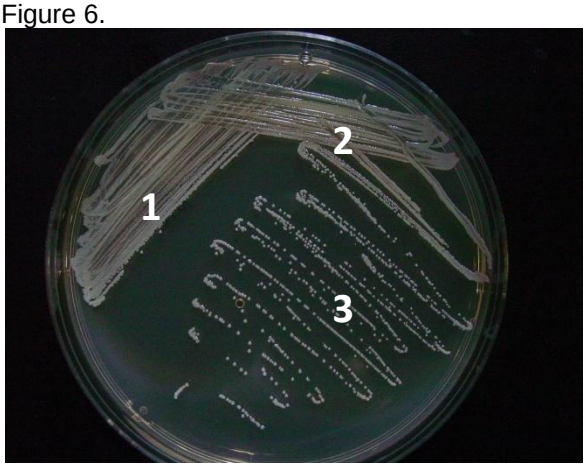
Upper respiratory tract: Appropriate specimens to identify pathogens causing upper respiratory tract infections include samples from the nasopharynx, throat, oral ulcerations, and inflammatory material from the nasal sinuses.

All specimens should be stored at 4ºC until delivered to the laboratory (to inhibit growth of normal flora). *Neisseria gonorrhoeae* is particularly susceptible to dehydration, so swabs must be inoculated directly to plate media or put into an appropriate transport medium.

Lower respiratory tract specimens (particularly sputum) are assessed for quality (lack of contaminating oral respiratory tract flora and epithelial cells) through a Gram stain. If the specimen shows a lack of PMNs but many epithelial cells and oropharyngeal flora, the specimen will be rejected by the laboratory and another specimen must be collected for culture.

Specific pathogens or normal respiratory flora are quantified in the culture report using the terms "many," "moderate," or "few." "Many" refers to the observation that the specific pathogen is growing in the first, second, and third quadrant of an agar plate (Figure 6). "Moderate" growth refers to the fact that the organism is growing in the first and second quadrant; whereas "few" means that the organism of interest is growing only in the first quadrant. "Rare" means that fewer than 10 colonies are isolated on the plate.

Figure 6.



It is important to note that cultures for *Legionella pneumophila* are a separate order (i.e. media used to detect *Legionella pneumophila* will not be inoculated if only a sputum culture is ordered). The routine setup of all pulmonary fluid specimens for *Legionella* culture will no longer be performed. As an alternative to the full *Legionella* culture, the laboratory will begin to offer a highly sensitive, rapid EIA for the detection of *L*. *pneumophila* serogroup 1 antigen in the urine of patients suspected of having legionellosis.

MYCOBACTERIOLOGY

General – *Mycobacterium* spp. are typically placed into one of three groups based upon their growth characteristics and, in some cases, their phylogenetic relatedness.

M. tuberculosis complex: This group includes *M. tuberculosis, M. bovis, M. africanum, M. microti, M. pinnipedii and M. canettii.* These organisms, which grow very slowly (14-21 days), are of extreme public health importance due to person-to-person spread.

Slowly growing nontuberculous mycobacteria: This group includes, among others, the *M. avium* complex (MAC), *M. genavense, M. kansasii,* and *M. ulcerans.*

Rapidly growing Mycobacteria: This group includes, among others, *M. fortuitum, M. abscessus,* and *M. chelonae.*

Staining – Due to a high mycolic acid content in their cell wall, *Mycobacterium* spp. stain poorly using the Gram stain method. Therefore, AFB smears for mycobacteria are screened by fluorescent Auramine O stain and confirmed positive by the Ziehl-Neelsen stain. Bacteria that stain positive with the Ziehl-Neelsen stain are called acid-fast bacteria (or AFB) because they resist decolorization with acidified organic solvents and retain the carbol fuschisin dye, appearing red. The positive acid-fast stain by Ziehl-Neelsen should not be confused with a positive "modified" acid-fast stain, which is used to detect partial or weakly acid-fast aerobic actinomycetes including *Nocardia* spp*., Gordonia* spp*., Rhodococcus* spp*.,* and *Tsukamurella* spp*.*

Specimen requirements – Typical specimens submitted for *Mycobacterium* spp. isolation include sputum, tissue, or sterile body fluid (including blood). It should be noted that specimens submitted on swabs or stool specimens are not acceptable for isolation of *Mycobacterium* spp.

Timing – Specimens are decontaminated and concentrated in the Mycobacteriology laboratory using a procedure that minimizes contamination by non-mycobacterial organisms*.* A specialized fluorescent stain (Auramine-O), which is highly sensitive, is used to screen all specimens for the presence of mycobacteria*.* All positive smears are confirmed using the highly specific Ziehl-Neelsen stain. AFB-positive smears are called to the ordering physicians. Specimens are plated onto an egg-based media (Lowenstein-Jensen or LJ) as well as liquid media. All specimens are held for 8 weeks. Blood cultures for *Mycobacterium* spp., which are drawn into the Bactec Myco/F Lytic bottle, are held for six weeks and are monitored continuously using our standard Bactec blood culture instrument. Positive cultures are first tested using a DNA probe test (not a PCR based approach) which can detect *Mycobacterium tuberculosis* complex*, M. kansasii, M. avium*-complex, and *M. gordonae.* All *Mycobacterium* species are identified using conventional biochemical techniques or through DNA sequencing. An amplified test is available for *M. tuberculosis* from sputum samples only.

Susceptibility testing – Susceptibility testing for mycobacterial isolates is a sendout test performed at Creighton Medical Laboratories or ARUP. Susceptibilities are determined on all medically significant *Mycobacterium* species isolated.

Mycobacterium Amplified Direct Test – A PCR test is now available in the laboratory for detection of *M. tuberculosis* complex from direct patient specimens. Approved specimens include sputum and BAL. The test is performed on Tuesdays and Fridays. It is recommended that all patients with a **high** clinical suspicion of TB be tested by this method because of the high sensitivity/specificity and the rapid turnaround time. All AFB smear positive specimens will automatically be reflexed to this test. The test is FDA-approved for AFB smear-positive specimens (sensitivity 96.9%, specificity 100%) and for AFB smear-negative specimens (sensitivity 72%, specificity >99%).

VIROLOGY

Virus detection – There are four general ways in which viral infections can be detected: culture, direct viral antigen detection, serology, or nucleic acid detection.

Culture – Viral culture is based upon the inoculation of specimen into specific cell lines and detection of cytopathic effect (CPE) within those cells; specific CPE is representative of a specific virus. This initial observation is then typically confirmed using virus-specific antibody. There are 4 different viral culture orders – general virus culture (VCGVI), CMV culture (VCCMV), HSV culture (VCHSV), and VZV culture (VCVZV). Specimen is inoculated into tissue culture cell lines and shell vials (for VCCMV only). Cell lines for each virus are selected for their ability to propagate the suspected viruses. The use of shell vials normally results in faster detection of virus due to an enhancement of virus antigen production during the centrifugation step of the procedure. Essentially, centrifugation allows any amount of virus present in the specimen to be spun down into direct contact with the cells. This allows the virus to begin its replication cycle sooner than it would if the virus were to attach to a cell by happenstance (as would happen without centrifugation). After incubation, the shell vials are stained with CMV-specific monoclonal antibodies, and a report is issued at 24 hours. The tissue culture cell lines are examined for 14 days before being reported as negative. In our laboratory, the following viruses can be detected using culture: HSV, VZV, Adenovirus, CMV, and Enterovirus. If SARS is suspected, do not send specimen for culture; page the Nebraska Public Health Laboratory Special Pathogens Laboratory at 888-5588.

a. Herpes simplex virus (HSV) culture (culture is held for 7 days).
b. Cytomegalovirus (CMV) culture (culture is held for 21 days; although shell vial results [detection of early antigen] are available after 1 day).
c. General virus culture (culture is held for 14 days)
d. Varicella-zoster virus (VZV) culture (culture is held for 14 days).

Nucleic Acid Amplification Test – Viruses that cause respiratory infections can be detected using an FDA-approved Respiratory Viral Panel (RVP) test. This test is capable of simultaneous detection and identification of multiple respiratory viruses using a qualitative nucleic acid multiplex PCR assay. Viruses detected by this methodology include Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Respiratory Syncytial Virus (RSV) subtype A, RSV subtype B, Human Metapneumovirus, Rhinovirus, Adenovirus, and Parainfluenza viruses (1, 2, and 3). The acceptable specimen is a nasopharyngeal swab placed in viral transport media, or 2-3 ml of nasopharyngeal wash, or bronchioalveolar lavage (BAL). This new methodology replaces the previously used shell vial technique and standard cell culture for respiratory viruses. The test will be performed Monday, Thursday, and Saturday with additional testing days during respiratory viral season.

Direct viral antigen detection – HSV and VZV can be detected directly from skin lesions using a direct fluorescent antibody (DFA) test. Call the microbiology laboratory (552-2090) for instructions and the Specimen Receiving Laboratory (559-7616) for test materials if a DFA test for either HSV or VZV is required.

Serology – Both IgM (acute) and IgG antibody titers can be assessed for a number of viral entities including: Epstein Barr Virus (EBV), CMV, HSV, measles virus (MeV), mumps virus (MuV), HIV, and West Nile virus (WNV). Note that EBV, MeV, and MuV cannot be cultured. Additional testing is available through a reference laboratory. Call the Laboratory Sendout Department at 599-9353 for questions about sendout tests.

Nucleic acid detection – A number of viruses can also be detected using molecular methodologies-these tests are offered by the molecular diagnostics department. Specific questions regarding specimen collection, etc. should be discussed with the molecular diagnostics laboratory (559-7630). The following tests are currently offered: Parvovirus, HHV-6, Enterovirus, HSV, VZV, CMV, EBV, BK, JC, HIV, and Norovirus. Quantitative viral load tests are also available for EBV, CMV, JC, and HIV.

Specimen collection – With a few exceptions (listed below) specimens sent to the laboratory for viral culture should be collected either using a swab containing viral transport medium or within viral transport media. For instance, cultures for HSV or VZV from lesions should be collected using a viral transport medium containing swab. It is important to note that these swabs are distinct from the typical swab for bacterial culture. All tissue specimens should be placed in viral

transport medium-it is best not to use a swab when collecting tissue from any source. The three exceptions when viral cultures do not need to be in viral transport medium are: 1) a nasal wash for respiratory virus culture, 2) blood culture for CMV (collect 5 ml blood in a sodium heparin tube and order CMV buffy coat), and 3) sterile fluid (such as CSF) where specimen should not be diluted. Sterile fluids not placed in viral transport media should be kept at 4ºC until transported to the microbiology laboratory.

Guidelines for specimen collection can be found at: http://www.preceptor.com. Then follow links to Laboratory services, section specific policies (Microbiology specimen collection guidelines).

MYCOLOGY

Specimen collection – The ideal specimens for fungal isolation are either tissue, sterile body fluid, or blood. If a tissue specimen is to be tested for the presence of fungi, it is important that part of the specimen is sent to the microbiology laboratory **before** the specimen is fixed in formalin for histological examination. Blood to be tested for fungus should be added to a separate blood culture bottle (Bactec Myco/F Lytic bottle) that is specially formulated for fungal and mycobacterial growth. It is important to note that the growth of moulds from specimens that originate from non-sterile sites should be interpreted with caution. In most instances, these saprophytic moulds are contaminants.

Timing of reports – Moulds may take 3-4 weeks to grow, whereas yeasts grow rather rapidly and can usually be identified within 3-5 days. Tissue, biopsy, bone marrow, and autopsy specimens will be finalized at 6 weeks; all other specimens will be finalized at 4 weeks.

Susceptibility Testing – Yeast susceptibility testing is performed using the Sensititre YeastOne susceptibility test, which is a microtiter broth dilution method. This test has been validated in house and is not FDA approved. It is used to determine antifungal susceptibility (MIC) of rapidly growing yeasts including *Candida* species, *Cryptococcus* species, and miscellaneous other rapid growing yeast species from sterile sites including blood, CSF, synovial fluids, pleural fluids, and pericardial fluids. The panel contains appropriate dilutions of antifungal agents and a colorometric dye, Alamar Blue. Yeast growth in the panel will be observed by colorimetric change from blue (no growth) to red (growth). The MIC is the lowest concentration of antifungal agent preventing the development of a red growth well, i.e. the first blue “no growth” well. This method is not approved for testing molds. Mold isolates to be tested for AST are sent to a reference laboratory (San Antonio, Texas) for evaluation when requested. Please call the Mycology laboratory if susceptibility testing is desired on a particular isolate (552-2090).

PARASITOLOGY

Ova and Parasites – An O&P test should be ordered on patients presenting with a history of chronic diarrhea (> 10 days). It is **not** appropriate to order an O&P test if the patient develops diarrhea while in the hospital. Due to the low incidence of most parasitic infections in the United States and Nebraska, stool specimens for Ova and Parasite are routinely tested only for *Giardia lamblia* and *Cryptosporidium parvum* through an EIA test. However, if the patient has a travel history that includes regions of the world where parasitic infections are endemic, microscopic evaluation for ova and parasites can be ordered. Please contact the microbiology lab if this is the case (552-2090).

Timing of Reports – A *Giardia/Cryptosporidium* antigen test is available M,W,F. If a specimen is received by 0900 on these days, the test will be completed the same day. Full ova and parasite workup (i.e., with appropriate foreign travel history) is available M-F with results available the following day.

Malaria smears – Malaria smears are performed in the hematology department; please call the hematology laboratory (559-7640) with questions if malaria is suspected.

Ectoparasites – The microbiology laboratory also identifies insect vectors associated with disease (e.g. lice, ticks, scabies). Please call the microbiology laboratory (552-2090) with questions regarding identification.

CLINICAL MICROBIOLOGY FELLOWSHIP

Program Description – The Department of Pathology and Microbiology, in collaboration with the Nebraska Medical Center, sponsors a Clinical Microbiology Fellowship Program that is accredited by the Committee on Postgraduate Educational Programs (CPEP) of the American Academy of Microbiology. This 2-year program provides the fellow hands-on experience in the basic disciplines of clinical microbiology (i.e., bacteriology, mycobacteriology, mycology, parasitology, virology, molecular microbiology, public health microbiology and serology). Fellows are selected for their potential as future directors of diagnostic microbiology laboratories and as leaders in public health.

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INTERPRETATION OF VIRAL DIAGNOSTIC TESTS

1. HEPATITIS

What defines hepatitis?

- Increased ALT
- The three most common causes of hepatitis are prescription drugs, obesity, and alcohol.

Hepatitis A Virus (HAV)

Test	Result	Interpretation
HAV IgM	Positive	Active Infection
HAV IgM	Negative	Not Infected
HAV Ab total	Positive	Exposure to HAV or vaccinated (immune)
HAV Ab total	Negative	Indeterminate; does not preclude prior exposure (existing Ab may be undetectable)

Hepatitis B Virus (HBV)

HBsAg	HBsAb	HBeAg	HBeAb	Interpretation	Notes	Follow-up
+	-	±	-	Acute or chronic HBV infection	A positive surface antigen means HBV is present and can spread to others. A positive HBeAg confirms actively replicating virus. If HBeAg is positive, this is considered wild type HBV. If HBeAg is negative and the patient is still replicating virus, this is considered mutant HBV. Approximately 2% of acute infections in adults will progress to chronicity.	Check HBV DNA. Repeat serology for clearance of HBsAg and/or resolution of chronicity; serum ALT to monitor disease activity
+	-	-	+	Carrier or early seroconversion	A positive surface antigen means HBV is present and can spread to others. A positive HBeAb usually means no replication is occurring.	Check HBV DNA. If negative, patient is a “carrier”.
+	-	+	+	Decreasing infectivity	Very rare results	Repeat serology for resolution; serum ALT to monitor disease activity
NA	+	NA	NA	Immune	Presence of HBsAb indicates immunity, which can occur via vaccination or prior acute infection. NOTE: If both HBsAg (+) and HBsAb (+), the patient is infected with two or more strains of HBV.	
-	-	-	-	Not immune/not infected	At risk for infection	Recommend vaccination series

HBV DNA assay should be performed in any patient with a positive HBsAg to determine whether active replication is occurring.

HBcAb is only relevant when dealing with acute HBV infection because HBcAb may be positive during serologic gap/window between seroconversion from HBsAg positivity to HBsAb positivity. With chronic HBV infection, HBsAg remains positive; thus, no serologic gap/window occurs.

Hepatitis C Virus (HCV)

HCV Ab Test *	HCV RNA	Interpretation
Positive	Positive	Active infection
Positive	Negative	If risk factors exist, cleared acute viremia (15%) or a sustained viral response after antiviral therapy; no risk for reactivation
Negative	Not needed	Not infected

*Enzyme immunoassay (EIA) or enhanced chemiluminescence immunoassay (CIA)

Occupational Exposure (Needlestick Injuries)

Time	Tests
Immediately post-exposure	ALT, AST, HBsAg, HBsAb, HCVAb*, HCV RNA
1 month post-exposure	Repeat
3 months post-exposure	Repeat

*Becomes positive eight weeks after acute infection

2. HERPES SIMPLEX VIRUS (HSV)

Test	Result	Interpretation	Recommendation/Notes
Culture of vesicles or ulcers	Positive	Active infection	Confirm by staining w/ specific monoclonal antibodies establishes the diagnosis. Culture from recurrent late disease is much less sensitive.
ELISA (Serology)	Positive	Prior exposure or active infection	Distinguishes HSV-1 and HSV-2
Direct Cytologic Exam	Positive	Active infection	Use Wright-Giemsa stain followed by Tzanck smear=see multinucleated giant cells. Negative test does not rule out diagnosis. Does not differentiate HSV-1, HSV-2, and zoster.
PCR	Positive	Active infection	Detects HSV in tissue, CSF, or cell samples. Sensitive, specific and rapid. Distinguishes HSV-1 and HSV-2.
Western blot or Immunoblot	Positive Negative	Prior exposure No prior exposure	Detects glycoprotein G; distinguishes HSV-1 and HSV-2. Western blot is gold standard for antibody detection (IgM and IgG).

3. VARICELLA ZOSTER VIRUS (VZV)

Test	Result	Interpretation	Recommendation/Notes
PCR	Positive	Active infection	88% sensitive in stained smears and 97% sensitive in unstained smears
Wright-Giemsa stain followed by Tzanck smear	Positive	Active infection	75% sensitive but also positive in herpes simplex
Immunofluorescent Staining	Positive	Acute Infection	Diagnostic of acute infection; more sensitive than culture
In situ hybridization	Positive	Primary Infection	Can demonstrate virus in peripheral blood mononuclear cells in primary infection in 24 hours
ELISA (Serology)	Positive	Prior exposure or active infection	A negative test does not rule out VZV infection because sample may have been collected prior to appearance of detectable IgG. Thus, if negative, repeat in 2-3 weeks.

4. CYTOMEGALOVIRUS (CMV)

Test	Result	Interpretation	Recommendation/Notes
Shell-vial culture (Gold Standard)	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation.
CMV IgM	Positive	Indicates exposure	Usually detected in primary infection except in immunocompromised patients. However, false positives are not uncommon. Should be confirmed by culture. Can also see false negatives in immunocompromised patients.
CMV IgG	Positive	Indicates exposure	Produced early in infection and persists life-long.
Intranuclear Inclusions	Positive	Active CMV replication	Inclusions in epithelial cells in urine sediment and liver biopsy are diagnostic. More useful in infants than adults. Presence of true CMV infection is determined by active replication PLUS clinical correlation.
PCR for CMV DNA in urine, CSF or serum	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation. The higher the number of viral copies in serum, the higher the probability of true infection.
DNA & RNA hybridization	Positive	Active CMV replication	Presence of true CMV infection is determined by active replication PLUS clinical correlation.

5. EPSTEIN-BARR VIRUS (EBV)

Test	Result	Interpretation	Recommendation/Notes
Heterophile Agglutination (Paul-Bunnell test)	Positive	EBV infection	"Spot" tests are now performed at the initial test. False positives may occur in leukemia, malignant lymphoma, malaria, rubella, hepatitis & pancreatic carcinoma
Titers, in situ hybridization	Positive	EBV infection	EBV can be confirmed in liver biopsy by in situ hybridization. Titers ≤1:56 may occur in normal persons and in pts w/ other illnesses. A titer of ≥1:224 is presumptive evidence of Infectious Mononucleosis (IM). Therefore, a differential absorption test should be performed using guinea pig kidney and beef cell antigens.
PCR	Positive	EBV replication	Presence of true EBV infection is determined by active replication PLUS clinical correlation. The higher the number of viral copies in serum, the higher the probability of true infection.

IgG-VCA	IgM-VCA	IgD (EA)	EBNA	Interpretation	Notes
-	-	-	-	No evidence of infection	At risk for infection
+	-	-	+	Consistent with prior infection	Immune
±	+	±	-	Consistent with primary infection	IgG becomes positive later. EA decreases later. Repeat in 2-3 weeks for IgG.
±	-	±	±	Potential lack of true Abs	If patient is less than 15 months old, serology may be due to the presence of maternal antibodies
+	±	+	+	Consistent with convalescence of primary infection or reactivation of latent infection	If patient is less than 20-25 years old
				or reactivation of latent infection	If patient is greater than 20-25 years old
+	+	-	+	Consistent with convalescence of primary infection	
-	-	+	-	Unknown	Repeat 2-4 wks.

6. **HUMAN HERPESVIRUS-6 (HHV-6)**

Test	Result	Interpretation	Recommendations/Notes
IgM Immunofluorescence Assay	Positive	Primary infection or reactivation	
IgG Immunofluorescence Assay	Positive	Primary infection or reactivation	
PCR	Positive	Primary Infection or reactivation	
Blood Mononuclear Cells Culture	Positive	Infection	Has a sensitivity of 86% and a specificity of 100%
Anticomplement Immunofluorescence Assay (ACIF)	Positive	Infection	Subjective results, less accurate than EIA
Enzyme Immunoassay (EIA)	Positive	Infection	More objective results

NOTE: Nearly 100% of Americans are seropositive. PCR is commonly positive, indicating low-level replication (occurs in ~50% of stem cell transplant patients and ~25% of young healthy adults).

Abbreviations and Notes:

Abbreviation/Symbol	Definition
EBNA	Epstein-Barr nuclear antigen
ELISA	Enzyme-linked immunosorbent assay
HBsAg	Hepatitis B surface antigen
HBsAb	Hepatitis B surface antibody
HBcAb	Hepatitis B core antibody
HBeAg	Hepatitis e antigen; if present indicates high infectivity
HBeAb	Hepatitis e antibody; if present indicates low/no infectivity
IgD (EA)	Anti-D antibody; Early antigen antibody
IM	Infectious mononucleosis
NA	Not applicable
PCR	Polymerase chain reaction
VCA	Viral capsid antigen

ANTIMICROBIAL FORMULARY

NOTE: The most recent antimicrobial formulary can be found online at www.formchecker.com/FormChecker/servlet/FormSearch

Inpatient Formulary Agents

Aminoglycosides
- Amikacin IV/IH
- Gentamicin IV
- Neomycin PO
- Tobramycin IH/IV

Antifungals
- Amphotericin B Top/IV
- Liposomal Amphotericin B IV
- Clotrimazole PO/Top
- Fluconazole PO/IV
- Flucytosine PO
- Itraconazole PO
- Micafungin IV
- Nystatin PO/Top
- Voriconazole PO/IV
- *Posaconazole PO*

Antimalarials
- Chloroquine PO
- Hydroxychloroquine PO
- Primaquine PO
- Pyrimethamine PO
- Quinine PO

Antimycobacterial Agents
- Ethambutol PO
- Isoniazid PO
- Pyrazinamide PO
- Rifabutin PO
- Rifampin PO/IV

Antiprotozoals
- Atovaquone PO
- *Trimetrexate IV*

Antiretrovirals
- Abacavir PO
- Atazanavir PO
- Darunavir PO
- Efavirenz PO
- Emtricitabine PO
- Fosamprenavir PO
- Lamivudine PO
- Lopinavir-ritonavir PO
- Nevirapine PO
- Raltegravir PO
- Ritonavir PO
- Tenofovir PO
- Zidovudine PO/IV

Antivirals
- Acyclovir PO/IV
- Amantadine PO
- Famciclovir PO
- Foscarnet IV
- Ganciclovir PO/IV
- Oseltamivir PO
- Ribavirin IH
- Rimantadine PO
- Valacyclovir PO
- Valganciclovir PO
- Zanamivir IH

Carbapenems
- Meropenem IV
- Ertapenem IV

Cephalosporins
- Cefazolin IV
- Cefepime IV
- *Cefotaxime IV*
- Cefoxitin IV
- Ceftazidime IV
- Ceftriaxone IV
- Cefuroxime PO/IV
- Cephalexin PO

Fluoroquinolones
- Ciprofloxacin PO/IV
- Moxifloxacin PO/IV

Glycopeptides
- Vancomycin PO/IV

Lipopeptides
- *Daptomycin IV*

Macrolides
- Azithromycin PO/IV
- Clarithromycin PO
- Erythromycin PO/IV

Miscellaneous
- Aztreonam IV/IH
- Chloramphenicol IV
- Clindamycin PO/IV
- Colistimethate IV
- Dapsone PO
- Drotrecogin alfa IV
- *Fosfomycin PO*
- Sulfisoxazole PO
- Metronidazole PO/IV
- Nitrofurantoin PO
- Pentamidine IV
- Polymyxin B IV
- Quinupristin-dalfopristin IV
- Sulfadiazine PO
- Sulfamethoxazole-Trimethoprim PO/IV
- *Tigecycline IV*
- Trimethoprim PO

Oxazolidinones
- Linezolid PO/IV

Penicillins
- Amoxicillin PO
- Amoxicillin/clavulanate PO
- Ampicillin PO/IV
- Ampicillin/sulbactam IV
- Dicloxacillin PO
- Oxacillin IV
- Penicillin G IV
- Penicillin G procaine IM
- Penicillin G procaine and benzathine IM
- Penicillin VK PO
- Piperacillin IV
- Piperacillin/tazobactam IV

Tetracyclines
- Doxycycline PO
- Minocycline PO
- Tetracycline PO

Outpatient Formulary Agents

Aminoglycosides
- Amikacin IV
- Gentamicin IV
- Neomycin PO
- Paromomycin PO
- Streptomycin IM
- Tobramycin IH/IV

Antifungals
- Fluconazole PO
- Flucytosine PO
- Griseofulvin PO
- Itraconazole PO
- Ketoconazole PO
- Nystatin PO
- Posaconazole PO
- Terbinafine PO
- Voriconazole PO

Antihelmintics
- Albendazole PO
- Ivermectin PO

Mebendazole PO
Praziquantel PO
Thiabendazole PO

Antimalarials
Atovaquone-proguanil PO
Chloroquine PO
Hydroxychloroquine PO
Mefloquine PO
Primaquine PO
Pyrimethamine PO
Quinine PO

Antimycobacterial Agents
Ethambutol PO
Isoniazid PO
Isoniazid/rifampin PO
Isoniazid/rifampin/pyrazinamide PO
Pyrazinamide PO
Rifabutin PO
Rifampin PO

Antiprotozoals
Atovaquone PO

Antiretrovirals
Abacavir PO
Abacavir /Lamivudine PO
Abacavir/lamivudine/zidovudine PO
Atazanavir PO
Darunavir PO
Didanosine PO
Efavirenz PO
Efavirenz/Emtricitabine/Tenofovir PO
Enfuvirtide SubQ
Etravirine PO
Emtricitabine PO
Emtricitabine/tenofovir PO
Fosamprenavir PO
Indinavir PO
Lamivudine PO
Lamivudine/zidovudine PO
Lopinavir-ritonavir PO
Maraviroc PO
Nelfinavir PO
Nevirapine PO
Raltegravir PO
Ritonavir PO
Stavudine PO
Tenofovir PO
Tipranavir PO
Zidovudine PO/IV

Antivirals
Acyclovir PO/IV
Adefovir PO
Amantadine PO
Cidofovir IV
Entecavir PO
Famciclovir PO
Foscarnet IV
Ganciclovir PO/IV
Interferon alfacon-1 SubQ
Lamivudine HBV PO
Oseltamivir PO
Palivizumab (Murine) IM
Peginterferon alfa-2a SQ
Peginterferon alfa-2b SQ
Ribavirin PO
Ribavirin-IFN alfa-2B
Rimantadine PO
Telbivudine PO
Valacyclovir PO
Valganciclovir PO
Zanamivir IH

Cephalosporins
Cefaclor PO
Cefadroxil PO
Cefazolin IV
Cefdinir PO
Cefixime PO
Cefpodoxime PO
Cefprozil PO
Ceftazidime IV
Ceftibuten PO
Ceftriaxone IV
Cefuroxime PO/IV
Cephalexin PO
Loracarbef PO

Carbapenems
Meropenem IV
Ertapenem IV

Fluoroquinolones
Ciprofloxacin PO/IV
Levofloxacin PO/IV
Moxifloxacin PO
Norfloxacin PO
Ofloxacin PO

Glycopeptides
Vancomycin PO/IV

Macrolides
Azithromycin PO/IV
Clarithromycin PO
Erythromycin PO/IV
Telithromycin PO (ketolide)*

Miscellaneous
Aztreonam IV/IH
Clindamycin PO/IV
Clofazimine PO*
Colistimethate IV
Dapsone PO
Erythromycin-Sulfisoxazole PO
Fosfomycin PO
Furazolidone PO
Lincomycin PO/IV/IM
Methenamine PO
Metronidazole PO/IV
Nitrofurantoin PO
Pentamidine IH
Sulfadiazine PO
Sulfamethoxazole-Trimethoprim PO/IV
Tigecycline IV
Trimethoprim PO

Oxazolidinones
Linezolid PO/IV

Penicillins
Amoxicillin PO
Amoxicillin/clavulanate PO
Ampicillin PO/IV
Dicloxacillin PO
Oxacillin IV
Penicillin G procaine IM
Penicillin G benzathine IM
Penicillin G procaine & benzathine IM
Penicillin VK PO

Tetracyclines
Demeclocycline PO
Doxycycline PO
Minocycline PO
Oxytetracycline PO
Tetracycline PO

ITALICS = restricted agent
***= compassionate use**

Note: inclusion of an agent within this guideline does not necessarily indicate TNMC formulary status

ANTIMICROBIAL COSTS (Updated April 2010)

Drug Name	Route	DDD* (g)	# of times/day	Acquisition Price	Labor Cost	Inpatient Cost/Day**	AWP pricing	Outpatient Cost/Day***
Amikacin	IV	1	3	$6.70	$10.50	$17.20	$9.03	N/A
Amphotericin B	IV	0.035	1	$6.81	$3.50	$10.31	$17.15	N/A
AmphoB (liposomal)	IV	0.35	1	$367.50	$3.50	$371	$1372	N/A
Amoxicillin	PO	1	2	$0.17	$2.50	$2.67	$0.74	$1.47
Ampicillin	IV	2	4	$6.17	$14	$20.17	$16.75	N/A
Ampicillin/Sulbactam[#]	IV	8	4	$22.03	$14	$36.03	$37.41	N/A
Anidulafungin	IV	0.1	NF	NF	NF	NF	$225	N/A
Augmentin (500mg)	PO	1	2	$1.36	$2.50	$3.86	$7.57	$6.10
Azithromycin	IV	0.5	1	$7.27	$3.50	$10.77	$20.63	N/A
Azithromycin	PO	0.3	1	$3.59	$1.25	$4.84	$9.33	$6.11
Aztreonam	IV	4	3	$111.99	$10.50	$122.49	$153.24	N/A
Capreomycin	IV	1	NF	NF	NF	NF	$25.54	N/A
Caspofungin	IV	0.05	NF	NF	NF	NF	$412.01	N/A
Cefaclor	PO	1	NF	NF	NF	NF	$7.79	$8.75
Cefazolin	IV	3	3	$2.39	$10.50	$12.89	$7.20	N/A
Cefdinir	PO	0.6	NF	NF	NF	NF	$10.23	$1.75
Cefepime	IV	2	2	$11.57	$7	$18.57	$40.36	N/A
Cefotaxime	IV	4	3	$9.80	$10.50	$20.30	$18.48	N/A
Cefotetan	IV	4	NF	NF	NF	NF	$56.90	N/A
Cefoxitin	IV	6	4	$23.05	$14	$37.05	$67.50	N/A
Ceftazidime	IV	4	2	$20.09	$7	$27.09	$52.20	N/A
Ceftizoxime	IV	4	NF	NF	NF	NF	$47.48	N/A
Ceftriaxone	IV	2	1	$8.19	$3.50	$11.69	$12.00	N/A
Cefuroxime	IV	3	2	$5.50	$7	$12.50	$27.05	N/A
Cefuroxime	PO	0.5	2	$2.92	$2.50	$5.42	$8.02	$3.49
Cephalexin	PO	2	2	$0.23	$2.50	$2.73	$4.90	$2.06
Chloramphenicol	IV	3	4	$42.89	$14	$56.89	$89.63	N/A
Ciprofloxacin[#]	IV	0.8	2	$4.18	$7	$11.18	$11.25	N/A
Ciprofloxacin	PO	1	2	$0.12	$2.50	$2.62	$10.37	$1.01
Clarithromycin	PO	0.5	2	$0.31	$2.50	$2.81	$4.52	$6.38
Clindamycin	IV	1.8	3	$3.31	$10.50	$13.81	$12.26	N/A
Clindamycin	PO	1.2	3	$1.89	$3.75	$5.64	$14.87	$2.65
Colistimethate (colistin)[Ŧ]	IV	0.15	2	11.55	$7.00	$18.55	$57.00	$11.44
Daptomycin	IV	0.28	1	$103.98	$3.50	$107.48	$126.85	N/A
Dicloxacillin	PO	2	4	$1.40	$5	$6.40	$4.80	$4.99
Doripenem	IV	1.5	NF	NF	NF	NF	$140.29	N/A
Doxycycline	IV	0.1	1	$3.55	$3.50	$7.05	$14.75	N/A
Doxycycline	PO	0.1	1	$0.08	$1.25	$1.33	$1.16	$0.99
Ertapenem	IV	1	1	$54.86	$3.50	58.37	$62.76	$36.23
Erythromycin	IV	1	2	$14.06	$7	$21.06	$24.01	N/A
Erythromycin (Not EES)	PO	1	2	$0.52	$2.50	$3.02	$0.89	$0.95
Ethambutol	PO	1.2	1	$2.48	$1.25	$3.73	$5.36	$6.32
Fluconazole	IV	0.2	1	$5.71	$3.50	$9.21	$14.60	N/A
Fluconazole	PO	0.2	1	$0.19	$1.25	$1.44	$13.61	$4.82
Gentamicin	IV	0.24	3	$2.38	$10.50	$12.88	$4.86	N/A
Griseofulvin	PO	0.5	NF	NF	NF	NF	$6.58	$6.20

Imipenem	IV	2	NF	NF	NF	NF	$159.34	N/A
Isoniazid	PO	0.3	1	$0.11	$1.25	$1.36	$0.21	$0.85
Itraconazole (caps)	PO	0.2	2	$14.27	$2.50	$16.77	$23.29	$6.63
Ketoconazole	PO	0.2	NF	NF	NF	NF	$0.79	$2.21
Levofloxacin	IV	0.5	NF	NF	NF	NF	$43.82	N/A
Levofloxacin	PO	0.5	NF	NF	NF	NF	$13.06	$13.15
Linezolid	IV	1.2	2	$163.48	$7	$170.48	$222.70	N/A
Linezolid	PO	1.2	2	$127.57	$2.50	$130.07	$173.80	$165.54
Meropenem	IV	2	4	$60.20	$14	$74.20	$149.86	N/A
Metronidazole	IV	1.5	3	$4.61	$10.50	$15.11	$7.83	N/A
Metronidazole	PO	2	3	$0.19	$3.75	$3.94	$2.77	$0.85
Micafungin	IV	0.1	1	$98.22	$3.50	$101.72	$228.14	N/A
Minocycline	PO	0.2	2	$0.55	$2.50	$3.05	$6.66	$0.85
Moxifloxacin	IV	0.4	1	$11.67	$3.50	$15.17	$42.70	N/A
Moxifloxacin	PO	0.4	1	$2.53	$1.25	$3.78	$13.05	$10.45
Nitrofurantoin	PO	0.2	4	$1.18	$5	$6.18	$3.73	$5.65
Oxacillin	IV	2	4	$13.55	$14	$27.55	$21.99	N/A
Penicillin G	IV	3.6	4	$3.29	$14	$17.29	$48.08	N/A
Penicillin VK	PO	2	4	$0.48	$5	$5.48	$1.88	$2.48
Piperacillin/Tazobactam	IV	14	4	$70.79	$14	$84.79	$88.76	N/A
Piperacillin	IV	14	4	$45.21	$14	$59.21	$58.46	N/A
Posaconazole	PO	0.8	4	$96.38	$5	$101.38	$120.91	$124.18
Pyrazinamide	PO	1.5	1	$1.69	$1.25	$2.94	$3.62	$4.36
Quinupristin/Dalfopristin	IV	1.5	3	$394.39	$10.50	$404.89	$499.70	N/A
Rifabutin	PO	0.15	1	$8.62	$1.25	$9.87	$11.08	$12.04
Rifampin	IV	0.6	2	$44.15	$7	$51.15	$141.52	N/A
Rifampin	PO	0.6	1	$2.12	$1.25	$3.37	$5.15	$4.91
Streptomycin	PO	1	NF	NF	NF	NF	$14.65	$7.86
Sulfisoxazole	PO	4	NF	NF	NF	NF	$4.35	$5.10
Tetracycline	PO	1	4	$0.08	$5	$5.08	$0.24	$0.98
Tigecycline	IV	0.1	2	$105.14	$7	$112.14	$135.12	N/A
Ticarcillin/clavulanate	IV	15	NF	NF	NF	NF	$78.29	N/A
Tobramycin	IV	0.24	3	$3.51	$10.50	$14.01	$12.71	N/A
Trimethoprim	PO	0.4	2	$0.92	$2.50	$3.42	$2.74	$3.70
Trimethoprim-Sulfa	IV	0.32	3	$5.88	$10.50	$16.38	$1.09	N/A
Trimethoprim-Sulfa	PO	0.32	2	$0.41	$2.50	$2.91	$1.71	$1.10
Vancomycin	IV	2	2	$10.27	$7	$17.27	$32.50	N/A
Vancomycin	PO	2	NF	NF	NF	NF	$285.25	$66.22
Voriconazole	IV	0.4	2	$197.18	$7	$204.18	$268.60	N/A
Voriconazole	PO	0.4	2	$67	$2.50	$69.50	$91.27	$68.88

*DDD=defined daily dose according to the WHO (http://www.whocc.no/atcddd/); ** Cost to the institution (based on acquisition cost plus labor); *** TNMC Outpatient Pharmacy price for a cash-paying customer; # Modified DDD based on commonly prescribed dose; ₸ No DDD provided by the WHO, based on commonly prescribed dose; NF = Non-formulary

ANTIMICROBIAL CONCEPTS AND TIPS

Pharmacodynamics and Therapeutic Drug Monitoring

Pharmacokinetics versus pharmacodynamics

Pharmacokinetics mathematically describe the relationship of antibiotic concentration to time. Terminology that is typically associated with pharmacokinetics includes: absorption, distribution, metabolism, elimination, half-life, volume of distribution, and area under the concentration-time curve (AUC).

Pharmacodynamics describe the relationship of antibiotic concentration to pharmacologic effect or microorganism death. The three main pharmacodynamic parameters that are used are the peak to minimal inhibitory concentration ratio (peak/MIC), the AUC to MIC ratio (AUC/MIC), and the time the drug concentration remains above the MIC (T>MIC).

Concentration independent versus concentration dependent

Concentration independent (time dependent) means that the rate and extent of microorganism killing remain unchanged regardless of antimicrobial concentration. The pharmacodynamic parameter that is most often predictive of outcome for concentration independent drugs is T>MIC, although the AUC/MIC can be used because the AUC takes both the antimicrobial concentration and time into account. Examples of concentration independent antimicrobials include: beta-lactams, vancomycin, macrolides, aztreonam, carbapenems, clindamycin, tetracyclines, quinupristin/dalfopristin, flucytosine, and azole antifungals.

Concentration dependent (time independent) means that the rate and extent of microorganism killing are a function of the antimicrobial concentration (increase as the concentration increases). The pharmacodynamic parameter that is most often predictive of outcome for concentration dependent drugs is peak/MIC, although the AUC/MIC can be used because the AUC takes both the antimicrobial concentration and time into account. Examples of concentration dependent antimicrobials include: fluoroquinolones, aminoglycosides, and amphotericin B.

Bacteriostatic activity versus bactericidal activity

Bacteriostatic activity refers to the inhibition of bacterial growth, while bactericidal activity refers to killing the bacteria.

Minimum inhibitory concentration (MIC) – The MIC is defined as the lowest concentration of antibiotic that completely inhibits growth of the specific organism being tested.

Minimum bactericidal concentration (MBC) – The MBC is defined as the lowest concentration of antibiotic at which bacteria are killed.

Most of the available evidence supports the use of a bactericidal agent when treating endocarditis, meningitis or osteomyelitis. However, data do not exist to support this practice for other infectious diseases.

Pharmacodynamic properties do not remain constant for all antimicrobials in a class for all microorganisms. In other words, if a drug is concentration dependent and bactericidal against one organism, that does not mean that it, or all the other drugs in its class, are concentration dependent and bactericidal against all organisms. However, because of a lack of data characterizing the pharmacodynamic properties of various antimicrobials against several different organisms, we usually lump antimicrobials into one category.

Vancomycin Dosing

Vancomycin is considered to be a concentration independent or time dependent killer of bacteria. Therefore, increasing antibiotic concentrations beyond the therapeutic threshold will not result in faster killing or eliminate a larger portion of the bacterial population. Vancomycin dosing should be based upon actual body weight (ABW), is generally used at doses of 10-15 mg/kg, and dosing intervals should be renally adjusted per the chart below.

Estimated CrCl (mL/min)	Initial Dosing Interval
> 50 mL/min	Q12H
40-49 mL/min	Q24H
10-39 mL/min	Q48H
< 10 mL/min	Q48-96H;As needed based on trough

Vancomycin indications – Vancomycin is **NOT** recommended for:

- Routine surgical prophylaxis
- Treatment of a single positive blood culture for coagulase-negative staphylococci
- Empiric therapy of a febrile neutropenic patient where no evidence of gram-positive infection exists
- Continued empiric therapy if microbiologic testing does not confirm an infection due to a beta-lactam-resistant gram positive organism
- Selective gut decontamination
- MRSA colonization
- Primary therapy for mild or moderate *Clostridium difficile* infections
- Topical application or irrigation
- Treatment of MSSA or other susceptible gram-positive infections in dialysis patients
- Prophylaxis in CAPD patients
- Prophylaxis in low birth weight infants
- Systemic or local prophylaxis for indwelling central or local catheters

Vancomycin levels ARE recommended in the following settings:

- Serious or life-threatening infections. TROUGH ONLY.
- Patients receiving vancomycin/aminoglycoside or vancomycin/amphotericin B combination therapy. TROUGH ONLY.
- Anephric patients undergoing hemodialysis and receiving infrequent doses of vancomycin for serious systemic infections. RANDOM TROUGH 4 hours after dialysis.
- Patients receiving higher than usual doses of vancomycin (adults: > 20 mg/kg/dose, pediatrics: > 60 mg/kg/day). INITIAL PEAK & TROUGH. Once therapeutic, do not repeat levels if fluid status and renal function are stable.
- Patients with rapidly changing renal function (50% increase/decrease or 0.5 mg/dl increase/decrease in SCr over 24-48 hours). RANDOM TROUGH only.
- Morbidly obese patients. TROUGH ONLY.
- Reaffirm a seriously abnormal or unusual serum concentration (i.e., line draws, inappropriate times, etc.). TROUGH ONLY.
- Neonates: a) determine a therapeutic level has been achieved after culture results have been reported and b) monitor serum levels with prolonged therapy >10 days. INITIAL: PEAK AND TROUGH; TROUGH ONLY after therapeutic levels achieved for prolonged administration with stable renal function.
- Patients receiving prolonged (>14 days) vancomycin therapy. TROUGH ONLY.

Monitoring is NOT recommended in the following settings:

- Patients treated for less than five days.
- Patients receiving oral vancomycin.
- Patients with stable renal function who are treated for up to 14 days for mild to moderate infections.

Drug level recommendations

Drug		Time to Obtain	Therapeutic Range	Hospital Cost
Vancomycin *levels not routinely recommended *	Trough	½ hour before infusion	10-20 mcg/mL	$9.71
	Peak	1 hour after infusion	25-40 mcg/mL	$9.71

Aminoglycoside Dosing

Aminoglycosides are concentration dependent antibiotics, meaning that as aminoglycoside concentration increases, the rate and extent of bacterial killing increases.

Once Daily Dosing – The theories behind once daily dosing (ODA) include:

a. Aminoglycosides have concentration dependent activity. The rate of bacterial killing increases as drug concentration is increased. Investigators suggest optimizing the aminoglycoside peak/MIC ratio to a value ≥ 10:1 to maximize bacterial killing.
b. The combination of a high peak and an "aminoglycoside-free" interval will help to reduce the selection and the emergence of resistant organisms (by eliminating the adaptive resistance phenomena), and minimize aminoglycoside-associated toxicity, which has been associated with elevated trough concentrations.
c. A high peak concentration of aminoglycosides leads to a longer duration of post-antibiotic effect (PAE).
d. **Exclusion criteria -** pregnancy, breastfeeding, burns (>20%), ascites, cystic fibrosis, cirrhosis, dialysis, solid organ transplants, neutropenia, endocarditis, and CrCl < 20 mL/min. PLEASE NOTE: Once daily dosing should be considered in all patients for which an aminoglycoside is ordered for a suspected or documented Gram-negative rod infection, except for those that meet the exclusion criteria.

ODA Dosing Guidelines

- Use Actual body weight (ABW)
- If patient is obese (>20% over ideal body weight - IBW) use dosing body weight (DBW)

  DBW = IBW + [0.4 (ABW - IBW)]
- Tobramycin/ gentamicin - dose at 4 to 7 mg/kg
- Amikacin – dose at 15 mg/kg

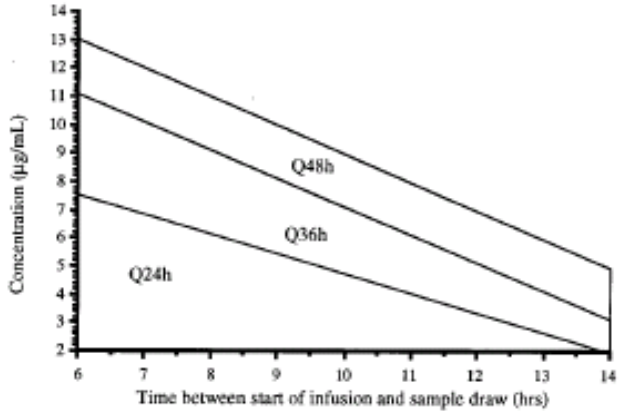
Estimated CrCl (mL/min)	Initial Dosing Interval
> 60 mL/min	Q24H
40-59 mL/min	Q36H
20-39 mL/min	Q48H
< 20 mL/min	Not recommended

ODA Therapeutic Monitoring and Dose Adjustment

Levels should be obtained only in the following situations:

- Random serum level 10-12 hours **AFTER THE START** of the infusion of the first dose to confirm appropriate serum level.
- Confirm an appropriate serum concentration after dosage adjustment.
- Suspected toxicity (oto- or nephro-) or when there is a change in or impaired renal function while on maintenance therapy.
- Reaffirm a seriously abnormal or unusual serum concentration (i.e., potential line draws, inappropriate times, etc.)
- Weekly monitoring of prolonged therapy with aminoglycosides
- Dosage adjustments should be made according to the Hartford Nomogram (see below).
- **Important Notes:**
  - Because the Hartford Nomogram was based on a dose of 7mg/kg, if a lower dose is being used, the resultant level should be multiplied by a factor equal to 7 mg divided by the dose used. Example: If a patient is receiving 5mg/kg/day and the 10h post-dose level was 2 mcg/mL, you would multiply the level by 1.4 (7/5) to give a level of 2.8 mcg/mL. This adjusted level is the one you would plot on the Hartford nomogram.
  - If using amikacin, plot ½ of the serum concentration on the nomogram.
- If the level falls on the line, choose the longer interval for administration.
- If the aminoglycoside level falls off the nomogram, traditional dosing should be used.

Hartford Nomogram



Aminoglycoside levels should be obtained according to the following guidelines (not for extended interval/once daily dosing):

a. Patient not responding to therapy as expected.
b. Suspected toxicity (oto- or nephro-) or patient has a change in or impaired renal function while on maintenance therapy.
c. Reaffirm a seriously abnormal or unusual serum concentration (i.e., potential line draws, inappropriate times, etc.)
d. To determine that a therapeutic level has been achieved after culture results have been reported and the decision to continue the aminoglycoside has been made.
e. Initial dosage check for prophylactic or empiric therapy in neutropenic patients or suspected *Pseudomonas* infections (i.e., cystic fibrosis or ventilator-dependent patients).
f. Weekly monitoring of prolonged therapy with aminoglycosides.

Desired Levels for Various Infections

Cost to the institution for an aminoglycoside level
gentamicin → $10.43
tobramycin → $13.75
amikacin → $15.78

Medical Condition	Desired Peak	Desired Trough
Gentamicin/ Tobramycin		
Synergy (Gram-positives)	3-5	<1
UTI, endometriosis, pyelonephritis	4-6	<1
Tissue Infections, pneumonia, sepsis*	6-8	<2
Cystic Fibrosis	10-12	<1
Amikacin		
Moderate Infections	15-25	<5
Severe Infections	25-40	<10

*For more severe infections, such as pneumonia or sepsis, we usually recommend pushing the peak more towards 8 mcg/mL due to penetration issues and better outcomes shown with higher peaks.

Double coverage

Gram-negative Bacteria

The use of double coverage (two antibiotics used to provide coverage for the same organism) is based upon the following assumptions: the combination provides a broad spectrum of coverage for empiric treatment, before you know the identification and susceptibility of the offending pathogen; the

combination may provide additive or synergistic effects against the pathogen; the combination of antibiotics may decrease or prevent the emergence of resistant bacteria.

Inappropriate initial therapy has been shown to cause increased morbidity and mortality, specifically related to Gram-negative infections (usually *Pseudomonas* and *Acinetobacter* spp.). Thus, double coverage serves the purpose of providing broad spectrum initial empiric coverage. No evidence exists to support the superiority of combination therapy over monotherapy. Thus, once culture identification and susceptibilities have been reported, de-escalation to a single agent is recommended.

Many studies have evaluated various antibiotic combinations, most frequently a β-lactam and an aminoglycoside, for the treatment of Gram-negative infections. The majority of these studies have found no differences between various regimens in terms of clinical and microbiologic outcome as well as mortality rates. These findings were confirmed in at least two meta-analyses.

Anaerobes

Anaerobic pathogens are normal flora of the oral cavity and the gastrointestinal tract. While oral anaerobic flora are mostly gram-positive organisms such as *Peptococcus* and *Peptostreptococcus spp.,* the principal anaerobic intestinal flora are gram-negative bacilli such as *Bacteroides fragilis*, *Prevotella melaninogenica*, and *Fusobacterium spp.* Gram-positive oral anaerobes are widely covered by most of the orally-available agents, including penicillin. However, antibiotic activity against the most common intestinal anaerobic bacteria, *Bacteroides spp.*, is variable.

Anaerobic coverage is indicated in a variety of infectious processes, including but not limited to aspiration pneumonia, intra-abdominal infection, gynecologic infection, and diabetic foot ulcer infection. Antimicrobial agents with appreciable anaerobic activity include the following:

- Amoxicillin/clavulanate
- Ampicillin/sulbactam
- Cefotetan
- Cefoxitin
- Clindamycin
- Doripenem
- Ertapenem
- Imipenem
- Meropenem
- Metronidazole
- Moxifloxacin
- Piperacillin/tazobactam
- Ticarcillin/clavulanate
- Tigecycline

Double anaerobic coverage is the use of any combination of the above agents, which is prevalent at The Nebraska Medical Center. Redundant anaerobic coverage is the third most common problem intervened upon by the Antimicrobial Stewardship Program, accounting for approximately 20% of the interventions.

Available susceptibility and clinical data do not support this practice. The following susceptibility data from 2005-2007 were observed for the *B. fragilis* group, the most common pathogenic gram-negative anaerobes:

RESISTANCE RATES OF VARIOUS ANTIBIOTIC AGENTS AMONG *B. FRAGILIS* GROUP ISOLATES

Antibiotic Agent (No. of Isolates Tested)	Resistance breakpoint (mg/L)	% Resistant[a]
Metronidazole (6574)	≥32	<0.1
Piperacillin-tazobactam (1351)	≥128	0.3
Ampicillin-sulbactam (1351)	≥32	5.5
Cefoxitin (1351)	≥64	9.1
Meropenem (1351)	≥16	0.4
Ertapenem (1351)	≥16	0.9
Clindamycin (1351)	≥8	36
Moxifloxacin (1351)	≥8	40.7
Tigecycline (1351)	≥16	4.3

[a]Isolates categorized according to CLSI breakpoints. Adapted and modified from Snydman DR, Jacobus NV, McDermott LA, et al. Lessons learned from the anaerobe survey: historical perspective and review of the most recent data (2005-2007). *Clin Infect Dis*. 2010;50 Suppl 1:S26-33.

With regard to gram-positive anaerobes, all the agents listed above maintain excellent activity. For example, moxifloxacin was shown to have excellent activity against gram-positive anaerobic cocci such as *Peptostreptococcus* spp with MICs as low as 0.25mg/L (range 0.25-1mg/L).

Double anaerobic coverage is not necessary and puts the patients at risk for additional drug toxicities. No data or guidelines support double anaerobic coverage in clinical practice, with two clinical exceptions (see below).

Exceptions:

1. Metronidazole can be added to another agent with anaerobic activity when being used to treat *Clostridium difficile* infection.
2. Clindamycin can be added to another agent with anaerobic activity when being used for the treatment of necrotizing fasciitis.

ANTIMICROBIAL RESTRICTION AND UTILIZATION GUIDELINES

Certain antimicrobials are restricted and TNMC and these restrictions are noted below. Criteira for appropriate use a number of agents have been developed. These guidelines have been drafted to provide criteria for which use of specific antimicrobials is considered appropriate. These guidelines should not replace clinical judgment in patient-specific situations but should serve to help clinicians make appropriate antimicrobial choices.

Antimicrobial Restictions:

Restricted anti-infective approval process:

1. All orders for restricted anti-infectives must be reviewed and approved by an infectious diseases (ID) service (or other service as outlined below). The ordering physician is responsible for contacting an approving service.
2. If an order is received by pharmacy and it is not clear that use criteria are met or approval has been gained, the pharmacist will enter the order to remain active for 24 hours (exception, CMV-IG see table) and contact the ordering team to request they obtain approval. Because the order will be stopped in 24 hours, the review and approval must be initiated within 24 hours of the original order.
3. If use is approved, ID will relay this information to the ordering physician as well as to the pharmacy. If the restricted anti-infective is thought to be inappropriate, ID will provide alternative recommendations and communicate these recommendations to the physician originating the order.
4. ID may decide that a formal consultation is necessary for approval. In this instance, a formal ID consultation will be required for use of the restricted agent.

Drug	**Approving services**	**Indications not requiring approval**	**Note**
Colistin (IV and inhaled)	ID, Pulmonary	Approval required for all indications	Requires formal consultation by ID or pulmonary service
CMV-IG (Cytogam)	Transplant ID	P&T-approved order sets containing the agent (visceral transplant)	First dose is not dispensed without approval
Daptomycin (Cubicin)	ID	FDA-approved indications (skin/skin structure infections, *S. aureus* bacteremia)	
Fosfomycin (Monurol)	No approval required for simple cystitis	Simple cystitis treatment	Documented susceptibility required if using more than one dose
Posaconazole (Noxafil)	ID, Heme/Onc	Approval required for all indications	
Tigecycyline (Tygacil)	ID	Approval required for all indications	

Cefepime

Criteria for Use:

1. Serious infections due to Gram-negative organisms susceptible to cefepime but resistant to other, more narrow-spectrum agents.
2. Empiric therapy in serious infections in which Gram-negative or mixed aerobic organisms, including *Pseudomonas aeruginosa*, are suspected.
3. Culture documented *Pseudomonas aeruginosa* infection that is susceptible to cefepime.
4. Empiric treatment in febrile neutropenia, usually in combination with another agent.

5. Part of initial, empiric therapy for serious respiratory tract infections in which multidrug-resistant organsisms, such as *P. aeruginosa*, are suspected. Note: Empiric therapy should be streamlined to definitive, targeted therapy as soon as cultures and susceptibilities are reported.

Colistin (IV/IH)
Criteria for Use:
1. Infections due to gram-neative pathogens which are resistant to other agents
2. Use of colistin requires either ID or Pulmonary service consultation for approval.

Daptomycin
Criteria for Use:
1. Requires approval from Infectious Diseases for any indication other than those listed below.
2. Complicated skin and skin structure infection due to multidrug-resistant Gram-positive organisms. Daptomycin is generally considered for use in patients failing or intolerant to therapy with vancomycin. *Dose = 4 mg/kg*
3. Bacteremia and/or endocarditis due to multidrug-resistant Gram-positive organisms in a patient failing/intolerant of therapy with vancomycin. *Dose = 6 mg/kg*

Note: Daptomycin has been associated with elevations in CK. Baseline and weekly monitoring is recommended. Concomitant statin therapy should be discontinued while patient is receiving daptomycin.

Ertapenem:
1. Culture-proven infection due to bacteria resistant to other broad-spectrum antibiotics, such as cefepime, but susceptible to ertapenem (except *Pseudomonas* and *Acinetobacter*).
2. Culture-documented serious infection with *Enterobacter, Morganella,* or *Citrobacter* species. Administration of a third-generation cephalosporin is not recommended for these organisms due to an inducible beta-lactamase.
3. Serious infection suspected of being polymicrobial and/or involving anaerobic bacteria in patients intolerant of piperacillin/tazobactam or ampicillin/sulbactam (or with resistance to these agents).
4. Complicated intra-abdominal infections where other beta-lactam agents are not appropriate due to intolerance or resistance.

Note: Although ertapenem has been approved for surgical prophylaxis, at TNMC it is not recommended for routine surgical prophylaxis because its spectrum of activity includes organisms infrequently associated with elective surgery.

Fosfomycin:
Criteria for Use:
1. Single dose fosfomcyin for simple cystitis in uncomplicated UTIs can be used without restriction
2. Use for any other indication or duration requires documented sensitivity to the agent
    a. Bacterial isolates are not routinely tested for susceptibility to fosfomycin but susceptibility testing is available by request in the microbiology laboratory (Please contact 552-2090 if this is desired)
    b. The agent will not be dispensed for use until susceptibility has been documented
3. An ID consult is strongly recommended for all uses outside of simple cystitis

Linezolid
Criteria for Use:
1. Infections due to MRSA. Linezolid is generally considered for use in patients failing or intolerant to therapy with vancomycin.
2. Infections due to VRE, including bacteremia.
3. Initial, empiric therapy for respiratory tract infections in patients in whom MRSA is suspected. Linezolid is generally considered for use in patients failing or intolerant to

therapy with vancomycin. Note: Empiric therapy should be streamlined to definitive, targeted therapy as soon as cultures and susceptibilities are reported.

Note: Linezolid has been associated with thrombocytopenia and anemia, particularly when therapy is continued beyond two weeks. Weekly monitoring of CBC is recommended while receiving linezolid.

Meropenem

Criteria for Use:

1. Culture-proven infection due to bacteria resistant to other broad-spectrum antibiotics, such as cefepime, but susceptible to meropenem.
2. Culture-documented serious infection with *Enterobacter, Morganella, Acinetobacter,* or *Citrobacter* species. Administration of a third-generation cephalosporin is not recommended for these organisms due to an inducible beta-lactamase.
3. Serious infection suspected of being polymicrobial and/or involving anaerobic bacteria in patients intolerant of piperacillin/tazobactam or ampicillin/sulbactam (or with resistance to these agents)
4. Complicated intra-abdominal infections where other beta-lactam agents are not appropriate due to intolerance or resistance.
5. Part of initial, empiric therapy for serious respiratory tract infections in which multidrug-resistant organsisms, such as *P. aeruginosa*, are suspected. Note: Empiric therapy should be streamlined to definitive, targeted therapy as soon as cultures and susceptibilities are reported.
6. Meropenem should be used at the higher dose of 2g IV q8hr in patients with CNS infections, infectious due to gram-negative pathogens with an MIC=4, and cystic fibrosis.

Micafungin

Criteria for Use:

1. Invasive aspergillosis in a patient failing/intolerant of therapy with amphotericin.
2. Candidal infections refractory to amphotericin and triazoles.
3. Invasive candidiasis (non-CNS) due to non-albicans species.
4. Empiric therapy in patients at risk for invasive candidiasis due to non-albicans species.

Note: Not recommended for infections of the urinary tract due to poor penetration. Patients with document susceptibility to fluconazole should be de-escalated to this agent (preferably orally) if possible.

Tigecycline

Criteria for Use:

1. Treatment of multi-drug resistant pathogens where other agents (beta-lactams, etc.) are either not active or contra-indicated due to severe allergy or resistance
2. Use of tigecycline has been associated with increased mortality in comparison with other agents and its use is restricted to ID approval

Vancomycin

Criteria for Use:

1. Treatment of serious infections due to beta-lactam resistant Gram-positive organisms.
2. Surgical prophylaxis in a patient allergic to beta-lactam antibiotics. **Therapy should not continue beyond 24 hours after the end of the surgical procedure.**
3. Treatment of infections due to Gram-positive organisms in the setting of beta-lactam allergy.

Voriconazole

Criteria for Use:

1. Treatment of proven or probable invasive aspergillosis.
2. Treatment of serious *Scedosporium apiospermum* and *Fusarium* spp. infections.
3. Treatment of invasive candida infections refractory to amphotericin B and other triazoles.
4. Prophylaxis of aspergillosis in patients meeting one of the following criteria: severe graft-versus-host disease and high-dose steroid treatment, remission induction therapy for

acute myelogenous leukemia, or history of aspergillus infection with indication to undergo additional immunosuppressive therapy.

Note: Not recommended for infections of the urinary tract due to poor penetration.

ANTIMICROBIAL CLINICAL PRACTICE GUIDELINES

Antibiotic and Ethanol Lock Therapy

NOTE: Please use Antibiotic or Ethanol Catheter Lock Order Form.

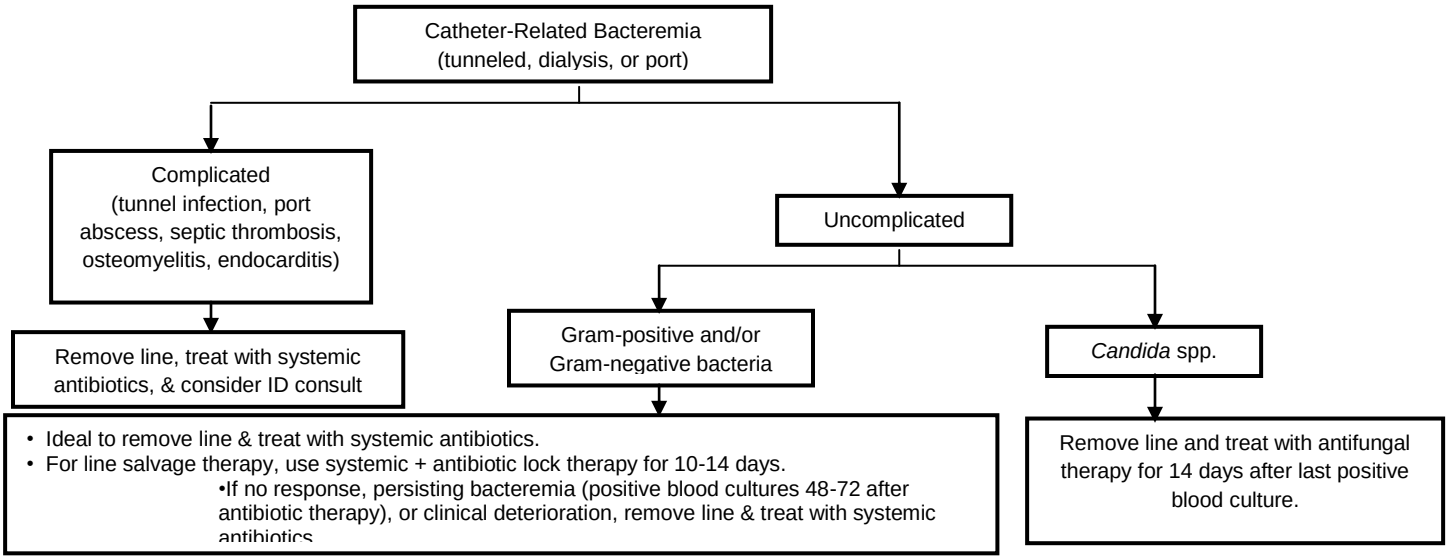
Diagnosis of an Intravascular Device-related Infection:

1. Growth of the same organism from at least one percutaneous blood culture and a catheter tip.

OR

2. Growth of the same organism from two blood cultures, one obtained peripherally and one obtained via the line PLUS differential time to positivity (positive line culture result is obtained at least 2 hours earlier than a positive peripheral blood culture result). NOTE: Other methods can be used for diagnosis; refer to the following article:
   Mermel LA, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49:1-45.

Algorithm:



Available Antibiotic Solutions (in normal saline; concentrations represent final concentrations)

Vancomycin 2.5 mg/ml plus or minus heparin 2500 units/ml (100 units/ml for pediatrics)
Gentamicin 2 mg/ml plus or minus heparin 2500 units/ml (100 units/ml for pediatrics)
Vancomycin 2.5 mg/ml + gentamicin 2 mg/ml plus or minus heparin 2500 units/ml (100 units/ml for pediatrics)

If you need to use an antibiotic not listed on this form or you are considering antibiotic lock therapy for prophylaxis rather than treatment, please consult the Infectious Disease service.

Antibiotic Lock Procedure

Dwell time for antibiotic lock solution should be for a period of at least 6 h at least twice per day (total of at least 12 h).

1. Withdraw contents of lumen (antibiotic lock solution) and discard.
2. Flush catheter with normal saline.
3. Administer ordered medication through line.
4. Flush catheter with normal saline.

5. Instill volume of antibiotic lock solution to fill lumen of catheter.
6. Be sure to aspirate antibiotic lock solution before using line to administer medications.

Ethanol Lock Technique for Prevention and Treatment of Central line-Associated Bloodstream Infections (CLA-BSIs)

Within 24 hours of intravascular catheter insertion, complex matrices, called biofilms, are formed, in which microorganisms are harbored (Figure 1). These microorganisms can detach from the biofilm and seed the bloodstream, causing central line-associated bloodstream infections (CLA-BSIs). Microorganisms within biofilms are more difficult to eradicate with systemic antibiotic therapy due to their sessile nature and biofilm interactions with host immunity. Thus, antibiotic lock therapy [instillation of a highly concentrated antimicrobial solution into the lumen of the catheter for a particular dwell time (refer to Antibiotic Catheter Lock Clinical Pathway at www.nebraskamed.com/asp)] has been advocated as a means to eradicate such organisms However, a primary concern for the use of antibiotic lock therapy is the potential increased risk of antimicrobial resistance due to the selective pressure caused by antimicrobial exposure.

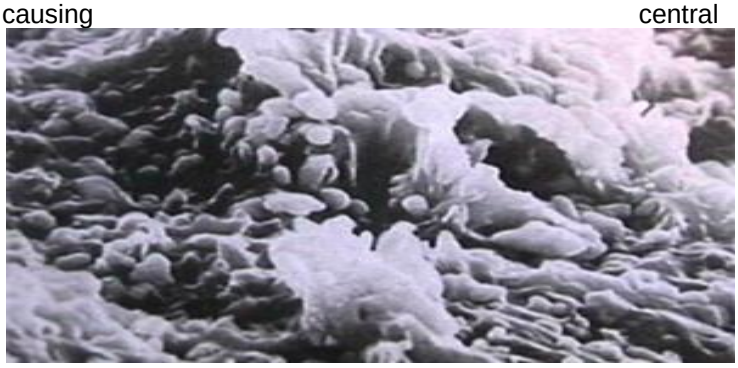


Figure 1. Biofilm on intravascular catheter (Source: www.ivteam.com)

Ethanol lock therapy (ELT) has been proposed as a potential mechanism to eradicate organisms in biofilms and hence, treat or prevent CLA-BSIs, but decrease the risk of antimicrobial resistance. Additional benefits associated with ELT include the facts that ethanol is readily available and inexpensive.

In vitro data suggest that the integrity of silicone or polyurethane catheters is not clinically significantly affected by exposure to a 70% ethanol solution, although the data are limited regarding different manufacturers and catheter polymers. Thus, before using ELT, the physician should confirm that ethanol is compatible with the catheter polymer (Table 1). Several human clinical studies have demonstrated the efficacy and safety of ELT in adult and pediatric patients for both treatment (in conjunction with systemic antibiotics) and prevention of CLA-BSIs. However, these studies are limited by small sample sizes and variability in ELT protocols. No data exist for patients < 3 months old or pregnant/breastfeeding women. Thus, the risk:benefit ratio should be carefully weighed in these situations of limited data and potential for increased risk.

While multiple studies using ELT report very mild or no adverse effects, these studies are limited by retrospective design and/or small sample size. Side effects reported included tiredness, headaches, dizziness, light-headedness, nausea, and tasting alcohol. Notably, three of the five studies used a protocol whereby the ethanol was flushed through the line rather than aspirated. In the studies where the ethanol was withdrawn from the catheter, the only adverse effect reported was the taste of alcohol (n=1). Theoretical ethanol-related toxicities, such as central nervous system depression, arrhythmias, local venous irritation, and flushing, have not been reported in any studies using ELT.

ELT may be considered for patients at The Nebraska Medical Center who meet the following criteria:
1. Require salvage of current intravascular catheter because of inability to place catheter elsewhere
OR
2. Need to prevent CLA-BSI in a patient with a history of recurrent CLA-BSIs and limited alternatives for intravascular access.

Before beginning ELT, please consult an Infectious Diseases service.

Lock Procedure
Use a 70% ethanol solution. Dwell time for ethanol lock solution should be for a period of at least 4 h daily. Port and lumen identity and volume of solution to be used (usually 1.5-3 mL) must be specified by the physician.
1. Withdraw contents of lumen (ethanol lock solution) and discard.
2. Flush catheter with normal saline.
3. Administer ordered medication through line.

4. Flush catheter with normal saline.
5. Instill volume of ethanol lock solution to fill lumen of catheter.
6. At the conclusion of the lock period, aspirate ethanol lock solution before using line to administer medications.

*****HEPARIN SHOULD NOT BE ADMINISTERED CONCOMITANTLY WITH ELT DUE TO FORMATION OF A PRECIPITATE*****

ELT should NOT be used for peripheral catheters or peripherally-inserted central catheters (PICCs) because of low risk of infection and lack of data, respectively. In pediatric patients and those with underlying liver dysfunction, appropriate consideration should be given to limiting systemic alcohol exposure (i.e., use the appropriate volume to fill the lumen without spillage into the systemic circulation) in order to minimize the potential risk of systemic or hepatic toxicity.

Lock Order

When ordering ELT, please write the following in the Orders section of the medical record:
"70% ethanol ___mL to be locked into _____ (port/CVC & lumen identity) for ___h daily for ___ days. Follow ethanol lock policy."

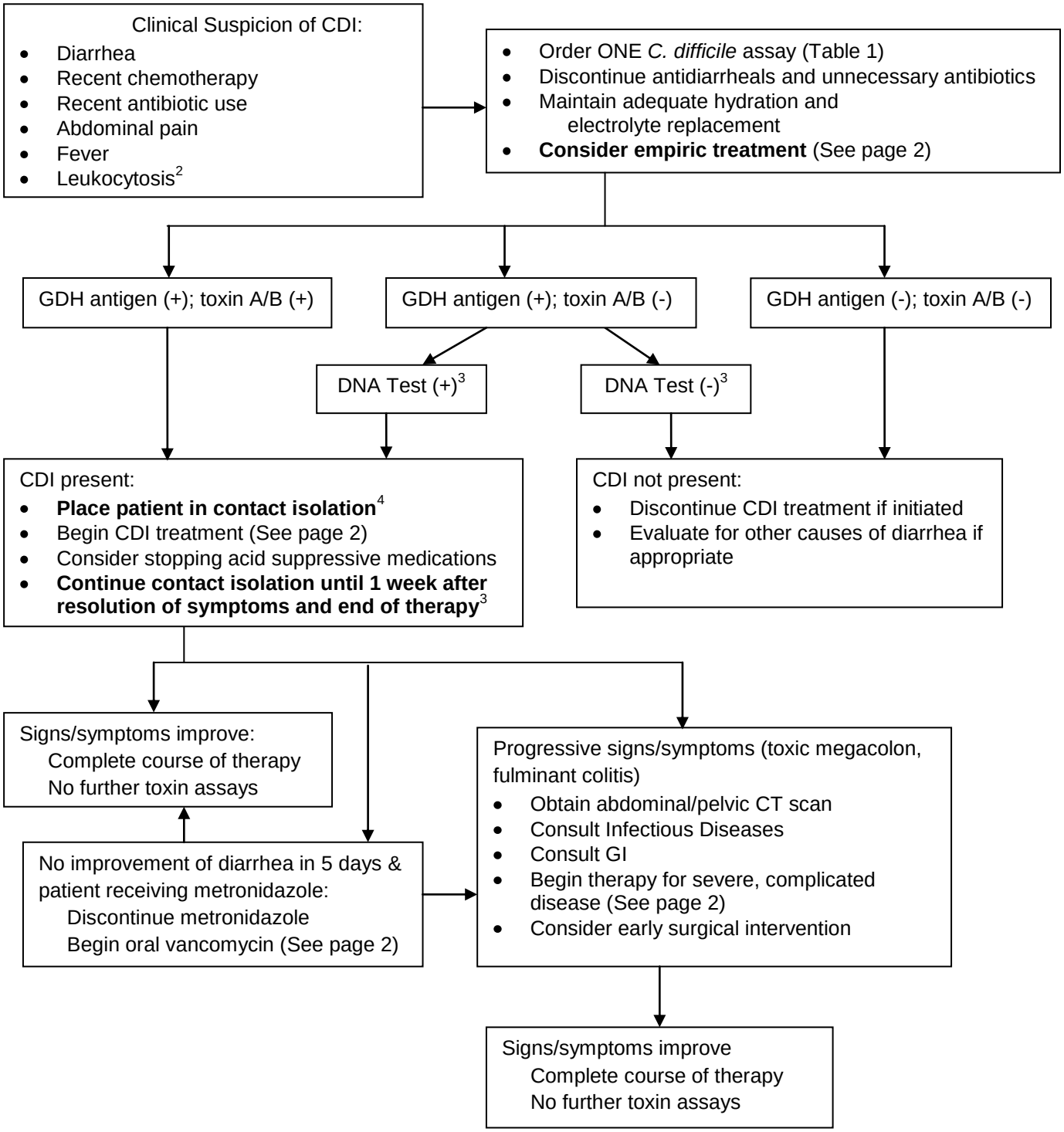
Table 1. Intravascular Catheters in Use at The Nebraska Medical Center and Compatibility with Ethanol
NOTE: If ethanol lock therapy is desired for a catheter that is not on this list, contact the manufacturer to ensure compatibility.

Catheter	Polymer	Compatible with ≥70% Ethanol?
AngioDynamics & Horizon Medical Products		
Dialysis Even More Flow catheter kit	Carbothane	No
DuraFlow dialysis kit	Carbothane	No
DuraFlow straight basic 24 cm hemodialysis kit	Carbothane	No
Port Smart CT 9.6 Fr outer diameter detached silicone catheter	Silicone	No
Triple lumen apheresis CV-332	Polyurethane	No
Arrow International		
9 Fr Central venous access kit two lumen used w/7.5-8 Fr	Polyurethane	No
Central venous catheter SGL 7 Fr 16cm PU SS-14701	Polyurethane	No
Double lumen 7 Fr CVP catheter	Polyurethane	No
Tray – Central venous 18g catheter single lumen over 20g intro scalpel 18g extra thin 4.8 Fr 80cm	Polyurethane	No
Triple lumen 7 Fr 20cm catheter AK-15703-CDC	Polyurethane	No
Triple lumen catheter kit 5.5 Fr 13cm	Polyurethane	No
Triple lumen catheter 7 Fr 30cm (LX)	Polyurethane	No
Triple lumen central venous catheter 7 Fr X 18g	Polyurethane	No
Triple lumen pedi catheter 5.5 Fr 8cm	Polyurethane	No
Bard		
Abramson triple lumen 15mm diameter 15in length drain sump, latex free w/filter	Polyurethane	No
Bard dual lumen port 9.5 Fr	Silicone	Yes
Broviac 6.6 Fr single lumen ingrowth cuff w/ peel stylet	Silicone	Yes
Broviac catheter single lumen 2.7 Fr single lumen ingrowth cuff	Silicone	Yes
Broviac catheter single lumen 4.2 Fr Ped	Silicone	Yes
Chronic femoral hemodialysis catheter 16 Fr 27cm	Polyurethane	No
Groshong catheter single lumen 8 Fr ingrowth/1 antimicrobial cuff	Silicone	Yes
Groshong port 7.0 Fr single lumen	Silicone	Yes
Hemosplit long term hemodialysis catheter 16 Fr 19cm	Polyurethane	No
Hemosplit long term hemodialysis catheter 16 Fr 23cm	Polyurethane	No
Hemosplit long term hemodialysis catheter 16 Fr 27cm	Polyurethane	No
Hickman catheter 9 Fr	Silicone	Yes
Hickman catether 9.6 Fr single lumen ingrowth/4 antimicrobial cuff	Silicone	Yes
Hickman 13.5 x 36 x 19 chronic hemodialysis double lumen	Silicone	Yes
Hickman catheter 13.5 x 40 x 23 hemodialysis dual lumen	Silicone	Yes
Hickman catheter 13.5 x 45 x 28 chronic dual hemodialysis straight antimicrobial cuff	Silicone	Yes
Hickman catheter 13.5 x 50 x 33 hemodialysis tray chronic dual straight antimicrobial cuff	Silicone	Yes

Hickman catheter dual lumen 7 Fr	Silicone	Yes
Hickman DL 12 Fr 0600620	Silicone	Yes
Hickman triple lumen 12 Fr peel apart introducer kit	Silicone	Yes
Infusi-Port implantable access port	Polyurethane	No
ISP MRI port with 6 Fr attachable Chronoflex catheter	Polyurethane	No
MRI infusion port 9.6 Fr ATT open ended peel apart introducer	Silicone	Yes
Port Power 8 Fr Chronoflex	Silicone/ polyurethane	No
Port Power MRI device w/ 8 Fr Chronoflex catheter	Polyurethane	No
Port Power MRI device w/ 8 Fr polyurethane catheter	Polyurethane	No
Single MRI infusion port 9.6 Fr pre-att open ended	Silicone	Yes
Slim Port dual catheter 7 Fr	Silicone	Yes
Vitacuff dialysis catheter 60cm	Silicone	Yes
Cook Group Incorporation		
Arterial femoral 3 Fr x 8cm single lumen pedi central line	Polyurethane	Yes
Double lumen central venous catheter 4 Fr	Polyurethane	No
Double lumen pedi 5 Fr catheter	Polyurethane	Yes
Peritoneal dialysis kit 8.5 Fr x 8cm	Polyurethane	Yes
Tray – single lumen central venous catheter 3 Fr 8cm	Silicone	Yes
Edwards Lifesciences		
Triple lumen CVC w/oximetry kit	Polyvinyl chloride	No
Kendall Company		
Femoral dialysis catheter 11.5 Fr	Carbothane	Unknown
Mahurkar 13cm triple lumen catheter	Carbothane/silicone	Unknown
Mahurkar 16cm triple lumen catheter	Carbothane/silicone	Unknown
Mahurkar 20cm triple lumen catheter	Carbothane/silicone	Unknown
Mahurkar 24cm triple lumen catheter	Carbothane/silicone	Unknown
Peritoneal dialysis catheter 62cm	Silicone	Unknown
Medcomp		
Hemodialysis catheter 8 Fr x 24cm	Silicone	Yes
Hemodialysis double lumen catheter set 12.5 Fr x 28cm	Silicone	Yes
Hemodialysis double lumen catheter set 12.5 Fr x 32cm	Silicone	Yes
Navilyst Medical		
Chest port 45-215	Polyurethane	Unknown
Port CT compatible 8 Fr 2.6mm OD 1.6mm ID 75cm length plastic power injectable	Polyurethane	Unknown
Vaxcel chest port 7 Fr	Polyurethane	Unknown
Vaxcel chest port 9 Fr	Polyurethane	Unknown
Vaxcel dialysis catheter 15 Fr x 23cm	Carbothane	Unknown
Vaxcel dialysis catheter 14 Fr x 19cm	Carbothane	Unknown
Vaxcel dialysis catheter 14 Fr x 28cm	Carbothane	Unknown
Sims Portex		
Portacath 8.4 Fr 76cm single lumen 21-4055	Polyurethane	No
Portacath II 6 Fr single lumen 21-4083-01 low profile	Polyurethane	No
Portacath II 8.5 Fr single lumen 21-4071 low profile	Polyurethane	No
Spire Biomedical		
Alta Gold tunneled catheter	Carbothane/ polyurethane	Unknown
Decathlon Gold dialysis catheter 28cm	Carbothane/ polyurethane	Unknown
Decathlon Gold dialysis catheter 32cm	Carbothane/ polyurethane	Unknown
Double lumen dialysis catheter 24 Fr 19cm	Silicone	Unknown
Double lumen dialysis catheter 28 Fr 23cm	Silicone	Unknown
Double lumen dialysis catheter 32 Fr 27cm	Silicone	Unknown
Double lumen dialysis catheter 36 Fr 31cm	Silicone	Unknown

Table created July 2009 based on information provided by manufacturers.

Clinical Pathway for *Clostridium difficile* Infection (CDI)[1]



[1]**Prophylaxis for CDI with metronidazole or vancomycin is NOT warranted.**
[2]Isolated leukocytosis is not an indication for treatment of CDI.
[3]DNA Test = Illumigene™ test for presence of C. difficile pathogenicity locus
[4]Universal glove use required. Gown required for any substantial contact with the patient or environment. Soap and water hand hygiene is necessary. Environmental Services will clean the room with a bleach solution weekly and at discharge.

Treatment Recommendations for CDI

Treatment for initial episode of CDI and the first recurrence* of CDI should be the same. See below for recommendations for treatment of CDI beyond the first recurrence.

Mild-Moderate Infection:

Metronidazole[Ŧ] 500 mg PO q8h x 10 days
(Very limited data on IV use, use same dose IV only if ileus or toxic megacolon, or otherwise unable to take PO.)
Pediatric dosing: 30 mg/kg/day PO divided q6h x 10 days; not to exceed 4 g/day

Severe Infection (WBC > 20,000 or SCr ≥ 1.5x baseline):

Vancomycin 125 mg PO q6h x 10 days (DO NOT treat with IV vancomycin)
Pediatric dosing: 40 mg/kg/day PO divided q6-8h x 10 days; not to exceed 2 g/day

Severe, Complicated Infection (i.e., hypotension or shock, ileus, toxic megacolon, fulminant colitis):

Consult ID Services.
Consult General Surgery for evaluation for possible colectomy
Metronidazole[Ŧ] 500 mg IV q8h + vancomycin 125 mg PO q6h +/- vancomycin enema 500 mg in 100 mL of 0.9% NaCl; instill via Foley catheter q6h and retain for 1h

Recurrent CDI beyond 1st recurrence*:

Vancomycin 125 mg PO q6h x 10 days followed by,
Vancomycin 125 mg PO q12h x 7 days, 125 mg PO q24h x 7 days, then 125 mg PO every 3 days x 14 days

Discontinue acid suppressive medications if possible:

The use of acid suppressive medications (ASM) and especially proton pump inhibitors (PPI) has been associated with an increased risk of developing CDI. Also patients with CDI who are continued on ASM have a higher recurrence rate of CDI. It is recommended these agents be discontinued if medically possible.

*Recurrence is defined as the re-appearance of signs/symptoms of CDI within two months of previous CDI episode for which signs/symptoms had resolved. Treatment of the first recurrence should be with the same antibiotic used for the initial episode.
[Ŧ]Metronidazole should not be used in pregnant/lactating women.

Testing Recommendations for CDI

***Clostridium difficile* Assay Results**

GDH Result	Toxin Assay Result	Interpretation	Recommendations
Negative	Negative	No C. difficile present	No further action. Repeat testing is discouraged.
Positive	Positive	Toxigenic C. difficile is present	Utilize contact isolation precautions and begin therapy according to management algorithm. Repeat testing is discouraged.
Positive	Negative	Non-toxigenic C. difficile or false-negative toxin assay	DNA confirmatory test for toxin performed. Interpret based on this result
Negative	Positive	Indeterminate	Repeat test x 1.

Specimen and Order:

- Liquid stool only (i.e. stool conforms to the container) and only one specimen per patient in 24 hours

    - Non-liquid stool will not be processed by the microbiology lab
- Order one test for *C. difficile* at a time. **Do not order multiple tests for *C. difficile.***

Testing Interpretation:

GDH and toxin negative: No *C. difficile* is present (Negative Predictive Value >99%)

- Repeat testing is not recommended due to poor yield
- At TNMC over the first 2 months of use of the GDH/toxin assay only 2 of 147 (1.4%) episodes of repeat testing after an initially negative stool resulted in the diagnosis of toxigenic *C. difficile*. The cost in patient charges of repeat testing was roughly $37,000 per diagnosed episode
- The likelihood of a false positive test result increases dramatically with each repeated test due to lower pretest probability in the test population. PPV of a repeated test is approximately 30 and 50% and results in more false positives than true positives
- Repeat testing could be considered if several days have passed and the clinical syndrome has changed

GDH and toxin positive: Toxigenic *C. difficile* is present (Positive Predictive Value ~99%)

- Treat as appropriate if symptoms suggestive of CDI are present (refer to guidelines above)
- Repeat testing after a positive is not recommended for at least 14 days and no test of cure should be performed

GDH positive, toxin negative: *C. difficile* may be present.

- Repeat testing is NOT recommended as this practice has not resulted in an increased detection of toxin positive stools
- DNA Confirmatory test (Illumigene™) will be performed daily on all GDH +, toxin negative stools
- **DNA Confirmatory Test (+)**
    - *C. difficile* with toxin gene is present
    - Treat as appropriate if symptoms suggestive of CDI are present
- **DNA Confirmatory Test (-)**
    - 2 possibilities: 1) *C. difficile* is present and does not have the toxin gene or 2) false positive GDH
    - No treatment indicated

Isolation/Infection Control Recommendations for CDI

- All patient care units will use the same procedures for testing, treatment, and isolation
- Presumptive isolation on units where it is currently in use (SOTU, OSCHU, PICU, etc) may continue, but otherwise is not routinely necessary
- GDH and toxin negative patients **AND** GDH positive, toxin negative, DNA test negative patients = No isolation necessary
- GDH and toxin positive patients **AND** GDH positive, toxin negative, DNA test positive patients = Initiate CDI contact isolation precautions
    - Isolation procedures include: Universal glove use, gown use for any substantial patient or environmental contact, and soap and water hand hygiene after patient or environment contact
    - Patients will remain in isolation for 1 week after treatment is completed and they are asymptomatic (no diarrhea)
- Environmental Services will perform routine bleach cleaning of rooms of all patients with *C. difficile* infection (CDI) weekly and at patient discharge

Community-Acquired Pneumonia Pathway for Adults

Purpose
To provide a framework for the initial evaluation and management of the immunocompetent, adult patient with bacterial causes of CAP based on recent literature and guidelines. Delays in the initiation of appropriate antibiotic therapy can increase mortality, and therapy should not be postponed for the purpose of performing diagnostic studies in patients who are clinically unstable. Antibiotics should be administered within 4 hours of presentation.

Definitions:
Community-Acquired Pneumonia (CAP) is defined as pneumonia that occurs within 48 hours of hospital admission or in a patient presenting with pneumonia who does not have any of the characteristics of healthcare associated pneumonia (hospitalized in an acute care hospital for two or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic).
Severe CAP can be defined by eleven criteria: (1) need for invasive mechanical ventilation, (2) septic shock with the need for pressors, (3) respiratory rate ≥30 breaths/min, (4) PaO2/FiO2 < 250, (5) multilobar pneumonia (6) confusion/disorientation, (7) uremia (BUN >20mg/dl), (8) leucopenia (WBC <4000cells/mm3), (9) thrombocytopenia (platelets <100,000 cells/mm3), (10) hypothermia (core temperature <36°C), (11) hypotension requiring aggressive fluid resuscitation. The need for ICU admission can be defined by using a rule requiring the presence of one of the factors numbered 1-2 or three of the factors 3-11.

Diagnosis and Management:
All patients thought to have pneumonia should have a chest X-ray. All admitted patients should have an assessment of gas exchange (oximetry or arterial blood gas), complete blood cell count and differential, complete metabolic panel. Clinical indications for more extensive testing of patients admitted to the hospital are found below.

Indication	Blood Culture	Sputum Culture	*Legionella* urinary antigen	Pneumococcal urinary antigen	Other
ICU admission	X	X	X	X	X[a]
Failure of outpatient antibiotics		X	X	X	
Cavitary infiltrates	X	X			X[b]
Leukopenia	X			X	
Active alcoholic	X	X	X	X	
Chronic severe liver disease	X			X	
Severe obstructive/structural lung disease		X			
Asplenia	X			X	
Travel within prior 2 weeks			X		X[c]
Positive *Legionella* urinary antigen result		X[d]	NA		
Positive pneumococcal urinary antigen result	X	X		NA	
Pleural effusion	X	X	X	X	X[e]

[a]Endotracheal aspirate or bronchoalveolar lavage if intubated.
[b]Fungal and tuberculosis cultures.
[c]*Legionella*, *Coccidioides, Hantavirus, Burkholderia pseudomallei,* avian influenza, and SARS are all potential considerations depending on the area of travel.
[d]Special media for *Legionella*.
[e]Thoracentesis and pleural fluid cultures.
Therapy should not be delayed if a sputum culture cannot be obtained. HIV serology, with consent, should be considered, especially for patients aged 15-54 years. For patients with severe CAP, pre-treatment blood cultures, urinary antigens for *Legionella* and *S. pneumoniae*, and sputum culture should be ordered. Empiric antibiotics should be initiated while awaiting culture and susceptibility results.

The decision to admit a patient should be based on clinical judgment with consideration of age, co-morbid conditions, and factors that may compromise the safety of home care. Additionally, a CURB-65 score may be calculated to assist in patient disposition decisions. If a CURB-65 score is used, outpatient care is recommended for a score of 0-1, inpatient care for a score of 2, and ICU care for a score of 3 or more (see appendix A). The PORT Severity Index is another score that may be calculated to assist in patient disposition decisions. If a PORT score is used, home care is recommended for risk classes I, II, and III (see appendix B).The recommended discharge criteria are that, during the 24 h prior to discharge, the patient should have no more than one of the following characteristics: temperature > 37.8°C, pulse > 100 bpm, respiratory rate > 24 breaths/min, systolic blood pressure < 90 mm Hg, and blood oxygen saturation <90%.

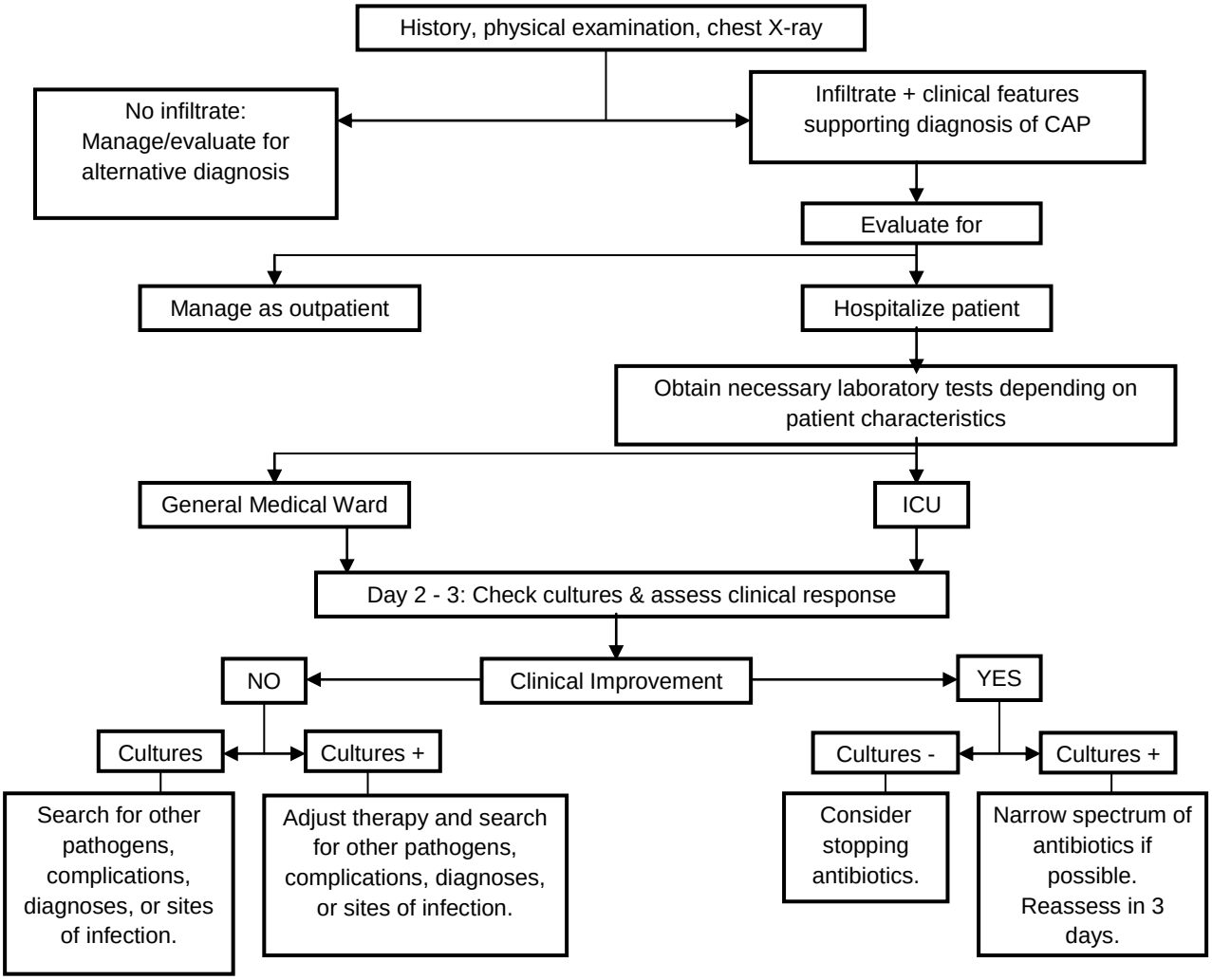
Antibiotic Selection:
The key decision in initial empiric therapy is whether the patient has risk factors for healthcare associated pneumonia, in which case the Antibiotic Protocol for Adult NOSOCOMIAL Pneumonia Empiric Therapy must be used. Additional factors that must be considered are the treatment site for the patient (inpatient/outpatient, general ward/ICU), the presence of modifying factors, and the presence of risk factors for pseudomonas or CA-MRSA.

It is not necessary to start all CAP patients on intravenous therapy if they can tolerate oral therapy. However, if the patient is being admitted to the ICU, it is typically recommended that the patient receive at least 24 hours of intravenous therapy. Doxycycline, moxifloxacin, ciprofloxacin, and azithromycin all have excellent oral bioavailability.

Continuation of Therapy:
Broad-spectrum empiric antibiotic therapy must be accompanied by a commitment to choose pathogen-specific therapy once the culture and susceptibility results are known, which is usually within 48 – 72 hours. Clinical improvement usually becomes apparent after the first 48–72 hours of therapy, and therefore, the selected antimicrobial regimen should not be changed during this time unless progressive deterioration is noted or initial microbiologic studies so dictate.

The nonresponding patient should be evaluated for noninfectious mimics of pneumonia, unsuspected or drug-resistant organisms, extrapulmonary sites of infection, and complications of pneumonia and its therapy. Diagnostic testing should be directed to whichever of these causes is likely.

Algorithm:



Appendix A

CURB-65 Scoring System:

Patient Characteristic	Points assigned[a]
Confusion (based on specific mental test or disorientation to person, place, or time)	1
BUN level > 7 mmol/L (20 mg/dL)	1
Respiratory rate ≥ 30 breaths/min	1
Low blood pressure (systolic < 90 mmHg or diastolic ≤ 60 mmHg)	1
Age ≥ 65 years	1

[a] A total point score for a given patient is obtained by adding the points for each patient characteristic.

Score	Recommended site of care
0	Outpatient
1	Outpatient
2	Inpatient, wards
≥3	Inpatient, ICU

The Pneumonia PORT prediction rule:

1. Classify patient into risk class I if they are aged ≤ 50 years, have no neoplastic disease, liver disease, cerebrovascular disease, renal disease, or congestive heart failure, and have normal or only mildly abnormal vital signs and normal mental status.
2. Use the tables below to calculate a PORT score for those patients in risk classes II – V and determine site of care.

Patient Characteristic	Points asssigned[a]
Demographic factor	
Age	
Male	# of years of age
Female	# of years of age - 10
Nursing home resident	+10
Comorbid illnesses	
Neoplastic disease[b]	+30
Liver disease[c]	+20
Congestive heart failure[d]	+10
Cerebrovascular disease[e]	+10
Renal disease[f]	+10
Physical examination findings	
Altered mental status (disorientation, stupor, or coma)	+20
Respiratory rate > 30 breaths/min	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature < 35°C or > 40°C	+15
Pulse > 125 beats/min	+10
Laboratory or radiographic findings	
Arterial pH < 7.35	+30
Blood urea nitrogen > 30 mg/dL	+20
Sodium < 130 mEq/L	+20
Glucose > 250 mg/dL	+10
Hematocrit < 30%	+10
Arterial partial pressure of oxygen < 60 mm Hg[g]	+10
Pleural effusion	+10

[a] A total point score for a given patient is obtained by adding the patient's age in years (age – 10 for females) and the points for each applicable patient characteristic.
[b] Any cancer except basal or squamous cell cancer of the skin that was active at the time of presentation or diagnosed within 1 year of presentation.
[c] A clinical or histologic diagnosis of cirrhosis or other form of chronic liver disease such as chronic active hepatitis.
[d] Systolic or diastolic ventricular dysfunction documented by history and physical examination, as well as chest radiography, echocardiography, Muga scanning, or left ventriculography.
[e] A clinical diagnosis of stroke, transient ischemic attack, or stroke documented by MRI or computed axial tomography.
[f] A history of chronic renal disease or abnormal blood urea nitrogen and creatinine values documented in the medical record.
[h] An oxygen saturation value < 90% on pulse oximetry or intubation before admission is also considered abnormal.

Risk class	# of points	Mortality %	Recommended site of care
I	NA	0.1	Outpatient
II	≤ 70	0.6	Outpatient
III	71-90	2.8	Outpatient
IV	91-130	8.2	Inpatient
V	> 130	29.2	Inpatient

Antibiotic Protocol for Adult Community-Acquired Pneumonia Empiric Therapy

This pathway is to be used in adult (>18 yo), immunocompetent patients only. A consult from the Immunocompromised ID group is recommended when dealing with hematopoetic stem cell or solid organ transplant patients. All dosages are based on normal renal and hepatic function.

If patient has any of the following characteristics, use the Antibiotic Protocol for Adult NOSOCOMIAL Pneumonia Empiric Therapy:

- Hospitalization for 2 d or more in the preceding 90 d
- Residence in a nursing home or extended care facility
- Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy
- Home wound care
- Home infusion therapy
- Chronic dialysis within 30 d
- Antimicrobial therapy w/in 90 d

A. Not being admitted

1. No Modifying Factors Present (see below)

Azithromycin 500 mg PO qday **OR** Doxycycline* 100 mg PO q12h

2. Modifying Factors Present (age > 65 years, alcoholism, malignancy, asplenia, chronic heart/lung/liver/renal disease, diabetes mellitus, exposure to a child in a daycare center)**

Moxifloxacin* 400 mg PO qday **OR**

Cefuroxime or amoxicillin or amoxicillin/clavulanate **PLUS** azithromycin or doxycycline*

Cefuroxime 500 mg PO q12h
Amoxicillin 1 gram PO q8h
Amoxicillin/clavulanate 2 grams (extended release) PO q12h
Azithromycin 500 mg PO qday
Doxycycline* 100 mg PO q12h

B. Admitted to the Hospital***

1. General Medical Ward (non-ICU)

Moxifloxacin* 400 mg PO/IV qday **OR**

Ceftriaxone **PLUS** azithromycin or doxycycline*

Ceftriaxone 1 gram (2 grams if > 80 kg) IV qday
Azithromycin 500 mg PO/IV qday
Doxycycline* 100 mg PO/IV q12h

2. ICU (No Pseudomonas Risk Factors Present)

Ceftriaxone 1 g (2 g if > 80 kg) IV qday **PLUS EITHER** azithromycin 500 mg PO/IV qday or moxifloxacin* 400 mg PO/IV qday

Penicillin allergy: aztreonam 2 grams IV q8h plus moxifloxacin* 400 mg PO/IV qday

3. Pseudomonas Risk Factors Present (structural lung disease, >10mg prednisone/day, malnutrition)

Either General Ward or ICU

Cefepime 1 gram IV q6h**** **OR**
Piperacillin/tazobactam 4.5 grams IV q8h, infused over 4 hours **OR**
Meropenem 500 mg IV q6h
Penicillin allergy: aztreonam 2 grams IV q6h
PLUS EITHER
Ciprofloxacin***** 400 mg IV q8h **OR**
Aminoglycoside **PLUS** Azithromycin

Aminoglycosides – Gentamicin/tobramycin 5-7 mg/kg IV qday*****
Azithromycin 500 mg PO/IV qday

* Not recommended for use during pregnancy.

** Moxifloxacin is preferred due to reduced local susceptibility to the β-lactam options. Among the β-lactams, cefuroxime is preferred.

*** If community-associated methicillin-resistant *S. aureus* (CA-MRSA) is suspected, add vancomycin 15 mg/kg IV q12h or linezolid 600 mg IV/PO q12h. Trough levels for vancomycin should be approximately 15 mg/L – Consult the pharmacist.

**** Cefepime 2g IV q8h if neutropenia

*****Trough level for gentamicin/tobramycin once-daily dosing should be 0 mg/L – Consult the pharmacist.

Check pneumococcal and influenza vaccination eligibility and status.

Healthcare-Associated Pneumonia Pathway for Adults

Purpose:

To provide a framework for the initial evaluation and management of the immunocompetent, adult patient with bacterial causes of HAP, VAP, or HCAP based on recent literature and guidelines. Delays in the initiation of appropriate antibiotic therapy can increase mortality, and therapy should not be postponed for the purpose of performing diagnostic studies in patients who are clinically unstable.

Definitions:
Hospital Acquired Pneumonia (HAP) is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission.
Ventilator Acquired Pneumonia (VAP) is defined as pneumonia that arises more than 48–72 hours after endotracheal intubation.
Healthcare Associated Pneumonia (HCAP) includes pneumonia within 48 hours of hospital admission in any patient who was hospitalized in an acute care hospital for two or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic.

Diagnosis:
The clinical diagnosis of HAP, VAP and HCAP can be made if the patient has a new radiographic infiltrate PLUS at least two of the following: fever > 38°C, leukocytosis or leucopenia, or purulent secretions. Etiologic diagnosis generally requires a lower respiratory tract culture, but rarely may be made from blood or pleural fluid cultures.

To facilitate etiologic diagnosis, early bronchoalveolar lavage (BAL) sampling, either by mini-BAL technique plus semi-quantitative culture or conventional bronchoscopy with lavage and semi-quantitative culture, should be considered. The probability for a specimen with high yield is highest when the specimen is obtained early (before empiric antimicrobial therapy is started).

Management:
All patients with suspected HAP/VAP/HCAP should have a lower respiratory tract sample and blood sent for culture, and patients with HAP and HCAP should have sputum samples sent whenever possible before the administration of antibiotic therapy. Extrapulmonary infection should be excluded as part of the evaluation

Unless there is low clinical suspicion for lower respiratory tract infection, empiric antibiotics should be initiated

Antibiotic selection:
The key decision in initial empiric therapy is whether the patient has risk factors for multidrug resistant (MDR) organisms (see above risk factors for MDR organisms table).

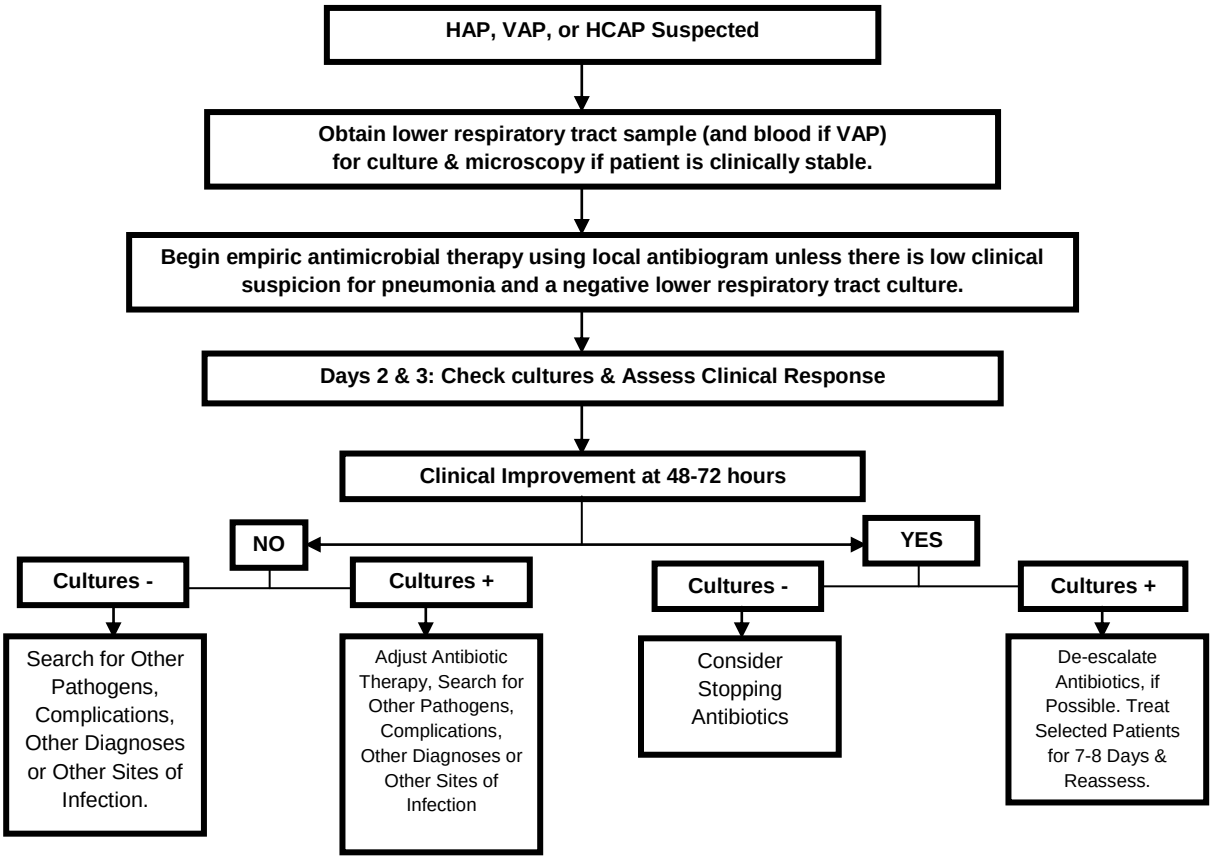
Continuation of Therapy:
Broad-spectrum empiric antibiotic therapy should be accompanied by a commitment to de-escalate antibiotics, on the basis of serial clinical and microbiologic data, to limit the emergence of resistance in the hospital.

All patients with HAP, VAP and HCAP should initially receive therapy intravenously, but conversion to oral/enteral therapy may be possible in certain responding patients. Clinical improvement usually becomes apparent after the first 48–72 hours of therapy, and therefore, the selected antimicrobial regimen should not be changed during this time unless progressive deterioration is noted or initial microbiologic studies so dictate. Clinical parameters including the white blood cell count and measures of oxygenation and core temperature have been used in several studies to define the normal pattern of resolution of HAP. The responding patient should have de-escalation of antibiotics, narrowing therapy to the most focused regimen possible on the basis of culture data.
The nonresponding patient should be evaluated for noninfectious mimics of pneumonia, unsuspected or drug-resistant organisms, extrapulmonary sites of infection, and complications of pneumonia and its therapy. Diagnostic testing should be directed to whichever of these causes is likely.

Efforts to reduce the duration of therapy are justified by studies of the natural history of the response to therapy. Data support the premise that most patients with VAP, who receive appropriate antimicrobial

therapy, have a good clinical response within the first 6 days. Prolonged therapy simply leads to colonization with antibiotic resistant bacteria, which may precede a recurrent episode of VAP.

Algorithm:



Antibiotic Protocol for Adult Nosocomial Pneumonia Empiric Therapy

This pathway is to be used in adult (>18 yo), immunocompetent patients only. An Infectious Diseases consult is recommended when dealing with complicated patients or immunocompromised patients (e.g., hematopoetic stem cell or solid organ transplant). All dosages are based on normal renal and hepatic function.

A. No known Risk Factors for Multidrug-Resistant (MDR; see table below) Pathogens and Early Onset Disease (< 5 d of hospital admission)

Ceftriaxone 1 gram (2 grams if > 80 kg) IV qday **OR**
Moxifloxacin[a] 400 mg PO/IV qday **OR**
Ampicillin/sulbactam 1.5 grams (3 grams if > 80 kg) IV q6h

B. **Known Risk Factors for MDR Pathogens (see table below) or Late Onset Disease (≥ 5 d of hospital admission)**

Vancomycin 15 mg/kg q12h[b] **OR**
Linezolid 600 mg IV q12h

PLUS

Cefepime 1 gram IV q6h[c] **OR**
Piperacillin/tazobactam 4.5 grams IV q8h, infused over 4 hours **OR**
Meropenem 500 mg q6h
Penicillin allergy: aztreonam 2 grams IV q6h plus clindamycin 900 mg IV q8h

PLUS[d]

Gentamicin 5-7 mg/kg IV qday[e] **OR**
Tobramycin 5-7 mg/kg IV qday[e] **OR**
Ciprofloxacin* 400 mg IV q8h

[a]Not recommended for use during pregnancy.
[b]Trough levels for vancomycin should be approximately 15 mg/L – Consult the pharmacist for pharmacokinetic evaluation. If methicillin-resistant *Staphylococcus aureus* (MRSA) with a vancomycin MIC of ≥ 2 mg/L is isolated, use of an alternative agent (linezolid) is recommended.
[c]Cefepime 2g IV q8h if neutropenia
[d] If Legionella is suspected, use an aminoglycoside plus azithromycin 500 mg IV qday.
[e]Trough level for gentamicin and tobramycin once-daily dosing should be 0 mg/L – Consult the pharmacist for pharmacokinetic evaluation.

RISK FACTORS FOR MULTIDRUG-RESISTANT ORGANISMS

- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit (antibiogram can be found on the intranet)
- Presence of risk factors for HCAP:
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic dialysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy

Check pneumococcal and influenza vaccination eligibility and status.
Give vaccinations if indicated.

The Nebraska Medical Center Guidelines for Management of Invasive Candidiasis

Purpose
To provide a framework for initial evaluation and management of immunocompetent and immunocompromised patients with suspected, probable, or proven invasive candidiasis (IC) based on the recent 2009 Clinical Practice Guidelines by the Infectious Disease Society of America. A summary of recommendations for the management of disseminated candidiasis in the neonatal population are also provided. The new guideline was updated to reflect newer antifungal agents, recent publications on the treatment of IC or suspected candidiasis as well as prophylaxis in high risk adult populations.

Definition
IC encompasses severe and invasive *Candida* infections that include candidemia, disseminated candidiasis, endocarditis, meningitis, endophthalmitis, and other deep tissue involvement. It excludes more superficial and less severe diseases such as oropharyngeal and esophageal candidiasis.

Risk Factors
Risk factors for IC include: prolonged and broad-spectrum antibiotics, central venous catheters, total parenteral nutrition, renal replacement therapy, neutropenia, bone marrow transplant, hematologic malignancies, solid organ transplant (liver and kidney), premature birth, gastrointestinal surgery, burns, implanted prosthetic devices, immunosuppressive agents (including glucocorticoids, chemotherapy,and immunomodulators), and prolonged intensive care unit (ICU) stay.[1] Risk factors for non-albicans species include glucocorticosteroid use, central venous catheter placement, prior fluconazole therapy, and preexisting candiduria.[2,3]

An evaluation of systemic candidemia at TNMC was performed and a prediction rule created to help clinicians determine the likelihood of individual patients developing this infection. Pertinent risk factors identified included: 1) Currently receiving broad-spectrum antibiotics (**BSAbx**), defined as carbapenems, fluoroquinolones, 2nd, 3rd, and 4th generation cephalosporins, beta-lactam/beta-lactamase inhibitor combinations, and tigecycline, 2) Presence of a central venous catheter (**CVC**), 3) Receipt of total parenteral nutrition (**TPN**), 4) Abdominal surgery within the last 7 days, 5) Steroid use, and 6) Length of stay (**LOS**) in the hospital. To calculate the risk of candidemia in an individual patient use the formula below and interpret as indicated. If the patient has the risk factor, then the value of that risk factor is 1 (i.e. Yes=1), if the patient does not have the risk factor, then the value is 0 (i.e. No=0). LOS should be entered as the exact number of days continuously hospitalized current assessment.

Prediction Rule = (1.54 x BSAbx) + (0.87 x CVC) + (0.92 x TPN) + (0.40 x Steroid) + (0.88 x Abdominal Surgery) + (0.04 x Pre-ICU LOS in days) =

Total < 2.45: No need for antifugals as probability of not developing candidemia 99.4% (NPV=99.4%)

Total ≥ 2.45: Consider antifungals on individual basis as probability of developing candidemia 4.7% (PPV 4.7%)

Recommended interpretation of the decision rule is if <2.45 no empiric antifungal is recommended as the risk for candidemia is exceedingly low. If result is ≥2.45 empiric therapy should be considered on an individual basis. The incidence level of candidemia in patients in this group does not meet the current guidelines standard of offering empiric therapy to patients who have a greater than 10% incidence of candidemia. Thus, the decision rule is more useful in determining who would not benefit from empiric therapy.

Antifungal Selection
Selection of an antifungal agent should take into account history of recent azole exposure, history of antifungal intolerances, the dominant *Candida* species based on epidemiologic and institution-specific surveillance data, susceptibility data, severity of illness, relevant comorbidities, and evidence of involvement of the central nervous system (CNS), cardiac valves, and/or visceral organs. Early antifungal initiation is critical to successful treatment outcomes. Empiric or prophylactic use of antifungals may reduce morbidity, mortality, and length of stay in critically ill patients, but widespread use of antifungals must be balanced against the risk of toxicity, costs, and emergence of resistance. Currently, the

prevalence of IC among adult ICU patients at TNMC is < 2%; thus, routine fungal prophylaxis in non-neutropenic ICU patients is **not** recommended at TNMC.

Susceptibility testing of *Candida* species is performed at TNMC on yeast isolates from sterile sites including blood, cerebrospinal fluid, synovial fluids, pleural fluids, and pericardial fluids. *Candida* species grow rather rapidly and can usually be identified within 3-5 days. Therapy should be guided by susceptibility testing results when available. In the absence of such results, Table 1 (see below) can be used.

Pharmacologic Considerations – There are 4 major antifungal categories (polyenes, triazoles, echinocandins, flucytosine). TNMC formulary antifungals are discussed briefly below.

1. Polyenes (amphotericin B deoxycholate and lipid amphotericin B formulations)
    - Antifungal category of choice for use in pregnant individuals with IC.
    - AmB-d (amphotericin B deoxycholate) – The most common adverse effects include nephrotoxicity, infusion-related reactions (chills, rigors, hypotension), and potassium and magnesium wasting.
    - LFAmB (lipid amphotericin B formulation) – Three formulations exist with similar spectra to AmB-d (see Table 1 below) but with less nephrotoxicity and higher costs. The TNMC formulary agent is liposomal amphotericin B (AmBisome®). LFAmB formulations possess different pharmacological properties and adverse events and should not be interchanged without careful consideration.
2. Triazoles (fluconazole, itraconazole, voriconazole, posaconazole) – Triazoles have varied activity against *Candida* (see Table 1 below). All triazoles have good oral bioavailability, and the oral formulations are preferred when possible. Fluconazole is the only azole with clinically significant urinary concentrations. All inhibit CYP450 to varying degrees, and careful evaluation for drug-drug interactions is warranted. Generally, avoid in pregnancy due to risks of fetal malformations.
    - Fluconazole is well absorbed orally (~90% bioavailability), is unaffected by food and gastric pH, and among all triazoles, has the greatest penetration into cerebrospinal fluid (CSF) and vitreous body with concentrations at least 50% of serum. Fluconazole urine concentrations reach 10-20 times serum concentrations. Adjust dose for creatinine clearance <50mL/min.
    - Itraconazole is generally reserved for mucosal candidiasis, and little data exist for IC. GI absorption differs for capsule versus solution. Acid-reducing agents decrease absorption of the capsule, while food and acidic beverages (such as carbonated drinks and cranberry juice) enhance absorption. Oral solution is better absorbed on an empty stomach. Renal elimination is minimal (active drug <0.03%; inactive metabolite 40%).
    - Voriconazole is effective for mucosal and IC, but is primarily used for step-down oral therapy for fluconazole-resistant, voriconazole-susceptible strains of *C. krusei* and *C. glabrata.* Voriconazole has good oral bioavailability, CSF (~50% of serum), and vitreous penetration. Oral bioavailability is not affected by gastric pH but is decreased when consumed with food. IV voriconazole is complexed to a cyclodextrin molecule, and should not be used if the CrCl is < 50 mL/min due to risk of accumulation of this molecule. Renal elimination of unchanged drug is insignificant, and thus dosage adjustment for renal insufficiency is not necessary. Voriconazole is the only triazole to require dosage reduction for mild-to-moderate hepatic impairment. Serum levels can vary widely between patients due to common polymorphisms in the primary metabolic enzyme. Drug-drug interactions are frequent and need careful consideration when beginning, altering, or discontinuing treatment. Contraindicated in pregnancy.
    - Posaconazole does not have an indication for treatment of primary candidiasis but demonstrates *in vitro* activity similar to that of voriconazole. Clinical data are inadequate to make evidence-based recommendation for treatment other than oropharyngeal candidiasis. Available only as oral suspension with high bioavailability especially when small doses are given frequently and administered with fatty foods and in acidic environments. Major excretion pathway is feces (~77%) with minimal urinary elimination (~14%). Therefore, dosage adjustment is not necessary in renal impairment. However, due to variability in posaconazole exposure in patients with creatinine clearance <20mL/min, patients should be monitored for breakthrough fungal infections.
3. Echinocandins (caspofungin, anidulafungin, micafungin) The TNMC formulary echinocandin is micafungin. Due to lack of data, these agents are generally avoided in pregnancy.
    - All agents are available parenterally only, dosed once daily, and do not require renal dose adjustment. Caspofungin requires dosage adjustment for moderate hepatic impairment (Child-Pugh class B). Echinocandins undergo nonenzymatic degradation and are not metabolized by the

CYP450 system, although caspofungin undergoes phase II metabolism. Echinocandins have negligible distribution into CSF and urine.

- Have a broad spectrum of activity and are similar to each other with respect to *in vitro* activity against *Candida* sp (see Table 1), with micafungin and anidulafungin having similar MICs that are generally lower than the MIC of capsofungin. *C. parapsilosis* has demonstrated less *in vitro* susceptibility to the echinocandins suggesting it may be less responsive to these drugs. However, the clinical significance of this finding is still unknown.
- Echinocandins are generally well tolerated. Adverse drug reactions are less frequent with micafungin and anidulafungin compared with caspofungin. Phlebitis (3.5-25% of patients) and elevated liver enzyme levels (1-15%) occur more often with caspofungin compared with micafungin and anidulafungin (< 8%)

4. Flucytosine has broad antifungal activity against most *Candida* species except *C. krusei.* Available orally only with good bioavailability. Most (>90%) is excreted unchanged in the urine, and dosage adjustment is necessary for renal dysfunction. Flucytosine is primarily used in combination with amphotericin B for invasive diseases such as meningitis or endocarditis and is rarely administered alone due to rapid emergence of resistance. Occasionally, flucytosine may be used for urinary tract infections when there are no other alternatives. Contraindicated in pregnancy.

Table 1. Spectra of Activity Against *Candida* Species of Various Antifungals

	Fluconazole	Voriconazole	Posaconazole	Itraconazole	Echinocandins	Amphotericin	Flucytosine
C. albicans	S	S	S	S	S	S	S
C. parapsilosis	S	S	S	S	S to R	S	S
C. tropicalis	S	S	S	S	S	S	S
C. glabrata	S-DD to R	S-DD to R	S-DD to R	S-DD to R	S	S to I	S
C. krusei	R	S	S	S-DD to R	S	S to I	I to R
C. lusitaniae	S	S	S	S	S	S to R	S
C. dubliniensis	S	S	S	S	S	S	S
C. guilliermondii	S	S	S	S	S to I	S to I	S
I= intermediately susceptible; R= resistant; S= susceptible; S-DD= susceptible dose-dependent							

Monitoring

- Therapeutic drug monitoring for itraconazole and voriconazole is recommended with extended treatment courses (e.g., ≥4 weeks) to ensure adequate absorption, monitor changes in dosages, monitor the addition of an interacting agent, and assess adherence. Timing of drug sampling for these agents is ill-defined. This is further complicated by nonlinear pharmacokinetics exhibited by itraconazole and voriconazole, making use of the half-life less applicable in determining the time of drug sampling. Therefore, multiple samples are needed to ensure effective and nontoxic concentrations are maintained.
    - Itraconazole blood concentrations vary widely and are generally higher (~30%) with solution than capsule formulation; however, wide inter-patient variability exists.
    - Itraconazole can be measured by high-performance liquid chromatography (HPLC) or bioassay. The results of bioassay are 2-10 times higher than those of HPLC because the bioassay measures both itraconazole and its active metabolite, hydroxyitraconazole. Determination of total antifungal activity by HPLC requires a separate assay for itraconazole and hydroxyitraconazole. The sum of itraconazole and its metabolite should be used in assessing drug levels.
    - Itraconazole levels should only be drawn after steady-state is achieved, which takes ~2 weeks due to its long half-life. The long half-life results in serum concentrations which vary little and allows for blood collection at any time in relation to drug administration.
    - Voriconazole nonlinear pharmacokinetics and genetic differences in metabolism account for observable intra-patient and inter-patient variability. Although the reported half-life of voriconazole is ~6 hours, this varies greatly depending on dose administered. Therefore, the recommendation is to obtain levels after 7 days of therapy to ensure steady state is reached. Drug toxicity has been observed at higher concentrations as well as reduced clinical response at lower concentrations.
    - The upper limit desired therapeutic level for voriconazole is currently 6mg/L, however this is unknown for itraconazole

- If flucytosine is used in infants, careful drug monitoring is recommended as clearance is directly proportional to the glomerular filtration rate (GFR). Very low birth weight infants may accumulate high plasma concentrations due to immaturity.
- Turnaround time for HPLC and liquid chromatography-mass spectrometry (LC-MS) is up to 1 week.

Table 2: Summary of desired reference ranges for antifungal monitoring

Drug	Lab assay	Desired trough levels		When to obtain levels
		Prophylaxis (mg/L)	Treatment (mg/L)	
Itraconazole	Bioassay HPLC and LC-MS	>0.5	>1-2	1-2 weeks
Voriconazole		0.5-6	1-6	1 week
Flucytosine		N/A	Peak (2hrs post dose): 50-100mg/L Trough: 25-50mg/L	≥2 weeks
LC-MS: Liquid chromatography-mass spectrometry; HPLC : High-performance liquid chromatography				

Length of therapy

Without obvious metastatic complications, duration of antifungal therapy for IC is 2 weeks (3 weeks for neonates) after documented clearance of *Candida* species from the bloodstream and resolution of symptoms.

Table 3: Treatment Guidelines; All dosages are based on normal renal/hepatic function.

Proven/Suspected Candidiasis Treatment			
	Preferred General Initial Therapy	**Alternative Therapy**	**Definitive Therapy/Notes**
CANDIDEMIA			
Treatment Candidemia Nonneutropenic Patient	• Fluconazole for less critically ill & without recent (≤3 months) azole exposure. • Micafungin for patients with moderately severe to severe illness or with recent azole exposure. • Transition from micafungin to fluconazole for isolates likely susceptible (*C. albicans)* if patient clinically stable. • Catheter removal strongly recommended	• Amphotericin B deoxycholate for intolerance or limited availability of preferred antifungals. AmBisome® may be used if needed due to toxicities associated with amphotericin B deoxycholate. • Voriconazole effective for candidemia but offers little advantage over fluconazole. Recommended as step-down therapy for selected cases of candidiasis due to susceptible *C. krusei* or *C. glabrata.* Generally reserved for aspergillosis.	• Infectious Disease (ID) consult recommended. • *C. glabrata*: micafungin preferred. o Transition to fluconazole or voriconazole not recommended without confirmation of isolate susceptibility. o If initially received fluconazole or voriconazole with clinical improvement and negative follow-up cultures, continuation of azole to therapy completion is reasonable. • *Candida parapsilosis:* fluconazole preferred. o If initially received micafungin with clinical improvement and negative follow-up cultures, continuation is reasonable. • *C. krusei:* micafungin, AmBisome®, or

Treatment Candidemia Neutropenic Patient	• Micafungin recommended for most. • Catheter removal strongly recommended.	• Fluconazole reasonable for less critically ill without recent azole exposure. • Voriconazole if additional mold coverage needed.	voriconazole preferred. • *C. lusitaniae*: fluconazole or micafungin preferred over amphotericin • **Document fungus clearance from bloodstream** • **Treat for 2 weeks AFTER documented clearance from bloodstream and resolution of symptoms** • **Ophthalmology evaluation/fundoscopic examination for all patients** • Consider trans-esophageal echocardiogram if blood cultures are persistently positive.
CANDIDIASIS			
Empiric Treatment Suspected Invasive Candidiasis in Nonneutropenia	• Similar to proven candidemia. Avoid azoles if recent exposure. • Consider for the critically ill with risk factors for IC and no other known cause of fever based on clinical assessment, serologic markers for IC, and/or culture data from nonsterile sites.	• Amphotericin B deoxycholate for intolerance or limited availability of preferred antifungals. AmBisome® may be used if needed due to toxicities associated with amphotericin B deoxycholate.	• Infectious Disease (ID) consult recommended.
Empiric Treatment Suspected Invasive Candidiasis in Neutropenia	• Micafungin • AmBisome® • Voriconazole	• Fluconazole: Do not use if recent azole exposure. • Itraconazole: Do not use if recent azole exposure. • Amphotericin B deoxycholate effective but carries higher risk of toxicity.	• Infectious Disease (ID) consult recommended.
Neonatal Disseminated Candidiasis Treatment	• Amphotericin B deoxycholate (1mg/kg daily) • Fluconazole (12mg/kg daily) • Treat for 3 weeks. • IV catheter removal strongly recommended.	• AmBisome® if urinary tract involvement excluded. • Micafungin should be used with caution and limited to situations in which resistance or toxicity precludes use of other agents.	• Infectious Disease (ID) consult recommended. • Lumbar puncture and ophthalmology evaluation recommended with sterile body fluid and/or urine cultures positive for *Candida* species. • Imaging of genitourinary tract, liver and spleen should be performed if results of sterile body fluid cultures are persistently positive.
Chronic disseminated	• Stable patients: Fluconazole • Severely ill: Amphotericin B deoxycholate 0.5-0.7mg/kg daily or AmBisome®, then switch to fluconazole once stable	• Micafungin then step down to fluconazole	• Infectious Disease (ID) consult recommended. • Transition from amphotericin or micafungin to fluconazole is preferred after several weeks of treatment. • Duration of treatment: until lesions resolved (usually months) • Treatment should be continued through periods of immunosuppression (chemotherapy or transplant).
CNS	• AmBisome® ± flucytosine for several weeks, then fluconazole daily	• Fluconazole (if patient cannot tolerate AmBisome®)	• Infectious Disease (ID) consult recommended. • Treat until signs and symptoms, CSF abnormalities, and radiologic abnormalities have resolved. • Remove intraventricular devices if possible.
Endocarditis	• AmBisome® ± flucytosine • Amphotericin B deoxycholate 0.6-1mg/kg daily ± flucytosine • Micafungin	• Stable patients with susceptible organisms and negative blood culture: step down to fluconazole	• Infectious Disease (ID) consult recommended. • Valve replacement, including prosthetic valves, strongly recommended. • If valvular replacement not feasible, chronic suppression with fluconazole is recommended.
Pericarditis, myocarditis, suppurative thrombophlebitis	• AmBisome® • Fluconazole • Micafungin	• If AmBisome® or micafungin used: step down to fluconazole once stable	• Infectious Disease (ID) consult recommended. • Several months of therapy is usually warranted for pericarditis or myocarditis. Pericardial window or pericardiectomy recommended. • At least 2 weeks of treatment after 1st negative blood culture is recommended for suppurative thrombophlebitis. Adjunctive surgical incision and drainage or vein resection is recommended for thrombophlebitis.
Osteomyelitis	• Fluconazole • AmBisome® for several weeks, then fluconazole	• Micafungin • Amphotericin B deoxycholate	• Infectious Disease (ID) consult recommended. • Transition from amphotericin or micafungin to fluconazole is preferred after several weeks of treatment. • Duration: 6-12 months • Surgical debridement often necessary.

Septic arthritis	• Fluconazole • AmBisome® for several weeks, then fluconazole	• Micafungin • Amphotericin B deoxycholate	• Infectious Disease (ID) consult recommended. • Transition from amphotericin or micafungin to fluconazole is preferred after several weeks of treatment. • Duration: 6 weeks • Surgical debridement for all cases and removal of infected prosthesis is recommended in most cases.
Endopthalmitis	• Amphotericin B deoxycholate 0.7-1mg/kg + flucytosine • Fluconazole	• AmBisome® • Voriconazole • Micafungin	• Infectious Disease (ID) consult recommended. • Surgical intervention is desired for patients with severe disease or vitreitis. • Duration: at least 4-6 weeks with resolution of infection based on serial ocular exams. • Diagnostic vitreal aspiration required if etiology unknown.
Candida from respiratory secretions	• Rarely indicates invasive candidiasis and should not be treated.		• *Candida* pneumonia and lung abscess are very uncommon, however colonization of bronchial tree is common in patients on ventilator. • Diagnosis of *Candida* pneumonia requires histopathological confirmation.
Candiduria: asymptomatic	• Treatment is generally not indicated with few exceptions noted below. • Neutropenic and neonates: manage as per invasive candidiasis outlined above • Urologic procedures: fluconazole 200- 400 mg (3–6 mg/kg) daily for several days before and after procedure	• Urologic procedures: Amphotericin B deoxycholate 0.3–0.6 mg/kg daily for several days before and after the procedure	• Remove urinary catheter if present. • Treat only high risk patients: neutropenic patients, infants with low birth weight, and patients who will undergo urologic manipulations. • If persistent or recurrent, image kidneys and collecting system to exclude abscess, fungus ball, or urologic abnormality.

Candiduria: symptomatic	• Complicated by disseminated candidiasis: treat as described for candidemia.
	• Cystitis:
	  ○ Fluconazole susceptible: Fluconazole 200 mg (3 mg/kg) PO daily for 2 weeks
	• Pyelonephritis:
	  ○ Fluconazole-susceptible: fluconazole PO 200–400 mg (3–6 mg/kg) daily for 2 weeks
	• Fungus balls
	  ○ Surgical intervention strongly recommended in non-neonates.
	  ○ Fluconazole 200–400 mg (3–6 mg/kg) daily
	  ○ Treat until symptoms resolved and urine cultures no longer yield *Candida* species.
		• Cystitis:
		  ○ Fluconazole resistant: Amphotericin B deoxycholate IV 0.3–0.6 mg/kg IV daily for 1–7 days OR flucytosine for 7–10 days
		• Pyelonephritis:
		  ○ Fluconazole-resistant: Amphotericin B deoxycholate IV 0.5–0.7 mg/kg daily ± flucytosine OR flucytosine for 2 weeks.
		• Fungus ball:
		  ○ Amphotericin B deoxycholate IV 0.5–0.7 mg/kg daily ± flucytosine
		  ○ Adjunct to systemic therapy: amphotericin B deoxycholate 50 mg/L of sterile water irrigation.
			• Remove urinary catheter if present.
			• Amphotericin B deoxycholate bladder irrigation, although not recommended, may be useful for fluconazole-resistant *C. glabrata* or *C. krusei.*
			• Fluconazole is mainstay. No other currently available azole is useful, because of minimal excretion of active drug into urine.
			• Echinocandins are not useful because of minimal excretion into urine.
			• Alternatives are oral flucytosine, systemic amphotericin B deoxycholate, and bladder irrigation with amphotericin B deoxycholate.
			• Avoid lipid amphotericin B formulations.

Peritonitis[11-13]	• Micafungin (preferred if critically ill) • Fluconazole	• Amphotericin B deoxycholate ± flucytosine	• Infectious Disease (ID) consult recommended. • **Use of antifungals for empiric therapy of peritonitis usually not warranted.** Consider in the setting of recurrent peritonitis following recent antibiotic treatment for bacterial peritonitis. • Peritoneal dialysis catheter removal with temporary hemodialysis is strongly recommended. • If *C. parapsilosis* is isolated, fluconazole preferred. • If *C. glabrata* is isolated, micafungin is preferred until fluconazole susceptibility can be confirmed.

ADULT DOSING (unless otherwise specified above) All doses are for normal renal/hepatic function.

• Fluconazole: loading dose 12mg/kg [800mg], then 6mg/kg [400mg] IV/PO daily • Itraconazole 200mg [3mg/kg] PO q12hr—acidic environment enhances absorption of capsule • Voriconazole: 6mg/kg [400mg] q12hr x 2 doses, then 3mg/kg [200mg] q12hr thereafter IV/PO	• Micafungin: 100mg IV q24hr • Amphotericin B deoxycholate (conventional): 0.5-1 mg/kg IV daily • Liposomal amphotericin B (AmBisome®): 3mg/kg IV daily (doses up to 5mg/kg/day are allowed only for NICU

	patients) • Flucytosine: 25 mg/kg PO QID

Prophylaxis in Surgery

NOTE: Use Antimicrobial Surgical Prophylaxis Order Form for all adult, inpatient surgical procedures except solid organ transplants. **Use Transplant Antimicrobial Surgical Prophylaxis Order Form** for all adult and pediatric solid organ transplant procedures.

Allergies – True drug allergy is based on the presence of a positive patient response to one or more of the following signs/symptoms: respiratory difficulty, hypotension, rash, or hives. In the absence of these findings, the patient likely experienced an adverse effect but NOT an allergic reaction to the antibiotic. An antibiotic of the same classification may be used for surgical prophylaxis.

Adult Antimicrobial Surgical Prophylaxis Recommendations

Surgery	Pre-op	Post-op
Abdominal (e.g., appendectomy (non-perforated), biliary, colorectal surgery of any type, gastroduodenal or small bowel surgery)	• Colorectal prep: Neomycin sulfate 1 g + erythromycin base 1 g PO at 19, 18, and 9 hours prior to surgery • Cefoxitin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** metronidazole 500 mg IV + gentamicin 80 mg (100 mg if greater than 80 kg) IV x 1 dose	No post-op dose needed.
Cardiac (e.g., coronary artery bypass graft (CABG), CABG with valve implant, pacemaker and other implants)	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose • **MRSA concern:** Vancomycin 1g IV + cefazolin 1g (2g if greater than 80kg) IV x 1 dose **Allergy:** vancomycin 1 g IV + gentamicin 80mg (100mg if > 80kg) x 1 dose	• Cefazolin 1 g (2 g if greater than 80 kg) q8h x 24h • **MRSA concern**: Vancomycin 1g q12h x1 dose + cefazolin 1g (2g if > 80kg) IV x 24h **Allergy**: vancomycin 1 g IV q12h X 24h + gentamicin 80mg (100mg if greater than 80kg) IV x1 dose (8h ater pre-op dose)
General: any implanted foreign body (e.g. hernia patch)	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy**: vancomycin 1 g IV x 1 dose	No post-op dose needed.

Gynecological: hysterectomy (abdominal, vaginal, or laparoscopic)	• Cefoxitin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** metronidazole 500 mg IV + gentamicin 80 mg (100 mg if greater than 80 kg) IV x 1 dose	No post-op dose needed.
Cesarean section [antibiotics should be administered as for other procedures (within 60 minutes prior to incision); *before* cord clamping]	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose • Cefoxitin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** metronidazole 500 mg IV + gentamicin 80 mg (100 mg if greater than 80 kg) IV x 1 dose	No post-op dose needed.
Head and Neck: clean procedures	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy**: clindamycin 900 mg IV x 1 dose	No post-op dose needed.
Clean-contaminated procedures (oropharyngeal mucosa is compromised)	• Cefazolin 1 g (2 g if > 80 kg) IV **+** metronidazole 500 mg IV x 1 dose **Allergy:** clindamycin 900 mg IV x 1 dose	• Cefazolin 1 g (2 g if >80 kg) IV **+** metronidazole 500 mg IV q8h x 24h **Allergy:** clindamycin 900 mg IV q8h x 24h
Neurosurgery: craniotomy, shunts, laminectomies, and spinal fusion (prosthetic material)	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** vancomycin 1 g IV x 1 dose	• Cefazolin 1 g (2 g if greater than 80 kg) IV q8h x 24h **Allergy:** vancomycin 1 g IV q12h x 24h
Orthopedic: internal fixation of fracture and joint replacement (hip or knee), any implanted foreign body	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** vancomycin 1 g IV x 1 dose **infusion should be completed before tourniquet is inflated if used** **Allergy:** clindamycin 600 mg IV x 1 dose	• Cefazolin 1 g (2 g if greater than 80 kg) IV q8h x 24h **Allergy**: vancomycin 1 g IV q12h x 24h **Allergy**: clindamycin 600 mg IV q8h x 24h
Thoracic: non-cardiac	• Cefazolin 1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** vancomycin 1 g IV x 1 dose	No post-op dosing needed.
Urologic (TURP only, otherwise ***indicated only for patients with known bacteriuria***)	• Ciprofloxacin 200 mg IV x 1 dose **Allergy:** trimethoprim/sulfamethoxazole 160 mg (trimethoprim component) IV x 1 dose	No post-op dosing needed.
Vascular: amputation (lower extremity for ischemia), arterial surgery, vascular access devices, implants, or repair	• Cefazolin1 g (2 g if greater than 80 kg) IV x 1 dose **Allergy:** vancomycin 1 g IV + gentamicin 80 mg (100 mg if > 80 kg) IV x 1 dose	• Cefazolin 1 g (2 g if greater than 80 kg) IV q8h x 24h **Allergy:** vancomycin 1 g IV q12h x 24h + gentamicin 80 mg (100 mg if greater than 80 kg) IV q8h x 24h

Adult Transplant Antimicrobial Surgical Prophylaxis Recommendations

Surgery	Pre-op	Post-op
Liver transplant (low risk; all patients not meeting high risk criteria below)	• Ampicillin/sulbactam 3 g IV x 1 dose **Allergy:** vancomycin 1 g IV + aztreonam 2 g IV x 1 dose	• Ampicillin/sulbactam 3 g IV q6h x 24h **Allergy:** vancomycin 1 g IV q12h + aztreonam 2 g IV q8h x 24h
Liver transplant (high risk) **or Small Bowel transplant** Considered high risk if patient meets the following criteria: re-transplant, requiring dialysis pre-transplant, surgical choledochojejunostomy, CMV+ donor/CMV- recipient	• Piperacillin/tazobactam 4.5 g IV x 1 dose **Allergy:** vancomycin 1 g IV + aztreonam 2 g IV x 1 dos	• Piperacillin/tazobactam 4.5 g IV q8h, infused over 4 hours x 24h **Allergy:** vancomycin 1 g IV q12h + aztreonam 2 g IV q8h x 24h
Kidney transplant **(*NOTE*: Do not adjust doses for renal dysfunction.)**	• Cefazolin 1 g (2g if over 80 kg) IV x 1 dose **Allergy:** clindamycin 600 mg IV + aztreonam 2 g IV x 1 dose	• Cefazolin 1 g (2g if over 80 kg) IV q12h x 24h **Allergy:** clindamycin 600 mg IV + aztreonam 1 g IV q8h x 24h
Kidney/Pancreas **(*NOTE*: Do not adjust doses for renal dysfunction.)**	• Cefoxitin 1 g (2g if over 80 kg) IV x 1 dose **Allergy:** clindamycin 600 mg IV + aztreonam 2 g IV x 1 dose	• Cefoxitin 1 g (2g if over 80 kg) IV q12h x 24h **Allergy:** clindamycin 600 mg IV + aztreonam 1 g IV q8h x 24h

Pancreas Transplant	• Cefoxitin 1 g (2g if over 80 kg) IV x 1 dose **Allergy:** clindamycin 600 mg IV + aztreonam 2 g IV x 1 dose	• Cefoxitin 1 g (2g if over 80 kg) IV q6h x 24h **Allergy:** clindamycin 600 mg IV + aztreonam 2 g IV q8h x 24h
Heart transplant **Ventricular Assist Device (LVAD/RVAD/BiVAD) or Heart Transplant in patient with VAD**	• Cefazolin 1 g (2g if over 80 kg) IV x 1 dose **Allergy**: vancomycin 1 g IV + aztreonam 2 g IV x 1 dose • Vancomycin 1 g IV + aztreonam 2 g IV x 1 dose	• Cefazolin 1 g (2g if over 80 kg) IV q8h x 24h • Allergy: vancomycin 1 g IV q12h + aztreonam 2 g IV q8h x 24h • Vancomycin 1 g IV q12h + aztreonam 2 g IV q8h x 48h

Pediatric Transplant Antimicrobial Surgical Prophylaxis Recommendations

Surgery	Pre-op	Post-op
Liver transplant (low risk; all patients not meeting high risk criteria below)	• Ampicillin/sulbactam 50 mg /kg IV x 1 dose (*dose based on ampicillin component*) Allergy: vancomycin 15 mg/kg IV + aztreonam 30 mg/kg IV x 1 dose	• Ampicillin/sulbactam 50 mg /kg IV q6h x 24h (*dose based on ampicillin component*) Allergy: vancomycin 15mg/kg IV q6h + aztreonam 30 mg/kg IV q8h x 24h
Liver transplant (high risk) **or Small Bowel transplant** Considered high risk if patient meets the following criteria: re-transplant, requiring dialysis pre-transplant, surgical choledochojejunostomy, CMV+ donor/CMV- recipient	Piperacillin/tazobactam 100 mg kg IV x ____kg x 1 dose over 30 minutes (*dose based on piperacillin component*) Allergy: vancomycin 15 mg/kg IV + aztreonam 30 mg/kg IV x 1 dose	Piperacillin/tazobactam 100 mg kg IV (over 4 hours) x 24h (*dose based on piperacillin component*) □ >40kg = q8h □ <40kg = q6h Allergy: vancomycin 15 mg/kg IV q6h + aztreonam 30 mg/kg IV q8h x 24h
Kidney transplant (*NOTE*: Do not adjust doses for renal dysfunction.)	Cefazolin 25 mg/kg IV x 1 dose Allergy: clindamycin 10 mg/kg IV + aztreonam 30 mg/kg IV mg x 1 dose	Cefazolin 25 mg/kg IV q12h x 24h Allergy: clindamycin 10 mg/kg IV q8h + aztreonam 15 mg/kg IV q8h x 24h

Kidney/Pancreas (*NOTE*: Do not adjust doses for renal dysfunction.)	Cefoxitin 30 mg/kg IV x 1 dose Allergy: clindamycin 10 mg/kg IV + aztreonam 30 mg/kg IV x 1 dose	Cefoxitin 30 mg/kg IV q12h x 24h Allergy: clindamycin 10 mg/kg IV 8qh + aztreonam 15 mg/kg IV q8h x 24h
Pancreas Transplant	Cefoxitin 30 mg/kg IV x 1 dose Allergy: clindamycin 10 mg/kg IV + aztreonam 30 mg/kg IV x 1 dose	Cefoxitin 30 mg/kg IV q6h x 24h Allergy: clindamycin 10 mg/kg IV + aztreonam 30 mg/kg IV q8h x 24h
Heart transplant **Ventricular Assist Device (LVAD/RVAD/BiVAD) or Heart Transplant in patient with VAD**	Cefazolin 25 mg/kg IV x 1 dose Allergy: vancomycin 15 mg/kg IV + aztreonam 30 mg/kg IV x 1 dose Vancomycin 15mg/kg IV + aztreonam 30 mg/kg IV x 1 dose	Cefazolin 25 mg/kg IV q8h x 24h Allergy: vancomycin 15mg/kg IV q6h + aztreonam 30 mg/kg IV q8h x 24h Vancomycin 15mg/kg IV q6h + aztreonam 30 mg/kg IV q8h x 48h

Sepsis Management in Adults

If patient has **all 3 of the below**, initiate Severe Sepsis Orders (pre-printed order form):

1. Suspected Infection
2. 2 out of 4 of the below
   - •Temperature greater than 100.4°F (38°C) or less than 96.8°F (36°C)
   - •Heart rate greater than 90 bpm
   - •Respiratory rate greater than 20 or PaCO2 less than 32 mmHg or mechanical ventilation
   - •WBC greater than 12,000 or less than 4,000 mm³
3. Systolic BP less than 90 mmHg after 1500 ml fluid bolus OR Serum lactate greater than or equal to 4 mmole/L

Sepsis Bundle: Antibiotic Selection Clinical Pathway

Early initiation of appropriate therapy is associated with improved outcomes in severe sepsis and septic shock and these guidelines are intended for use in patients with these syndromes only. Antibiotic choices should be based on the clinician's assessment of the most likely source of infection. Antibiotic therapy should be narrowed to target the isolated pathogen when culture results become available. Patients who have milder forms of infection may be more appropriately treated with narrow spectrum agents and antibiotic choices in these patients should be based upon current guidelines and clinical judgment.

Suspected Source of Infection	Suggested Antibiotics
Unknown‡	Vancomycin per clinical pharmacy consult **PLUS EITHER** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h ‡Consider Micafungin 100mg IV qday in patients at high risk for invasive candidiasis. Major risk factors predicting candidemia at TNMC include: 1) Broad-spectrum antibiotics, 2) Central venous catheter, 3) Receipt of TPN, 4) Abdominal surgery, and 5) Steroid use. Presence of 2 or fewer of the risk factors suggests a 99.4% chance of **not** developing candidemia, while patients with >2 risk factors have a 4.7% risk of developing candidemia. See Institutional Guidelines for the Treatment of Invasive Candidiasis for further information.
Intra-abdominal Source	Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h **OR** Metronidazole 500 mg IV q8h **PLUS** Cefepime 1g q6h hours **Note**: If risk factors for nosocomial or pseudomonas infection exist consider adding: Ciprofloxacin 400mg IV q8h or Gentamicin/tobramycin 5-7 mg/kg IV q24h
Urinary Tract	Ciprofloxacin 400 mg IV q12h **PLUS EITHER** Gentamicin 5-7 mg/kg IV single dose OR ceftriaxone 1g IV single dose **OR** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h **OR** Ampicillin 2 grams IV q6h **PLUS** Gentamicin 5-7 mg/kg IV qday*******
Skin/Soft Tissue: Staphylococcus spp.	Vancomycin per clinical pharmacy consult **OR** Linezolid 600 mg IV q12h **OR** Daptomycin 4 mg/kg q24h **OR** Oxacillin 2 grams IV q4h **if MRSA not suspected or ruled out**
Skin/Soft Tissue:	**Aggressive surgical debridement recommended**

Clostridium perfringens ("Gas gangrene"), Group A Streptococcus	Penicillin G 4 million units IV q4h **PLUS** Clindamycin 900 mg IV q8h
Skin/Soft Tissue: Polymicrobial Necrotizing fasciitis	**Aggressive surgical debridement recommended** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h
Community Acquired Pneumonia – No Pseudomonas Risk Factors **Excludes nursing home patients.**	Ceftriaxone 1 gram (2 grams if > 80 kg) IV q24h **PLUS EITHER** Moxifloxacin 400 mg IV q24h **OR** Azithromycin 500 mg IV q24h
Community Acquired Pneumonia – Pseudomonas Risk Factors (structural lung disease, >10mg prednisone/day, malnutrition) **Excludes nursing home patients.**	Cefepime 1g IV q6h **OR** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h **PLUS EITHER**** Ciprofloxacin 400 mg IV q8h **OR** Aminoglycoside PLUS Azithromycin Aminoglycosides – Gentamicin/tobramycin 5-7 mg/kg IV q24h******* Azithromycin 500 mg PO/IV q24h
Nosocomial Pneumonia, includes healthcare-associated pneumonia (HCAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) **Risk Factors for Multidrug Resistant (MDR) Bacteria** (definitions available at www.nebraskamed.com/asp) **Early onset HAP/VAP (<5 days) with NO known MDR risk factors**	**Risk Factors for Multidrug Resistant Bacteria** • Antimicrobial therapy in preceding 90 d • Current hospitalization of 5 d or more • Hospitalization for 2 d or more in the preceding 90 d • Residence in a nursing home or extended care facility • Home wound care • Home infusion therapy (including antibiotics) • Chronic dialysis within 30 d • Family member with multidrug-resistant pathogen • Immunosuppressive disease and/or therapy • High frequency of antibiotic resistance in the community or in the specific hospital unit. (Antibiogram available at www.preceptor.com—follow "Antibiogram" link) Vancomycin 15 mg/kg q12h*** OR** Linezolid 600 mg IV q12h **PLUS** Cefepime 1g IV q6h **OR** Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours **OR** Meropenem 500 mg IV q6h **PLUS**** Gentamicin 5-7 mg/kg IV qday***** OR** Tobramycin 5-7 mg/kg IV qday***** OR** Ciprofloxacin 400 mg IV q8h Ceftriaxone 1 gram (2 grams if > 80 kg) IV q24h **OR** Ampicillin/sulbactam 1.5 grams (3 grams if > 80 kg) IV q6h **PLUS** Moxifloxacin 400 mg PO/IV q24h **OR** Azithromycin 500mg PO/IV q24h

*Trough levels for vancomycin should be approximately 15 mg/L – Consult the pharmacist for pharmacokinetic evaluation
**If Legionella is suspected, use an aminoglycoside plus azithromycin 500 mg IV qday
***Use Hartford nomogram for dosing and obtain random level at 10 hrs – Consult pharmacist for pharmacokinetic evaluation

Guidelines for Treatment of Skin and Soft Tissue Infections

These guidelines are not intended to replace clinical judgment. The antimicrobials are not listed in order of preference, and therapeutic decisions should be based on a number of factors including patient history, comorbidities, suspected etiology, antimicrobial susceptibility patterns, and cost. In certain populations (e.g., intravenous drug abusers, immunosuppressed, travelers), the suspected organisms may include a broader range of organisms. The Infectious Diseases consult services are available for complex patient consultations and should be strongly considered in patients with any severe infections. Cultures should usually be obtained if I & D is performed and/or if there is a discrete collection of pus or drainage that would allow an appropriate culture specimen to be obtained.
Note: Refer to table for pediatric dosing.

Type of Infection	Suspected Organisms	Recommended Treatment
Non-culturable cellulitis (no purulent material or wound present)	*ß-hemolytic Streptococcus* (*Strep pyogenes* (group A strep)*, Strep agalactiae* (group B strep or GBS)*, Strep dysgalactiae* (group C strep)*, G streptococcus* (group G strep), Rarely *Staphyloccus aureus*	- Mild Cephalexin 250-500mg PO q6h **OR** Dicloxacillin 500mg PO q6h **PCN allergy**: Clindamycin 300 mg PO q8h* - Moderate-severe Cefazolin 1g (if ≥80kg 2g) IV q8h **OR** Oxacillin 2g IV q4h **PCN allergy:** Clindamycin 600 mg IV q8h -Severe systemic illness or no response/worsening at 48 hours consider vancomycin 10-15 mg/kg IV q12h[§] - If culture documented streptococcal infection: PCN VK 500 mg PO q6h OR Procaine PCN G 600,000 U IM bid OR Aqueous PCN G 1-2 MU IV q4-6h
Abscess, furuncles, carbuncles	*S. aureus*, including CA-MRSA and *ß-hemolytic Streptococcus* (less common)	**- I & D alone is likely adequate** Utility of antibiotics is unclear but are recommended in the following situations (see Purulent Cellulitis for options): • Severe or extensive disease (multiple sites) • Rapid progression of cellulitis • Signs/symptoms of systemic illness • Associated immunosuppression or comorbidities (diabetes, HIV, active neoplasm) • Extremes of age • Associated septic phlebitis • Sensitive area (face, hand, genitals) • Lack of response to I & D
Purulent cellulitis or abscesses meeting criteria for treatment	*S. aureus*, including CA-MRSA and *ß-hemolytic Streptococcus*	- I & D - Mild Cephalexin 250-500mg PO q6h **PLUS** TMP/SMX DS 1 tab PO q12h** OR Minocycline 100 mg PO q12h*** OR Doxycycline 100 mg PO q12h*** OR Clindamycin 300 mg PO q8h* - Moderate-severe Vancomycin 10-15 mg/kg IV q12h[§] Consult pharmacy for patient-specific dosing. - *If gangrene, immunocompromised and/or severe systemic symptoms treat as per necrotizing fasciitis guidance below*
Folliculitis	*S. aureus*, *P. aeruginosa* (hot tub)	- Warm compress - No antibiotics
Impetigo	*S. aureus*, including CA-	- Warm water soak

	MRSA, *S. pyogenes*	- Cephalexin 250 mg PO q6h **PLUS** TMP/SMX DS 1 tab** PO q12h OR Minocycline 100 mg PO q12h*** OR Doxycyline 100 mg PO q12h*** OR Clindamycin 300 mg PO q8h* OR Mupirocin ointment TID x 7d OR Retapamulin BID x 5d
Erysipelas	*S. pyogenes*, rarely *S. aureus*, including CA-MRSA, or *S. agalactiae*	- PCN VK 250-500 mg PO q6h OR Procaine PCN G 600,000 U IM q12h OR Aqueous PCN G 0.6-2 MU IV q6h OR Clindamycin 300 mg PO/600 mg IV q8h* - If concern for MRSA consider adding: TMP/SMX DS 1 tab** PO q12h
Diabetic foot ulcers	Diabetics: mixed aerobic and anaerobic flora. *S. aureus*. Consider Gram-negative organisms in immunocompromised patients or refractory patients. Consider anaerobes and fungi in IVDU.	**Assess for deep tissue infection/osteomyelitis** - Mild TMP/SMX DS 1 tab PO q12h** **PLUS** Amoxicillin/clavulanate 875/125 mg PO q12h OR Moxifloxacin 400 mg PO qday OR Ciprofloxacin 500 mg PO q12h **PLUS** clindamycin 300 mg PO q8h* - Moderate-severe[Ŧ] Vancomycin 10-15 mg/kg IV q12h[§] (Consult pharmacy for patient-specific dosing) **PLUS** Ampicillin/sulbactam 3 g IV q6h OR Ertapenem 1g IV QDAY OR Piperacillin/tazobactam 4.5g IV q8h, over 4 hours OR Meropenem 500 mg IV q6h **PCN allergy**: Consider ciprofloxacin/clindamycin or aztreonam/clindamycin.
Necrotizing fasciitis	Type I – mixed aerobic and anaerobic flora[Ŧ] Type II – *S. pyogenes*	- **Immediate surgical debridement** - Consider Infectious Disease consult - Ampicillin/sulbactam 3 g IV q6h OR Piperacillin/tazobactam 4.5g IV q8h infused over 4 hrs OR Meropenem 500 mg IV q6h **PCN allergy:** Consider ciprofloxacin/clindamycin or aztreonam/clindamycin. - MRSA concern consider vancomycin 10-15 mg/kg IV q12h[§] Consult pharmacy for patient-specific dosing - Aqueous PCN G 2-4 MU IV q4h **PLUS** clindamycin 900 mg IV q8h
Clostridial myonecrosis (gas gangrene)	*C. perfringens*, rarely *C. septicum*	- **Immediate surgical debridement** - Aqueous PCN G 2-4 MU IV q4 **PLUS** clindamycin 900 mg IV q8h
Bite wounds	Human: *S. viridans, S. aureus, Haemophilus* spp., *Eikenella corrodens,*	- Wound irrigation, evaluate for deep penetration - Prophylaxis for 3-5 days is recommended for non-infected wounds:

	Peptostreptococcus, *Fusobacterium, Porphyromonas, Prevotella*	Amoxicillin/clavulanate 875/125 mg PO q12h **PCN allergy**: Consider Clindamycin 300 mg PO q8h **PLUS** doxycycline 100 mg PO q12h** OR TMP/SMX 1 DS PO q12h OR ciprofloxacin 500mg PO q12h - Active Infection Ampicillin/sulbactam 3 g IV q6h OR Cefoxitin 2g IV q8h OR Clindamycin 900mg IV q8h **PLUS** [ciprofloxacin 400mg IV q12h **OR** TMP/SMX DS 1 tab PO q12h]
	Dog/cat: *Pasteurella multocida,* streptococci, staphylococci, *Fusobacterium, Bacteroides, Porphyromonas, Prevotella* Consider *Capnocytophaga canimorsus* in splenectomized dog bite patients.	- Consider tetanus booster and rabies vaccine. - Wound irrigation - Prophylaxis for non-infected bites wounds not recommended but should be considered in the following situations: • Deep puncture (especially cats) • Moderate or severe with crush injury • On hand or genitals • Near prosthetic material • Involves bone, joint, or poorly vascularized area • Patient is immunocompromised - Prophylaxis (3-5 days) and oral therapy: - Amoxicillin/clavulanate 875/125 mg PO q12h **OR** Clindamycin 300 mg PO q8h PLUS TMP/SMX 1 DS PO q12h* **OR** Cefuroxime 500 mg PO q12h PLUS Clindamycin 300 mg PO q8h - Severe infection requiring intravenous treatment: Ampicillin/sulbactam 3 g IV q6h **OR** Ceftriaxone 1g (2g if >80kg) IV qday PLUS metronidazole 500 mg IV q8h **OR** Ciprofloxacin 400 mg IV q12h PLUS metronidazole 500 mg IV q8h

CA-MRSA – community-associated methicillin-resistant *S. aureus*; I & D – incision and drainage; TMP/SMX – trimethoprim/sulfamethoxazole; PCN – penicillin

*If considering clindamycin for Staphylococci, susceptibility to clindamycin should be confirmed with the "D test" for isolates resistant to erythromycin. Call the Microbiology Laboratory at 552-2090.

**May consider using TMP/SMX DS 2 tabs PO bid for more severe infections. Monitor for increased adverse effects, such as hyperkalemia and GI upset.

***Should not be used in pregnant women or children under the age of 8 years.

§Alternatives to vancomycin include linezolid 600 mg PO/IV q12h OR daptomycin 4 mg/kg IV q24h.

ŦTigecycline 100 mg IV load, then 50 mg IV q12h*** may be considered as an alternative.

Recommended Dosing for Pediatrics (excluding neonates)

Antimicrobial Agent	Recommended Dosing
Amoxicillin/clavulanate	Amoxicillin:clavulanate 14:1 – 45 mg/kg PO q12h 7:1 – 10-22.5 mg/kg PO q12h Range: 20-45 mg/kg/day 4:1 – 7-13.3 mg/kg PO q8h Range: 20-40 mg/kg/day divided q 8h

	Maximum daily dose: 2 g (amoxicillin component) **All doses represent the amoxicillin component
Ampicillin/sulbactam	25-100 mg/kg (ampicillin component) IV q6h Maximum daily dose: 8 g (ampicillin component)
Aqueous PCN G	25,000-100,000 U/kg IV q4-6h Range: 100,000-400,000 U/kg/day Maximum daily dose: 24 mU
Cefuroxime	10-15 mg/kg PO q8-12h Maximum daily dose: 1 g
Cephalexin	6.25-37.5 mg/kg PO q6h Maximum daily dose: 4 g
Ciprofloxacin	10-20 mg/kg PO q12h 10-15 mg/kg IV q8-12h Maximum daily dose: 800 mg
Clindamycin	2.5-10 mg/kg PO q6-8h Range: 10-30 mg/kg/day Maximum daily dose: 1.8 g 6.25-10 mg/kg IV q6-8h Range: 25-40 mg/kg/day Maximum daily dose: 4.8 g
Daptomycin	Safety not established in pediatrics.
Doxycycline	Not to be used in children under 8 years old. 1-4 mg/kg PO q12-24h Range: 2-4 mg/kg/day Maximum daily dose: 200 mg
Linezolid	10 mg/kg PO/IV q8-12h Maximum daily dose: 1.2 g
Meropenem	20 mg/kg IV q8h Maximum daily dose: 1.5 g
Minocycline	Not to be used in children under 8 years old. 2 mg/kg PO bid or 4 mg/kg PO qhs Maximum daily dose: 200 mg
Moxifloxacin	Safety not established in pediatrics.
PCN VK	6.25-16.7 mg/kg PO q6-8h Range: 25-50 mg/kg/day Maximum daily dose: 3 g
Piperacillin/tazobactam	100 mg/kg (piperacillin component) IV q6-8h Range: 150-400 mg/kg/day (piperacillin component) Maximum daily dose: 16 g (piperacillin component) **NOTE:** all doses must be infused over 4 hours, except in NICU patients
Tigecycline	Safety not established in pediatrics.
TMP/SMX	4-6 mg/kg (trimethoprim component) PO bid Maximum daily dose: 160 mg (trimethoprim component)
Vancomycin	10 mg/kg IV q6h Maximum daily dose: 4 g

Renal Dosage Adjustment Guidelines for Antimicrobials

The pharmacists will automatically adjust the doses of any of the antimicrobials included in the protocol according to the estimated creatinine clearance (generally using the Cockroft-Gault equation for patients ≥ 18 years old and the Schwartz equation for patients < 18 years old). This protocol does NOT include patients in the neonatal intensive care unit. For other pediatric patients less than 1 year of age the pharmacist must discuss the dose adjustment with the medical team who initiated the order. When a change is necessary, the pharmacist will write a new order in the Orders section of the medical record indicating the new dosage "per protocol" and enter the order in Carecast as a protocol ("P") order. No physician signature will be required to authorize the revised dosing order.

The adjustments listed in the dosing guidelines will be made unless the physician writes "Do not adjust" when ordering the antimicrobial. For vancomycin and the aminoglycosides, a pharmacokinetic consult will be performed by the pharmacist, and the ordering physician will be contacted for dosage changes unless ordered as "pharmacy to dose." If written as "pharmacy to dose" dosing will be ordered by the pharmacist.

The most current version of the Renal Dosage Adjustment Guidelines for Antimicrobials and associated antimicrobial policies can be found online at the antimicrobial stewardship program (ASP) website: www.nebraskamed.com/asp

Please note:

- If there are no clear recommendations available, the pharmacist will not perform any automatic dosage adjustment. Consult with the physician.
- Accurate estimation of creatinine clearance and glomerular filtration rate from the Cockroft-Gault and Schwartz equations require serum creatinine concentrations to be at steady-state. Acute changes in renal function (indicated by changes in urine output & serum creatinine) render the Cockroft-Gault and Schwartz equations unreliable as serum creatinine is a delayed indicator of renal function. Furthermore, CrCl calculations may be significantly overestimated in patients with decreased muscle mass (e.g. elderly, paralysis). The pharmacist should use their clinical judgment regarding these changes and communicate their recommendations with the team as appropriate.
- Inclusion of an agent within this guideline **does not** necessarily indicate TNMC formulary status

Antimicrobial	Normal Dose	Renal Dosage Adjustment Based on CrCl Estimate (in ml/min)*
Abacavir (ABC)	Adult 600 mg PO q24h or 300 mg PO q12h Pediatric 8 mg/kg PO q12h	No adjustment necessary.
Acyclovir	Adult *PO* 200 mg PO 5x/day 400 mg PO 5x/day 800 mg PO 5x/day 400 mg PO q12h *IV* Mucocutaneous 5 mg/kg IV q8h Immunocompromised: 6.2 mg/kg q8h HSV encephalitis or varicella zoster virus 10 mg/kg IV q8h Immunocompromised: 12.4 mg/kg IV q8h - Pediatric *PO* 6.25-20 mg/kg PO q6h *IV* 15-20 mg/kg IV q8h	 CrCl 0-10: same dose q12h CrCl 11-25: same dose q8h CrCl 0-10: same dose q12h CrCl 11-25: same dose q8h CrCl 0-10: same dose q12h CrCl 0-10: 200 mg PO q12h CrCl 25-50: same dose q12h CrCl 10-24: same dose q24h CrCl <10: 2.5-3.1 mg/kg IV q24h CrCl 25-50: same dose q12h CrCl 10-24: same dose q24h CrCl <10: 5-6.2 mg/kg IV q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: dose as CrCl <10 - CrCl 10-25: same dose q8h CrCl <10: same dose q12h CrCl 25-50: same dose q12h CrCl 10-24: same dose q24h CrCl <10: 50% IV q24h‡ HD/CAPD: No data.
Amantadine	Adult 100 mg PO q12h or 200 mg daily	 CrCl 30-50: Administer 200 mg on day 1, then 100 mg/day CrCl 15-29: Administer 200 mg on day 1, then 100 mg on alternate days CrCl <15: Administer 200 mg every 7 days

	- <u>Pediatric</u> 1-9 years: 5 mg/kg/day PO in 2 divided doses (maximum dose: 150 mg/day) ≥10 years and < 40 kg: 5 mg/kg/day PO in 2 divided doses (maximum dose: 150 mg/day) ≥10 years and ≥40 kg: 100 mg PO q12h	HD: Administer 200 mg every 7 days CAPD: No supplemental dose is needed. - No clear recommendations.
Amikacin	<u>Adult</u> Extended interval dosing (most indications*): 15 mg/kg once daily • adjusted by serum level 6-14 hrs after start of infusion and Hartford nomogram (see PK training packet on ASP website[§]) 10 mg/kg/day may be used for UTIs - Traditional dosing 5 mg/kg IV q8h Monitoring of serum levels is recommended. *Refer to TNMC PK training packet on ASP website[§] for exclusions to extended-interval dosing - <u>Pediatric</u> Traditional dosing 5 mg/kg IV q8h	Extended interval dosing frequency determined by levels/Hartford nomogram - Traditional dosing (empiric, before levels): CrCl 51-90: 60-90% IV q12h[Ŧ] CrCl 10-50: 30-70% IV q12-18h[Ŧ] CrCl <10: 20-30% IV q24-48h[Ŧ] HD/CAPD: Dose according to levels.
Amoxicillin	<u>Adult</u> 250-1000 mg PO q8h <u>Pediatric</u> 12.5-25 mg/kg PO q8-12h (25-90 mg/kg/day) AOM: 90 mg/kg/day PO divided q8-12h	*Same for Adult & Pediatric* CrCl 10-30: same dose q12h CrCl <10: same dose q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: 250 mg PO q12h
Amoxicillin/clavulanate	<u>Adult</u> 500/125 mg PO q8h	CrCl 10-30: 250/125 mg PO q12h CrCl <10: 250/125 mg PO q24h

	875/125 mg PO q12h 1000/62.5 mg PO q12h (XR formulation) - <u>Pediatric</u> 15-45 mg (amoxicillin component)/kg 12h AOM: 22.5-45 mg/kg q12h [30-90 mg (amoxicillin component)/kg/day]	CrCl 10-30: 500/125 mg PO q12h CrCl <10: 500/125 mg PO q24h XR formulation NOT recommended with CrCl < 30. HD: Dose as daily CrCl <10. Give after dialysis on dialysis days. CAPD: 250/62.5 mg PO q12h - CrCl 10-30: same dose q12h CrCl <10: same dose q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: No clear recommendations.
Amphotericin B deoxycholate	<u>Adult & Pediatric</u> 0.7-1 mg/kg IV q24h	No adjustment necessary
Amphotericin B Liposomal	<u>Adult & Pediatric</u> 3 mg/kg IV q24h (Automatic dose substitution to 3 mg/kg, refer to policy on ASP website[§])	No adjustment necessary
Ampicillin	<u>Adult</u> *PO* 250-1000 mg PO q6h *IV* 1-2 g IV q4-6h - <u>Pediatric</u> *PO* 12.5-25 mg/kg PO q6h *IV* 25-100 mg/kg IV q6h	PO CrCl <10: same dose q12h IV CrCl 30-50: same dose q8h CrCl <30: same dose q12h HD: Dose as CrCl <10. Give after dialysis on dialysis days. CAPD: 250 mg PO/IV q12h - PO/IV CrCl <10: same dose q12h HD: Dose as CrCl <10. Give after dialysis on dialysis days. CAPD: No clear recommendations.
Ampicillin/sulbactam	<u>Adult</u> 1.5-3 g IV q6h	CrCl 30-50: same dose q8h CrCl 15-29: same dose q12h CrCl <15: same dose q24h

	- <u>Pediatric</u> 25-100 mg (ampicillin component)/kg IV q6h	HD: Dose daily as CrCl <15. Give after dialysis on dialysis days. CAPD: Dose as CrCl <15. - CrCl 15-29: same dose q12h CrCl <15: same dose q24h HD: Dose as daily CrCl <15. Give after dialysis on dialysis days. CAPD: Dose as CrCl <15.
Atazanavir (ATV) RTV=ritonavir PPI: proton pump inhibitor H2RA: histamine 2 receptor antagonist EFV: efavirenz TDF:tenofovir AUC: area under the curve	<u>Naïve</u> *Adult* ATV + RTV 300/100mg daily w/food Unable to tolerate RTV and/or on H2RA: ATV 400mg daily w/food With TDF, H2RA or PPI: ATV + RTV 300/100mg daily w/food With EFV: ATV+RTV: 400/100mg daily w/food *Pediatric* ≥6yr: 15-24kg; ATV+RTV 150/80mg daily; 25-31kg: 200/100mg daily; 32-38kg 250/100mg daily; ≥39kg 300/100mg daily w/food ≥13yr, ≥39kg and unable to tolerate RTV: ATV 400mg daily w/food <u>Experienced</u> *Adult* On H2RA: ATV + RTV 300/100mg daily w/food With TFV and H2RA: ATV+RTV 400/100mg daily w/food **NOTE**: PPI and EFV are contraindicated in treatment-experienced patients receiving atazanavir *Pediatric* ≥6yr: 25-31kg: ATV+RTV 200/100mg daily; 32-38Kg: 250/100mg daily; ≥39kg 300/100mg daily w/food	No renal adjustment necessary. PPI contraindicated in treatment experienced patients (package labeling) due to decrease in AUC by 75%. In naïve patients PPI should not exceed 20 mg omeprazole/day or equivalent. PPI should be given 12 hours prior to ATV. H2RA dose should not exceed equivalent of famotidine 20 mg q12h. ATV/RTV should be administered simultaneously with or 10 hours after H2RA ATV 400 mg once daily should be administered at least 2 hours before and at least 10 hours after the H2RA
Atovaquone	<u>Adult & Pediatric (>13yo)</u> 1500 mg PO divided q12-24h <u>Pediatric</u> 20 mg/kg PO q12h	No data.
Azithromycin	<u>Adult</u>	

	250-500 mg PO/IV q24h <u>Pediatric</u> 5-10 mg/kg PO q24h	No adjustment necessary. Caution advised if CrCl < 10 (AUC increased by 35%).
Aztreonam	<u>Adult</u> 1 g IV q8h Anti-pseudomonal/moderate-severe infection: 2 gm IV q8hr - <u>Pediatric</u> 30-60 mg/kg IV q6-8h	CrCl 10-30: same dose IV q12h CrCl <10: same dose IV q24h HD: Dose daily as for CrCl <10 and administer after dialysis on dialysis days. CAPD: Dose as CrCl <10. - CrCl 10-30: 50% IV at same interval[Ŧ] CrCl <10: 25% IV at same interval[Ŧ] HD: Dose as for CrCl <10 with an extra 3.25-7.5 mg/kg IV after dialysis. CAPD: Dose as CrCl <10.
Cefazolin	<u>Adult</u> 2 g IV q8h (All Gram-negative infections, *S. aureus* bloodstream infections, moderate-severe infections, patients >80kg) 1 g IV q8h (surgical prophylaxis for patients <80kg, simple urinary tract infections) - <u>Pediatric</u> 16.7-50mg/kg IV q8h	CrCl 10-50: same dose q12h CrCl <10: 1-2 g q24h HD: 1 gm IV q24hr, administered after HD -OR- 2 gm (~20 mg/kg) IV after each HD three times weekly CAPD: 500 mg IV q12h - CrCl 10-30: same dose q12h CrCl <10: same dose q24h HD: 2.5-7.5 mg/kg IV given only after dialysis. CAPD: No adjustment necessary.
Cefepime Refer to dosing protocol on ASP website[§]	<u>Adult</u> 1 g IV q6h --- Febrile Neutropenia: 2 g IV q8hr --- Mild-moderate UTI or community-acquired pneumonia not caused by *P. aeruginosa*: 1 g IV q12hr	CrCl 30-50: 1 g IV q8h CrCl 10-29: 1 g IV q12h CrCl <10: 1 g IV q24h --- CrCl 30-50: 2 g IV q12h CrCl 10-29: 1 g IV q12h CrCl <10: 1 g IV q24h --- CrCl 10-50: 1 g IV q24h CrCl <10: 500 mg IV q24h HD: Dose daily as CrCl <10.

	- <u>Pediatric</u> Pediatric ≥ 40 kg: see adult dose Pediatric <40 kg: 50 mg/kg IV q8-12h	Administer after dialysis on dialysis days. CAPD: Dose for CrCl <10. - CrCl 10-50: same dose q12 (for q8h dosing)-q24h (for q12h dosing) CrCl <10: 50% q24h[Ŧ] HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: 50 mg/kg IV q48h
Cefotaxime	<u>Adult</u> 1-2 g IV q8h (Therapeutic interchange to ceftriaxone in adults, see cephalosporin therapeutic interchange policy) - <u>Pediatric</u> 25-100mg/kg IV q6-8h (100-200mg/kg/day)	CrCl 10-50: same dose q12h CrCl <10: same dose q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: 1 g IV q24h - CrCl <20: same dose q24h HD: Dose daily as CrCl <20. Give after dialysis on dialysis days. CAPD: 50-100 mg/kg IV q24h
Cefoxitin	<u>Adult</u> 1-2 g IV q8h For coverage of *Enterobacteriaceae* (*E. coli, Klebsiella sp. Proteus sp.* etc*.):* 2 g IV q6h - <u>Pediatric</u> 20-40mg/kg IV q6h	CrCl 10-30: same dose q12h CrCl <10: same dose IV q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: 1 g IV q24h - CrCl 51-90: same dose q8h CrCl 10-50: same dose q12h CrCl <10: same dose q24-48h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: No clear recommendations.
Ceftazidime	<u>Adult</u> 1 g IV q8h Anti-pseudomonal dosing: 2 gm IV q8hr	CrCl 10-30: same dose q12h CrCl <10: 1 gm q24h HD: Dose daily as CrCl <10. Give

	- <u>Pediatric</u> 30-50 mg/kg IV q8h	after dialysis on dialysis days. CAPD: 1 g IV x1, then 500 mg IV q24h - CrCl 30-50: same dose q12h CrCl 10-29: same dose q24h CrCl <10: same dose q48h HD: Dose as CrCl <10. Give after dialysis on dialysis days. CAPD: 30-75 mg/kg IV x1, then 50% q24h[‡]
Ceftriaxone	<u>Adult</u> 1 g IV q24h Patients >80 kg: 2 g IV q24h Meningitis: 2 g IV q12h - <u>Pediatric</u> 25-100mg/kg IV q12-24h (50-100mg/kg/day)	No adjustment necessary. CAPD: 1 g IV q12h - No adjustment necessary.
Cefuroxime	<u>Adult</u> *PO* 250-500 mg PO q12h *IV* 1.5 g IV q8h - <u>Pediatric</u> *PO* Cefuroxime 10-15 mg/kg PO q12h *IV* 25-50mg/kg IV q8h	No adjustment necessary. CrCl 10-20: 1.5 gm IV q12h CrCl <10: 1.5 gm q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days. CAPD: Dose as CrCl <10. - No adjustment necessary. HD: Give after dialysis on dialysis days. CrCl 10-20: same dose q12h CrCl <10: same dose q24h HD: Dose daily as CrCl <10. Give after dialysis on dialysis days.

		CAPD: Dose as CrCl <10.
Cephalexin	Adult 250 - 1000 mg PO q6h - Pediatric 6.25-37.5 mg/kg PO q6h	 CrCl 50-90: same dose PO q8h CrCl <50: same dose PO q12h HD: Dose as CrCl <50. Give after dialysis on dialysis days. CAPD: Dose as CrCl <50. - CrCl 10-40: same dose q8h CrCl <10: same dose q12h HD: Dose as CrCl <10. Give after dialysis on dialysis days. CAPD: Dose as CrCl <10.
Chloramphenicol	Adult 12.5-25 mg/kg IV q6h Pediatric 6.25-25 mg/kg IV q6h	 No adjustment necessary.
Ciprofloxacin	Adult *PO* 250-750 mg PO q12h (consider 750mg q8h for pneumonia/severe infection) *IV* 400 mg IV q8-12h (q8h for pneumonia/severe infection) - Pediatric *PO* 10-20 mg/kg PO q12h *IV* 10-15 mg/kg IV q8-12h	 CrCl <30: same dose q24h HD/CAPD: Dose as CrCl <30 given after dialysis. CrCl <30: same dose q12 (for q8h regimen)-24h (for q12h regimen) HD/CAPD: Dose as CrCl <30 given after dialysis. - No clear recommendations.
Clarithromycin	Adult 0.5 – 1 g PO q12h Pediatric 7.5 mg/kg PO q12h	*Same for Adult & Pediatric* CrCl <30: 50% PO q12h[ǂ] HD: Dose as CrCl <30. Give after dialysis on dialysis days. CAPD: No adjustment necessary.
Clindamycin	Adult *PO* 150-450 mg PO q6-8h	

	IV Standard dose: 600 mg IV q8h Necrotizing fasciitis: 900 mg IV q8h <u>Pediatric</u> *PO* 2.5-10 mg/kg PO q6-8h (10-30 mg/kg/day) *IV* 6.25-10 mg/kg IV q6-8h (25-40 mg/kg/day)	No adjustment necessary.
Colistin base IV Restricted to ID service or pulmonary service consultation	<u>Adult</u> 5 mg/kg/day (lesser of actual or ideal body weight) colistin base IV divided in 2-3 doses	Use loading dose in renal dysfunction: Loading dose: 2.5 mg/kg IV q12h x2 doses. Maintenance dosing begins 24 hours after first loading dose CrCl >40: no adjustment needed CrCl 20-40: 75% IV q12h[ǂ] CrCl 10-19: 50% IV q12h[ǂ] CrCl <10, HD/CAPD: 50 mg IV q12h (after HD on HD days) SLED: While on SLED dose as CrCl>40 While off SLED dose as CrCl<10 See colistin dosing and restriction document available on ASP website[§]
Colistin base Inhaled Restricted to ID service or pulmonary service consultation	<u>Adult</u> 75-150 mg inhaled q12h <u>Pediatric</u> 30-75 mg inhaled q12h	No adjustment necessary See colistin dosing and restriction document available on ASP website[§]
Dapsone	<u>Adult</u> 50-100 mg PO q24h <u>Pediatric</u> 1-2 mg/kg PO q24h	No clear guidelines, but adjustment recommended.
Daptomycin Restricted to ID Service review and approval for non FDA-approved indications	<u>Adult</u> 6 mg/kg IV q24h UTI or skin/skin structure infection: 4 mg/kg IV q24h Safety and efficacy not established in pediatrics.	CrCl <30: same dose IV q48h HD: Dose as CrCl <30. Give after dialysis on dialysis days. CAPD: Dose as CrCl <30.
Darunavir (DRV)	<u>Naïve</u> *Adult*	

	DRV+RTV 800/100mg daily w/food *Pediatric* ≥6yrs; 20-29kg: DRV+RTV 375/50mg Q12H; 30-39Kg 450/60mg Q12H; ≥40kg 600/100mg Q12H <u>Experienced</u> *Adult* DRV+RTV 600/100mg Q12H w/food *Pediatric* No recommendations.	No adjustment necessary.
Dicloxacillin	<u>Adult</u> 250-500 mg PO q6h <u>Pediatric</u> 6.25-12.5 mg/kg PO q6h	No adjustment necessary.
Didanosine (enteric coated, DDI EC)	<u>Adult</u> **≥60kg** 400 mg EC PO q24h *if given with TDF: 250 mg PO q24h* **<60 kg:** 250 mg EC PO q24h *if given with TDF: 200 mg PO q24h* - <u>Pediatric</u> 100-120 mg/m^2 PO q12h	CrCl 30-59 & ≥60kg: 200 mg EC q24h CrCl 30-59 & <60kg: 125 mg EC q24h CrCl 10-29: 125 mg PO EC q24h CrCl <10, HD/CAPD: Dose as CrCl 10-29 and if patient is <60kg use oral solution instead of EC formulation - No clear recommendations except for HD. HD: 25% of total dose PO q24h$^{\mp}$
Doxycycline	<u>Adult</u> 100 mg PO/IV q12h <u>Pediatric</u> *not to be used in children < 8yo 1-4 mg/kg PO/IV q12-24h (2-4 mg/kg/day)	No adjustment necessary.
Efavirenz (EFV)	<u>Adult</u> 600 mg PO QHS (avoid food) <u>Pediatric</u> 200-600 mg PO q24h	No adjustment necessary.
Emtricitabine (FTC)	<u>Adult:</u> Capsule: 200 mg once daily Solution: 240 mg once daily	CrCl 30-49: Capsule: 200mg q48h; Solution: 120 mg q24h CrCl 15-29: Capsule: 200 mg q72h; Solution: 80 mg q24h CrCl <15: Capsule: 200 mg q96h; Solution: 60 mg q24h

	- Pediatric 0-3 months: Solution: 3 mg/kg/day 3 months to 17 years: Capsule: Children >33 kg: 200 mg once daily Solution: 6 mg/kg once daily; maximum: 240 mg/day	HD: Dose as CrCl <15. Give after dialysis on dialysis days. - No clear recommendations
Ertapenem	Adult 1 g IV q24h - Pediatric 15 mg/kg IV q12h	CrCl < 30: 500 mg IV q24h HD/CAPD: Dose as CrCl < 30 given after dialysis on dialysis days. - No clear recommendations.
Erythromycin	Adult *PO* 250-500 mg PO q6-12h *IV* 15-20 mg/kg/day IV divided q6-8h Pediatric *PO* 7.5-16.7 mg/kg PO q6-8h (30-50 mg/kg/day) *IV* 3.75-12.5 mg/kg IV q6h	*Same for Adult & Pediatric* CrCl <10: 50% PO/IV at same interval.[Ŧ] HD/CAPD: Dose as CrCl <10.
Erythromycin/sulfisoxazole	Adult 400 mg (erythromycin component) PO q6h Pediatric 10-16.7 mg (erythromycin component)/kg PO q6-8h [40-50 mg (erythromycin component)/kg/day]	No clear recommendations.
Ethambutol	Adult 15-25 mg/kg PO q24h (max. dose 2.5 grams) Pediatric 15-25 mg/kg PO q24h (max. dose 2.5 grams)	*Same for Adult & Pediatric* CrCl 10-50: same dose PO q24-36h CrCl <10: same dose PO q48h HD: Give dose only after dialysis. CAPD: Dose as CrCl <10.
Etravirine (ETV)	200 mg PO q12h with food	No adjustment necessary

Famciclovir	Adult 500 mg PO q8h (varicella zoster virus) Safety and efficacy not established in pediatrics.	 CrCl 40-59: same dose q12h CrCl 20-39: same dose q24h CrCl <20: 50% q24h‡ HD: 50% after each dialysis session.‡ CAPD: No clear recommendations.
Fluconazole	Adult Invasive candidiasis (susceptible *C. albicans, C. tropicalis, C. parapsilosis*): 800 mg (12 mg/kg) load x1dose then 400 mg (6 mg/kg) PO/IV q24h Esophageal candidiasis: 200 mg PO/IV q24h Oropharyngeal candidiasis: 100 mg q24h - Pediatric 3-12 mg/kg/day PO/IV q24h	Invasive candidiasis: CrCl 10-29: 800 mg (12mg/kg) load x1dose then 50% PO/IV q24h‡ CrCl <10: 800 mg (12 mg/kg) load x1dose then 25% PO/IV q24h‡ HD: 800 mg (12mg/kg) load x1dose then Then 400 mg (6 mg/kg) PO/IV after HD three times weekly CAPD: 50% PO/IV q24h‡ Esophageal/Oropharyngeal candidiasis: CrCl <30: 50% PO/IV q24h‡ HD: 100% PO/IV after each dialysis‡ CAPD: 50% PO/IV q24h‡ - CrCl 20-50: 50% PO/IV q24h‡ CrCl <20: 25% PO/IV q24h‡ HD: Give dose only after dialysis. CAPD: 25% PO/IV q24h‡
Flucytosine	Adult 50-150 mg/kg/day PO divided q6h - Pediatric 25-37.5 mg/kg PO q6h	 CrCl 10-50: same dose q12-24h CrCl <10: same dose q24h HD/CAPD: Give dose only after dialysis. - CrCl 20-40: same dose q12 CrCl 10-19: same dose q24h CrCl <10: same dose q48h HD/CAPD: Give dose only after dialysis.
Fosamprenavir (FPV) RTV = ritonavir EFV=efavirenz	ARV Naïve *Adult* FPV 1400mg q12h OR 1400mg + RTV 200mg daily OR 1400mg + RTV 100mg daily OR 700mg+ RTV 100mg q12h With EFV or NVP: 1400mg + RTV 300mg daily *Pediatric* 2-5yr: 30mg/kg q12h	 No adjustment necessary.

	≥6yr: 30mg/kg q12h OR FPV 18mg/kg+ RTV 3mg/kg q12h; (maximum dose: FPV 1400mg or RTV 200mg/day) <u>ARV Experienced</u> *Adult* FPV 700mg + RTV 100mg q12h *Pediatric* ≥6yr: FPV 18mg/kg + RTV 3mg/kg q12h (maximum dose: 1400mg+RTV 200mg/day)	
Foscarnet	<u>Adult</u> <u>Mucocutaneous HSV:</u> 40 mg/kg IV q8h <u>Disseminated CMV, induction:</u> 60 mg/kg IV q8h <u>Disseminated CMV, maintenance:</u> 90-120 mg/kg IV q24h . - <u>Pediatric</u> <u>Induction</u> 60 mg/kg IV q8h	**CrCl as ml/min/kg body weight** CrCl >1.0-1.4: 30 mg/kg IV q8h CrCl >0.8-1.0: 35 mg/kg IV q12h CrCl >0.6-0.8: 25 mg/kg IV q12h CrCl >0.5-0.6: 40 mg/kg IV q24h CrCl 0.4-0.5: 35 mg/kg IV q24h CrCl <0.4: Not recommended. CrCl >1.0-1.4: 45 mg/kg IV q8h CrCl >0.8-1.0: 50 mg/kg IV q12h CrCl >0.6-0.8: 40 mg/kg IV q12h CrCl >0.5-0.6: 60 mg/kg IV q24h CrCl 0.4-0.5: 50 mg/kg IV q24h CrCl <0.4: Not recommended. CrCl >1.0-1.4: 70-90 mg/kg IV q24h CrCl >0.8-1.0: 50-65 mg/kg IV q24h CrCl >0.6-0.8: 80-105 mg/kg IV q48h CrCl >0.5-0.6: 60-80 mg/kg IV q48h CrCl 0.4-0.5: 50-65 mg/kg IV q48h CrCl <0.4: Not recommended. HD: 40-60 mg/kg IV after each dialysis session - **CrCl as ml/min/kg body weight** <u>Induction</u> CrCl ≥ 1.6: 60 mg/kg/8h CrCl 1.5: 56.5 mg/kg/8h CrCl 1.4: 53 mg/kg/8h CrCl 1.3: 49.4 mg/kg/8h CrCl 1.2: 45.9 mg/kg/8h CrCl 1.1: 42.4 mg/kg/8h CrCl 1: 38.9 mg/kg/8h CrCl 0.9: 35.3 mg/kg/8h CrCl 0.8: 31.8 mg/kg/8h CrCl 0.7: 28.3 mg/kg/8h CrCl 0.6: 24.8 mg/kg/8h CrCl 0.5: 21.2 mg/kg/8h

	Maintenance 90-120 mg/kg IV q24h 40-60 mg/kg IV q12h	CrCl 0.4: 17.7 mg/kg/8h Maintenance CrCl 1-1.4: 70-90 mg/kg IV q24h CrCl 0.8-<1: 50-65 mg/kg IV q24h CrCl 0.6-<0.8: 80-105 mg/kg IV q48h CrCl 0.5-<0.6: 60-80 mg/kg IV q48h CrCl 0.4-<0.5: 50-65 IV q48h CrCl < 0.4: not recommended HD/CAPD: No data.
Fosfomycin sachet Susceptibility testing required for use other than a one time dose for uncomplicated cystitis ID Service consultation strongly recommended for use other than uncomplicated cystitis Refer to fosfomycin information on ASP website[§]	Adult Uncomplicated cystitis: 3g oral x 1 dose Complicated cystitis: 3 g oral q48h - Pediatric Pediatric ≥15 yrs: SEE ADULT DOSE Pediatric ≤14 yrs: Uncomplicated cystitis: 2g oral x 1 dose Complicated cystitis: 2g oral every 2 days Pediatric ≤1 yr: Uncomplicated cystitis: 1g oral x 1 dose Complicated cystitis: 1g oral every 2 days	 CrCl <50: same dose CrCl <50: 3g oral q72h - SEE ADULT DOSAGE If uncomplicated and CrCl<50: give same dose If complicated and CrCl<50: Age ≤14 yrs: 2g oral every 3 days Age ≤1 yr: 1g oral every 3 days
Ganciclovir	Adult *PO* 1 g PO q8h *IV* Induction: 5 mg/kg IV q12h Maintenance 5 mg/kg IV q24h - Pediatric *PO*	 CrCl 50-69: 1.5 g PO q24h or 500 mg PO q8h CrCl 25-49: 1 g PO q24h CrCl 10-24: 500 mg PO q24h CrCl <10: 500 mg PO 3x/week CrCl 50-69: 2.5 mg/kg IV q12h CrCl 25-49: 2.5 mg/kg IV q24h CrCl 10-24: 1.25 mg/kg IV q24h CrCl <10:1.25 mg/kg IV 3x/week CrCl 50-69: 2.5 mg/kg IV q24h CrCl 25-49: 1.25 mg/kg IV q24h CrCl 10-24: 0.625 mg/kg IV q24h CrCl <10: 0.625 mg/kg IV 3x/week HD (PO/IV): Dose as CrCl <10 given after dialysis sessions. -

	30 mg/kg PO q8h *IV* Induction: 5 mg/kg IV q12h Maintenance: 5 mg/kg IV q24h	No clear recommendations. CrCl 50-69: 2.5 mg/kg IV q12h CrCl 25-49: 2.5 mg/kg IV q24h CrCl 10-24: 1.25 mg/kg IV q24h CrCl <10:1.25 mg/kg IV 3x/week CrCl 50-69: 2.5 mg/kg IV q24h CrCl 25-49: 1.25 mg/kg IV q24h CrCl 10-24: 0.625 mg/kg IV q24h CrCl <10: 0.625 mg/kg IV 3x/week HD (PO/IV): Dose as CrCl <10 given after dialysis sessions.
Gentamicin	<u>Adult</u> Extended interval dosing (most indications*): 7 mg/kg once daily • adjusted by serum level 6-14 hrs after start of infusion and Hartford nomogram (see PK training packet on ASP website[§]) 5 mg/kg/day may be used for UTIs - Traditional dosing 1.5-2.5 mg/kg IV q8h Monitoring of serum levels is recommended. *Refer to TNMC PK training packet on ASP website[§] for exclusions to extended-interval dosing - <u>Pediatric</u> Traditional dosing 1.5-2.5 mg/kg IV q8h	Extended interval dosing frequency determined by levels/Hartford nomogram - Traditional dosing (empiric, before levels): CrCl 51-90: 60-90% IV q8-12h[Ŧ] CrCl 10-50: 30-70% IV q12h[Ŧ] CrCl <10: 20-30% IV q24-48h[Ŧ] HD/CAPD: Dose according to levels.
Imipenem	<u>Adult</u> 500 mg IV q6h For any other adult doses, use adjustment tables provided by Micromedex. - <u>Pediatric</u> 15-25 mg/kg IV q6h	<u>Adjusted by weight and CrCl. See Micromedex for adjustment.</u> HD: Dose as CrCl <20. Dose after dialysis on dialysis days. CAPD: Dose as CrCl <10 - CrCl 41-70: 50% IV q6h[Ŧ] CrCl 21-40: 35% IV q8h[Ŧ] CrCl 6-20: 25% IV q12h[Ŧ] HD: Same dose q12h, given after dialysis on dialysis days. CAPD: Dose as CrCl 6-20

Indinavir	Adult 800 mg PO q8h - Pediatric: 500 mg/m^2 PO q8h	No adjustment necessary. - No clear recommendations (<20% renal elimination).
Isoniazid	Adult 5 mg/kg PO q24h (max dose 300 mg daily) Pediatric 10-15 mg/kg PO q24h (max dose 300 mg daily)	No adjustment necessary. HD/CAPD: Give dose after dialysis on dialysis days.
Itraconazole	Adult 100-200 mg PO q12h Endemic fungi *(Histoplasmata sp. Coccidioides sp. Blastomycetes sp.*): 200 mg PO q8h x2days load then 200 mg PO q12h Pediatric 3-5 mg/kg PO q24h	No renal adjustment necessary. Avoid concomitant proton pump inhibitors or histamine receptor antagonists Suspension should be administered on an empty stomach Capsules should be administered with meal or acidic beverage Therapeutic drug monitoring should be considered. Goal steady-state trough obtained after 5-7 days of therapy for active disease >1mg/dL (sum of hyrdoxy-itraconazole and itraconazole)
Lamivudine (3TC)	Adult 150 mg q12h OR 300 mg PO q24h - Pediatric 2-4 mg/kg PO q12h	CrCl 30-49: 150 mg PO q24h CrCl 15-29: 150 mg PO x1, then 100 mg PO q24h CrCl 5-14: 150 mg PO x1, then 50 mg PO q24h CrCl <5: 50 mg PO x1, then 25 mg PO q24h (Note: because lamivudine is well-tolerated and available in 100 mg tablets, some practitioners will prescribe 50 mg PO daily (half of a 100 mg tablet) HD/CAPD: Dose as CrCl <5. - No clear recommendations (70% renal elimination).
Linezolid	Adult 600 mg PO/IV q12h Pediatric 10 mg/kg PO/IV q8-12h	No adjustment necessary.

Lopinavir/ritonavir (LPV/r)	Adult 400/100 mg PO q12h or 800/200 mg PO q24h (do not use once daily dosing in pts with >2 lopinavir resistance-associated substitutions, pregrancy, or patients receiving EFV, NVP, NFV, carbamazepine, phenobarbital, or phenytoin) Pediatric 10-13 mg (lopinavir component)/kg PO q12h	No clear recommendations, but adjustment probably not necessary (<3% renal elimination). Avoid once daily dosing in patients receiving HD
Maraviroc	150 mg PO q12h: when used concomitantly with a potent CYP3A inhibitor (with or without a CYP3A inducer) including protease inhibitors (except tipranavir/ritonavir), delavirdine, ketoconazole, itraconazole, clarithromycin, nefazadone, and telithromycin 600 mg PO q12h: when used concomitantly with a potent CYP3A inducer (without a strong CYP3A inhibitor) including efavirenz, etravirine, rifampin, carbamazepine, phenobarbital, and phenytoin. 300 mg PO q12h: when used concomitantly with tipranavir/ritonavir, nevirapine, raltegravir, all nucleoside reverse transcriptase inhibitors, and enfuvirtide	Caution in patients with hepatic impairment Caution in patients with CrCl<50
Meropenem Refer to dosing protocol on ASP website[§]	Adult Standard dose: 500 mg IV q6h Simple urinary tract infection: 500 mg IV q8h Meningitis, cystic fibrosis, meropenem MIC of 4 mcg/mL 2 g IV q8h - Pediatric 20-40 mg/kg IV q8h (q12h for neonates 7 days old and under)	 CrCl 25-49: 500 mg IV q8h CrCl 10-24: 500 mg IV q12h CrCl < 10: 500 mg IV q24h CrCl 25-49: 500 mg IV q12h CrCl 10-24: 250 mg IV q12h CrCl < 10: 500 mg IV q24h CrCl 25-49: 2 g IV q12h CrCl 10-24: 1 g IV q12h CrCl < 10: 1 g IV q24h HD/CAPD: Dose as CrCl < 10 given after dialysis on dialysis days. - No clear recommendations for neonates 7 days old under. For those over 7 days old: CrCl 10-24: Same dose IV q12h

		CrCl < 10: Same dose IV q24h HD/CAPD: Dose as CrCl < 10 given after dialysis on dialysis days.
Metronidazole	Adult 500 mg PO/IV q8h Pediatric 3.75-16.7 mg/kg PO/IV q6-8h (15-50 mg/kg/day)	*Same for Adult & Pediatric* CrCl <10 or severe hepatic dysfunction: consider 50% at same interval if >14 day duration[Ŧ] HD/CAPD: Give after dialysis on dialysis days.
Micafungin	Adult 50-150 mg IV q24h - Pediatric 1-4.5 mg/kg IV q24h	No adjustment necessary. - No clear recommendations.
Minocycline	Adult 100 mg PO q12h (200 mg PO qhs) Pediatric *not to be used in children < 8yo 2 mg/kg PO q12h (4 mg/kg PO qhs)	No adjustment necessary.
Moxifloxacin	Adult 400 mg PO/IV q24h Safety and efficacy not established in pediatrics.	No adjustment necessary.
Nelfinavir (NFV)	Adult 1250 mg PO q12h Pediatric 45-55 mg/kg PO q12h	No clear recommendations, but adjustment probably not necessary (<2% renal elimination).
Nevirapine (NVP)	Adult 200 mg PO q24h x14 days then increase to 200 mg PO q12h (immediate release tab) or 400 mg PO q24h (extended-release tab) Pediatric 4-7 mg/kg PO q12h	No adjustment necessary. Give dose after dialysis on dialysis days. Avoid if naïve and CD4 count > 250 cells/mm^3 in women and 400 cells/mm^3 in men
Nitrofurantoin	Adult 50-100 mg PO q12h Pediatric 1.25-1.75 mg/kg PO q6h	CrCl <50, HD/CAPD: Use is not recommended – will not reliably reach useful concentrations in urine and will have increased risk of toxicity
Oseltamivir	Adult 75 mg PO q12h Pediatric 30-75 mg PO q12h	*Same for Adult & Pediatric* CrCl 10-30: same dose PO q24h CrCl <10, HD/CAPD: No data.
Oxacillin	Adult	

	Methicillin-susceptible *S. aureus* bloodstream infections: 2g IV q4h Non-bloodstream infections 1-2g IV q4-6h <u>Pediatric</u> 16.7-50 mg/kg IV q4-6h (50-100 mg/kg/day)	No adjustment necessary.
Penicillin G	<u>Adult</u> 2 – 4 million units IV q4h - <u>Pediatric</u> 25,000-100,000 units/kg IV q4-6h (100,000-400,000 units/kg/day)	CrCl 10-50: 75% IV at same interval[+] CrCl <10: 2-4 million units q8h HD: Dose as CrCl <10. Give dose after dialysis on dialysis days. CAPD: Dose as CrCl <10. - CrCl 10-30: same dose q8h CrCl <10: same dose q12h HD: Dose as CrCl <10. Give dose after dialysis on dialysis days. CAPD: Dose as CrCl <10.
Penicillin VK	<u>Adult</u> 250-500 mg PO q6-8h <u>Pediatric</u> 6.25-16.7 mg/kg PO q6-8h (25-50 mg/kg/day)	No adjustment necessary. HD: Give dose after dialysis on dialysis days.
Pentamidine	<u>Adult</u> 4 mg/kg IV q24h - <u>Pediatric</u> 4 mg/kg IV q24h	No adjustment necessary. - CrCl 10-30: same dose q36h CrCl <10: same dose q48h
Piperacillin	<u>Adult</u> 3-4 g IV q4-6h - <u>Pediatric</u> 33.3-75 mg/kg IV q4-6h (200-300 mg/kg/day)	CrCl 10-50: same dose IV q6-8h CrCl <10: same dose IV q8h HD: Dose as CrCl <10. Give dose after dialysis on dialysis days. CAPD: Dose as CrCl <10. - CrCl 20-40: same dose q8h CrCl <20: same dose q12h HD: Dose as CrCl <20. Give dose after dialysis on dialysis days. CAPD: Dose as CrCl <20.
Piperacillin/tazobactam	<u>Adult</u>	

See dosing protocol on ASP website§	Extended 4hr infusion (standard at TNMC): 4.5 g IV q8h, infused over 4h Traditional, 30 minute infusion 3.375 g IV q6h or 4.5 g IV q8h Anti-pseudomonal dosing: 4.5 g IV q6h - <u>Pediatric</u> Extended infusion: over 40kg per adult dosing >2kg and ≤40kg, (all doses based on piperacillin component) 0-7 days: 100 mg/kg q12h, infused over 4h 8-28 days: 100 mg/kg q8h, infused over 4h >28 days: 100 mg/kg q6h, infused over 4h NOTE: all doses must be infused over 4 hours, except in NICU patients Traditional, 30 minute infusion 50-133.3 mg/kg (piperacillin) IV q6-8h [150-400mg/kg/day (piperacillin)]	Extended 4hr infusion (standard at TNMC): CrCl <20, HD/CAPD: 4.5 g IV q12h, infused over 4h Traditional, 30 minute infusion CrCl 20-40: 2.25 g IV q6h CrCl <20: 2.25 g IV q8h CrCl 20-40: 3.375 g IV q6h CrCl <20: 2.25 g IV q6h HD: Dose as CrCl <20 + 0.75 g IV after dialysis. CAPD: Dose as CrCl <20. - CrCl 20-40: 70%, same interval~~‡~~ CrCl <20, HD/CAPD: 70%, infuse q12h over 4 hours~~‡~~ CrCl 20-40: 70% IV q6h~~‡~~ CrCl <20: 70% IV q8h~~‡~~ HD/CAPD: No recommendations
Posaconazole Restricted to review and approval by the ID Service or the Hematology/Oncology Service	<u>Adult & Pediatric</u> (≥13 y.o.) 200-800 mg PO q6-24h (q6h dosing preferred for active disease due to saturable absorption) (Maximum 800 mg q24h) Take with high fat meal/nutritional supplement. Avoid concomitant use of proton-pump inhibitors & histamine receptor antagonists	No adjustment necessary. Therapeutic drug monitoring suggested. Obtain steady state trough (7 days). Goal for active disease is >1.25 mg/L
Primaquine	<u>Adult</u> 15-30 mg (primaquine base) PO q24h <u>Pediatric</u> 0.3 mg/kg (primaquine base) PO q24h	No clear recommendations, but adjustment probably not necessary (<1% renal elimination).
Pyrazinamide	<u>Adult</u> 25 mg/kg PO q24h (max dose 2gm PO for daily therapy)	CrCl <10: 15 mg/kg PO q24h HD: 25 mg/kg PO after each dialysis

	- <u>Pediatric</u> 10-40 mg/kg PO q12-24h (max dose 2gm PO for daily therapy) (20-40 mg/kg/day)	session. CAPD: No data. - CrCl <10, HD: 40 mg/kg PO 3x/week CAPD: No data.
Pyrimethamine	<u>Adult</u> 50-100 mg PO q24h <u>Pediatric</u> 1 mg/kg PO q12h	No adjustment necessary.
Quinupristin/dalfopristin	<u>Adult & Pediatrics</u> 7.5 mg/kg IV q8h	No adjustment necessary. No data for pediatrics.
Raltegravir (RAL)	<u>Adult and adolescent</u> ≥16yrs 400mg PO q12H With rifampin: 800 mg PO q12h <u>Pediatric</u> Not established in <16yrs	No adjustment necessary.
Ribavirin	<u>Adult</u> 400-600 mg PO q12h <u>Pediatric</u> 200-400 mg PO q12h	Same for Adult & Pediatric CrCl <50: Contraindicated.
Rifabutin	<u>Adult</u> 300 mg PO q24h <u>Pediatric</u> 5 mg/kg PO q24h	No adjustment necessary.
Rifampin	<u>Adult</u> Mycobacterial disease: 10 mg/kg (600 mg) PO daily Prosthetic valve infective endocarditis: 300 mg PO/IV q8h <u>Pediatric</u> 10-20 mg/kg PO/IV q24h	No adjustment necessary.
Rilpivirine (RVP)	<u>Adult</u>: 25 mg daily Do not coadminister with H2RA, PPI, or antacids	No dose adjustment necessary
Rimantidine	<u>Adult</u> 100 mg PO q12h - <u>Pediatric</u> 5 mg/kg PO q24h	CrCl <10: 100 mg PO q24h HD/CAPD: No data. - No clear recommendations.
Ritonavir (RTV)	<u>Adult</u>	

	100 mg PO q12h (in combination with another protease inhibitor) 100 mg PO q24h when coadministered with atazanavir or daily darunavir <u>Pediatric</u> 400 mg/m2 PO q12h	No adjustment necessary.
Saquinavir (SQV)	<u>Adult</u> 1000 mg PO q12h (w ritonavir 100 mg PO q12h) Not approved for use in pediatrics.	No data, but negligible renal clearance.
Stavudine (D4T)	<u>Adult</u> <60 kg: 30 mg PO q12h ≥60 kg: 40 mg PO q12h - <u>Pediatric</u> 1 mg/kg PO q12h	CrCl 26-50: 50% PO q12h‡ CrCl 10-25 and HD: 50% PO q24h‡ Give after dialysis on dialysis days. CAPD: No data. - CrCl 25-50: 50% PO q12h‡ CrCl <25: 50% PO q24h‡ HD: Dose as CrCl <25. Give after dialysis on dialysis days. CAPD: No data.
Sulfadiazine	<u>Adult</u> 2-4 g PO in 3-6 divided doses <u>Pediatric</u> 37.5 mg/kg PO q6h	No data.
Tenofovir (TDF)	<u>Adult</u> 300 mg PO q24h <u>Pediatric</u> 8 mg/kg PO q24h	Same for Adult & Pediatric CrCl 30-49: 300 mg q48h CrCl 10-29: 300 mg twice weekly CrCl <10: No data HD: 300 mg once weekly, given after dialysis if on a dialysis day. CAPD: No data.
Tetracycline	<u>Adult</u> 250-500 mg PO q6h - <u>Pediatric</u> *not to be used in children < 8yo 6.25-12.5 mg/kg PO q6h	CrCl >50-90: same dose PO q8-12h CrCl 10-50: same dose PO q12-24h CrCl <10: same dose PO q24h HD/CAPD: No data. - CrCl 50-80: same dose q8h CrCl 10-49: same dose q12h CrCl <10: same dose q24h HD/CAPD: No data.
Ticarcillin	<u>Adult</u> 3 g IV q4h	CrCl 30-60: 2 g IV q4h CrCl 10-30: 2 g IV q8h

	- <u>Pediatric</u> 25-75 mg/kg IV q4-6h (150-300 mg/kg/day)	CrCl <10: 2 g IV q12h HD: 2 g IV q12h with a 3 g IV supplement after each dialysis. CAPD: Dose as CrCl <10. - CrCl 10-30: same dose q8h CrCl <10: same dose q12h HD: Same dose 12h with dosing after dialysis. CAPD: Dose as CrCl <10.
Tigecycline (Restricted to ID Service review and approval)	<u>Adult</u> 100 mg IV load, then 50 mg IV q12h <u>Pediatric</u> Safety and efficacy not established in pediatrics.	Adults & Peds: Renal dysfunction: no adjustment necessary. Hepatic dysfunction, Child Pugh C: 100 mg IV load followed by 25 mg IV q12h
Tipranavir (TPV)	<u>Adult</u> 500 mg PO q12h (coadministered with ritonavir 200 mg PO q12h) <u>Pediatric</u> Safety and efficacy not established in pediatrics.	No data, but negligible renal clearance.
Tobramycin	<u>Adult & Pediatric</u> Extended interval dosing (most indications*): 7 mg/kg once daily • adjusted by serum level 6-14 hrs after start of infusion and Hartford nomogram (see PK training packet on ASP website§) 5 mg/kg/day may be used for UTIs - Traditional dosing 1.5-2.5 mg/kg IV q8h Monitoring of serum levels is recommended. *Refer to TNMC PK training packet on ASP website§ for exclusions to extended-interval dosing. - <u>Pediatric</u> Traditional dosing 1.5-2.5 mg/kg IV q8h	Extended interval dosing frequency determined by levels/Hartford nomogram - Traditional dosing (empiric, before levels): CrCl 51-90: 60-90% IV q8-12h‡ CrCl 10-50: 30-70% IV q12h‡ CrCl <10: 20-30% IV q24-48h‡ HD/CAPD: Dose according to levels.
Trimethoprim/sulfamethoxazole (TMP/SMX) 1 Bactrim DS tablet = 160mg(TMP)/800mg(SMX)	<u>Adult</u> PO Simple urinary tract infection: 1 Bactrim DS tablet PO q12h	Adults and Pediatrics, PO/IV Simple UTI, skin/skin structure, other infections CrCl <30: 50% of usual daily dose

Bactrim oral suspension = 40mg/5 mL (TMP)/ 200mg/5 mL (SMX)	Skin/skin structure infection/other infections: 1-2 Bactrim DS tablets PO q12h PCP treatment:15-20 mg/kg/day* (trimethoprim componenent) PO divided q6-8h IV Skin/skin structure infection: 10 mg/kg/day (ideal body weight) trimethoprim component divided q12h Severe Infections/PCP 15-20 mg/kg/day* (trimethoprim component) IV divided q6-8h *Ideal body weight, consider an adjusted body weight in severely ill obese patients. See equation for adjusted body weight at end of document - <u>Pediatric</u> PO/IV Simple urinary tract infection" 5 mg/kg (TMP) PO q12h Skin/skin structure infection/other infections: 10 mg/kg/day (TMP) IV divided q12h PCP treatment: 15-20 mg/kg/day (TMP) IV divided q6-8h	divided q12-24h HD: Dose as CrCl<30, administer after HD on HD days PCP treatment: CrCl 15-30: 15-20 mg/kg/day (trimethoprim component) q6-8h for 48 hours followed by 50% of usual daily dose divided q12h CrCl <15: 50% of usual daily dose divided q12h HD: Dose as CrCl<15, administer after HD on HD days
Valacyclovir	<u>Adult</u> 2 g PO q12h 1 g PO q8h 1 g PO q12h 1 g PO q24h 500 mg PO q12h	 CrCl 30-49: 1 g PO q12h CrCl 10-29: 500 mg PO q12h CrCl <10: 500 mg PO q24h CrCl 30-49: 1 g PO q12h CrCl 10-29: 1 g PO q24h CrCl <10: 500 mg PO q24h CrCl 30-49: no adjustment CrCl 10-29: 1 g PO q24h CrCl <10: 500 mg PO q24h CrCl 30-49: no adjustment CrCl 10-29: 500 mg PO q24h CrCl <10: 500 mg PO q24h CrCl 30-49: no adjustment CrCl 10-29: 500 mg PO q24h CrCl <10: 500 mg PO q24h

	500 mg PO q24h Safety and efficacy not established in pediatrics.	CrCl 30-49: no adjustment CrCl 10-29: 500 mg PO q48h CrCl <10: 500 mg PO 48h HD: Dose as CrCl <10. Give after dialysis on dialysis days. CAPD: 500 mg PO q48h
Valganciclovir	<u>Adult</u> Treatment, induction 900 mg PO q12h Treatment, maintenance 900 mg PO q24h Prophylaxis (dosing at TNMC) 450 mg PO q24h - <u>Pediatric</u> (Usual dosing at TNMC) Treatment 14 mg/kg PO q12h Maintenance or Prophylaxis 14 mg/kg PO daily	 CrCl 40-59: 50% PO same interval~~T~~ CrCl 25-39: 50% PO q24h~~T~~ CrCl 10-24: 50% PO q48h~~T~~ CrCl <10, HD/CAPD: Use is not recommended. CrCl 40-59: 50% PO same interval~~T~~ CrCl 25-39: 50% PO q48h~~T~~ CrCl 10-24: 50% PO twice weekly~~T~~ CrCl <10, HD/CAPD: Use is not recommended. CrCl 25-39: same dose PO q48h~~T~~ CrCl 10-24: 450 mg PO twice weekly~~T~~ CrCl <10, HD/CAPD: Use is not recommended. - CrCl 40-59: 50% PO same interval~~T~~ CrCl 25-39: 50% PO q24h~~T~~ CrCl 10-24: 50% PO q48h~~T~~ CrCl <10, HD/CAPD: Use is not recommended. CrCl 40-59: 50% PO same interval~~T~~ CrCl 25-39: 50% PO q48h~~T~~ CrCl 10-24: 50% PO twice weekly~~T~~ CrCl <10, HD/CAPD: Use is not recommended.
Vancomycin IV	<u>Adult</u> Standard*: 15-20 mg/kg IV q12h Consider loading dose in critically ill patients of 25 mg/kg x1dose	 *Dosing, therapeutic goals, and monitoring should be individualized for each patient; consult pharmacy. Refer to PK training packet on ASP website§ Troughs of 15-20 mcg/mL are

	- Pediatric 15-20 mg/kg IV q6h*	recommended for patients with MRSA bloodstream infections, endocarditis, meningitis, pneumonia, osteomyelitis, and septic arthritis. - CrCl 70-89: same dose q8h CrCl 46-69: same dose q12h CrCl 30-45: same dose q18h CrCl 15-29: same dose q24h CrCl <15, HD/CAPD: Measure trough levels to determine when to dose.
Vancomycin PO	125 mg PO q6h	No renal adjustment necessary
Voriconazole	Adult & Pediatric (>12 yo)* PO/IV Active disease: Loading dose of 6mg/kg PO/IV q12h x2doses, then 4 mg/kg PO/IV q12h Prophylaxis: 200 mg PO q12h (100 mg q12h if <40kg) Therapeutic drug monitoring is suggested. Voriconazole target trough at steady-state is 2 - 5.5 mg/L.	Hepatic dysfunction (Child Pugh A or B): 6mg/kg q12h x2doses then 50% of normal daily dose. Renal dysfunction: PO No adjustment necessary. IV CrCl <50, HD/CAPD: Caution with IV formulation due to accumulation of cyclodextrin vehicle.
Zanamivir IH	Adult and Pediatric ≥7 years Treatment: Two inhalations (10 mg total) twice daily for 5 days Adult and Pediatric ≥5 years Prophylaxis: Two inhalations (10 mg total) once daily for daily for 10 days	No adjustment necessary.
Zidovudine (AZT)	Adult PO: 300 mg PO q12h IV for intrapartum administration: 2 mg per kg body weight intravenously over 1 hour, followed by continuous infusion of 1 mg per kg body weight per hour. Refer to DHHS guidelines for dosage and duration for continuation post-partum - Pediatric PO: 160 mg/m2 PO q8h IV: 120 mg/m2 IV q6h	 CrCl <15, HD/CAPD: 100 mg PO q6-8h. Give after dialysis on dialysis days. CrCl <15, HD/CAPD: 1 mg/kg IV q6-8h. Give after dialysis on dialysis days. - No data.

*use Cockroft-Gault equation for patients ≥ 18 years old; use Schwartz method for patients < 18 years old

[Ŧ]When the recommended renal dosage adjustment is listed as a percentage change, this indicates that X% of the originally ordered dose should be given, NOT that the dose should be decreased by X%. For example, an adult with a CrCl between 10-50 ml/min would receive 30-70% of the originally ordered amikacin dose

[§]**Antimicrobial stewardship program (ASP) website:** www.nebraskamed.com/asp

Adults: Estimate of Creatinine Clearance using Cockroft-Gault equation

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) * \text{IBW}}{72 * \text{Scr}} \times 0.85 \text{(for females only)}$$

Scr = serum creatinine concentration in mg/dL; if patient is > 65 years old and Scr < 1 mg/dL, round up to 1.0

IBW = ideal body weight = IBW (males) = 50 + (2.3 x inches > 5 feet)

IBW (females) = 45.5 + (2.3 x inches > 5 feet)

NOTE: use actual body weight if less than ideal body weight

Adjusted body weight: ideal body weight + 0.4(actual body weight – ideal body weight)

Pediatrics: Estimate of Creatinine Clearance using Schwartz's equation

CrCl (ml/min) = K x L/Scr

K = Constant of proportionality that is age specific

Age	K
Preterm infants up to 1 year	0.33
Full-term infants up to 1 year	0.45
1-12 years	0.55
13-17 years female	0.55
13-17 years male	0.7

L = length or height in cm

Scr = serum creatinine concentration in mg/dL

Selected References

1. Gilbert DN, et al. *The Sanford Guide to Antimicrobial Therapy*, 38th Edition, 2008.
2. MICROMEDEX® Healthcare Series, 2012.
3. Livornese LL, et al. Use of antibacterial agents in renal failure. *Infectious Disease Clinics of North America*. 2004;18:551-79.
4. Taketomo CK, et al. *Pediatric Dosage Handbook*, 12th Edition, 2005.
5. Aronoff GR, et al. *Drug Prescribing in Renal Failure*, 4th Edition, 1999.

Dates Reviewed:

Antimicrobial Stewardship Program draft – October 2005, September 2008, January 2012

Medical Staff Pharmacy & Therapeutics Committee approved – April 2006, September 2008, October 2010, March 2012

Medical Staff Executive Committee approved – May 2006 **Updated March 2012**

ANTIMICROBIAL THEAPEUTIC INTERCHANGES

The most current version of the therapeutic interchange policies can be found online at http://www.preceptor.com/other/pharmadm/rxtipsite/default.asp.

Fluoroquinolones: Moxifloxacin

Before activating this interchange it is necessary for the pharmacist to verify the indication of the fluoroquinolone order. Moxifloxacin and ciprofloxacin are the fluoroquinolone antibiotics available on the inpatient formulary. Moxifloxacin is not eliminated through the kidneys. Therefore, the drug does not concentrate in the kidneys, and drug levels are not adequate to treat urinary tract infection; for urinary tract infections, interchange to ciprofloxacin should be performed. Additionally, when agents have been ordered for treatment of infection caused by *Pseudomonas* (including pneumonia or for empiric therapy of suspected pseudomonal infections), ciprofloxacin is the appropriate formulary agent. Conversely, when a fluoroquinolone has been ordered for treatment of suspected or documented community-acquired pneumonia (CAP), interchange to moxifloxacin should be performed because ciprofloxacin lacks activity against *Streptococcus pneumoniae,* one of the primary pathogens associated with CAP. Lastly, moxifloxacin is approved for monotherapy for intra-abdominal infections, but ciprofloxacin lacks anaerobic activity and must be used in combination with an anti-anaerobic agent for such infections. In summary, please refer to the following table for the preferred fluoroquinolone according to indication:

Moxifloxacin	**Ciprofloxacin**
CAP Single-agent therapy for intra-abdominal infections	Urinary tract infection Combination therapy for intra-abdominal infection (e.g., with metronidazole) Pseudomonal infections/cystic fibrosis

Interchange to moxifloxacin will occur per the below table:

Order written for:		**Dispense:**	
levofloxacin	250-750 mg IV q24h (adult)* 250-750 mg PO q24h (adult)*	Moxifloxacin	400 mg IV q24h 400 mg PO q24h • NO dosage adjustment necessary for renal or hepatic disease
gemifloxacin	320 mg PO q24h (adult)*		

*dosing/frequency adjustment recommended for renal or hepatic disease

Interchange to ciprofloxacin will occur per the below table!!:

Order written for levofloxacin	**Dispense ciprofloxacin**
250mg IV qd	200mg IV q12h
500mg IV qd	400mg IV q12h
750mg IV qd	400mg IV q8h*
250mg PO qd	250mg PO q12h
500mg PO qd	500mg PO q12h
750mg PO qd	750mg PO q12h

!!Ciprofloxacin dosing/frequency must be adjusted for renal impairment
*dose typically used for pseudomonal pneumonia

Beta-Lactams

Physicians may “opt out” of the therapeutic interchange program for clinical reasons by writing, “Do Not Substitute” in the Orders section of the chart.

For medications requiring renal dosage adjustment the therapeutic substitution should be performed on the dosage ordered and then the renal adjustment applied.

Penicillins

IF THIS IS ORDERED,	THIS WILL BE PROVIDED:
Cloxacillin (oral) (no longer manufactured) Nafcillin (IM/IV)	Dicloxacillin (½ dose and same frequency) Pediatrics: ½ dose and same frequency Oxacillin (IM/IV) (same dose and frequency) Pediatrics: same dose and frequency
Ticarcillin Timentin® 3.1g IV q4-6h Pediatrics: 200-300mg/kg/day (ticarcillin) divided q4-8h	Piperacillin (same dose and frequency) Pediatrics: same dose and frequency Piperacillin-tazobactam 4.5g IV q8h, infused over 4 hours (per dose substitution) Pediatrics: 100 mg/kg (piperacillin) q6-12h, infused over 4 hours

Ureidopenicillins (Piperacillin)

IF THIS IS ORDERED,	THIS WILL BE PROVIDED:
Piperacillin-tazobactaim 3.375-4.5g IV q6h Pediatrics: 150-400 mg/kg/d (piperacillin) divided q8h	Piperacillin-tazobactam 4.5g IV over 4h q8h Pediatrics: 100 mg/kg over 4h q6-12h

First-Generation Cephalosporins

IF THIS IS ORDERED:	THIS WILL BE PROVIDED:
Intravenous	
Cefazolin 1gm IV q6h Cefazolin 2gm IV q6h Pediatrics: 50-100mg/kg/day divided q6h	Cefazolin 1gm IV q8h Cefazolin 2gm IV q8h Pediatrics: 50-150mg/kg/day divided q8h
Oral	
Cefadroxil 500 – 1000 mg po bid Pediatrics: 30mg/kg/day divided q12h	Cephalexin 250 - 500mg po q6h Pediatrics: 25-150mg/kg/day divided q6h

Second-Generation Cephalosporins

IF THIS IS ORDERED:	THIS WILL BE PROVIDED:
Intravenous	
Cefotetan 1gm iv q12h Cefotetan 2gm iv q12h Pediatrics: 40-80mg/kg/day divided q12h	Cefoxitin 1gm iv q6h Cefoxitin 2gm iv q6h Pediatrics: 80-160mg/kg/day divided q6h
Cefamandole 500mg-1gm iv q4-8h Cefamandole 2 gm iv q4h Pediatrics: 50-150mg/kg/day divided q6h	Cefuroxime 750mg iv q8h Cefuroxime 1.5gm iv q8h Pediatrics: 75-150mg/kg/day divided q8h
Oral tablets/capsules	
Cefaclor 250mg po q8h Cefaclor 500mg po q8h	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Cefprozil 250mg po bid Cefprozil 500mg po bid	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Loracarbef 200mg po bid Loracarbef 400mg po bid	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid

Oral Suspensions (same conversions for pediatrics)	
Cefaclor 10 mg/kg bid Cefaclor 20 mg/kg bid	Cefuroxime 10mg/kg bid Cefuroxime 15 mg/kg bid
Cefprozil 7.5 mg/kg bid Cefprozil 15 mg/kg bid	Cefuroxime 10mg/kg bid Cefuroxime 15 mg/kg bid
Loracarbef 7.5 mg/kg bid Loracarbef 15 mg/kg bid	Cefuroxime 10mg/kg bid Cefuroxime 15 mg/kg bid

Third- Generation Cephalosporins

IF THIS IS ORDERED:	**THIS WILL BE PROVIDED:**
Intravenous	
For any population older than 4 weeks of age*: Cefotaxime 1g iv q8-12h Cefotaxime 2g iv q8-12h Pediatrics: 100-200mg/kg/day divided q6-8h	 Ceftriaxone 1g iv q24h Ceftriaxone 2g iv q24h Pediatrics: 50-100mg/kg/day divided q12-24h
If meningitis is suspected or confirmed: For any population older than 4 weeks of age*: Cefotaxime 2g iv q4-6h Pediatrics: 200mg/kg/day divided q6h	 Ceftriaxone 2g iv q12h Pediatrics: 100mg/kg/day divided q12-24h
Ceftizoxime 1gm iv q8-12h Ceftizoxime 2gm iv q8-12h Pediatrics: 150-200mg/kg/day divided q6-8h	Ceftriaxone 1g iv q24h Ceftriaxone 2g iv q24h Pediatrics: 100mg/kg/day divided q12-24h
Oral tablets/capsules	
Cefdinir 300mg po bid Cefdinir 600mg po qd	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Cefditoren 200mg po bid Cefditoren 400mg po bid	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Cefixime 200mg po q12h Cefixime 400mg po q24h	Cefuroxime axetil 250mg po bid Cefuroxime axetil 250mg po bid
Cefpodoxime 100mg po bid Cefpodoxime 200mg po bid	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Ceftibuten 400mg po qd	Cefuroxime axetil 250mg po bid Cefuroxime axetil 500mg po bid
Oral Suspensions *(same conversions for pediatrics)*	
Cefdinir 7 mg/kg bid	Cefuroxime 15 mg/kg bid
Cefixime 4 mg/kg bid Cefixime 8 mg/kg qd	Cefuroxime 10mg/kg bid Cefuroxime 15 mg/kg bid
Cefpodoxime 5mg/kg bid	Cefuroxime 15 mg/kg bid
Ceftibuten 9 mg/kg qd	Cefuroxime 15 mg/kg bid

*Ceftriaxone should not be used in infants with hyperbilirubinemia because of a concern for kernicterus.

Forth- Generation Cephalosporins: (applies to all adults and children >40kg)

IF THIS IS ORDERED:	**THIS WILL BE PROVIDED:**
Cefepime 1g q12hr	Cefepime 1g q12hr[a]
Cefepime 2g q12hr	Cefepime 1g q6hr
Cefepime 2g q8hr	Cefepime 1g q6hr
Cefepime 2g q8hr for "Neutropenic Fever"	Cefepime 2g q8hr*

[a]Only appropriate for community acquired pneumonia not due to *Pseudomonas aeruginosa* or for mild to moderate UTI. If 1g q12hr is ordered for any other indication, dose will be interchanged to 1g q6hr.

*Cefepime 2g q 8hrs is allowed only in neutropenic fever. Oordering clinicians must write the indication ("neutropenic fever") after ordering this dose. Pharmacists will review laboratory data in patients whom 2g q8h is ordered and no indication documented. If the Absolute Neutrophil Count (ANC) is ≤500 the 2g q8hr dose will be used. All other orders will be changed to 1g q6hr.

Carbapenems: Meropenem

Adults (≥18 years of age) and Children >50kg:

IF THIS IS ORDERED:	THIS WILL BE PROVIDED:
Meropenem 1g q8hr	Meropenem 500mg q6hr
Meropenem 1g q12hr	Meropenem 500mg q8h
Meropenem 500mg q8hr	Meropenem 500mg q8h
Meropenem 2g q8h	Meropenem 2g q8h
Imipenem/cilastatin 500mg q6h	Meropenem 500mg q6hr
Imipenem/cilastatin 500mg q8h	Meropenem 500mg q8h
Imipenem/cilastatin 1g q8	Meropenem 500mg q6hr
Imipenem/cilastatin 750mg q12h	Meropenem 500mg q8h
Imipenem/cilastatin 250mg q6h	Meropenem 500mg q8h

***For patients with a diagnosis of meningitis, cystic fibrosis or with microorganisms with a meropenem/ imipenem MIC of 4mg/L, the meropenem dose should be adjusted to 2 g q8hr. These are the only indications for which this dose is appropriate.**

Neonates & Pediatrics (<50kg):

Type of Infection	IF ORDERED	PROVIDED		
	Imipenem (mg/kg)	Meropenem (mg/kg)		Max dose
Sepsis and other indications	15-25 q6hr	Neonates 7 days & under	20 q12hr	--
		Neonates over 7 days/Children	20 q8hr	500 mg
Meningitis, cystic fibrosis, microorganisms with reported meropenem MIC of 4 mg/L	15-25 q6hr	Neonates 7 days & under	40 q12hr	--
		Neonates over 7 days/Children	40 q8hr	2 g

ANTIMICROBIAL IV TO PO CONVERSION PROTOCOLS

The most current version of the IV to PO Conversion Protocols can be found online at http://www.preceptor.com/other/pharmadm/tipsite/PocketCard.html.

Conversion Procedure:

1. Eligible patients will be identified by pharmacy based on the following criteria.
    a. Functioning GI tract
    b. Currently taking other PO or NG medications
    c. Patient is clinically improving
2. The pharmacist will stamp a short note (order) in the Orders section and the Progress section if necessary. The pharmacist will then enter the oral order into the computer system with start date entered 24 hours into the future.
3. If the physician feels that conversion to oral therapy is appropriate, but would like to use a different medication or dose, then he/she will discontinue the pharmacy initiated conversion order and write the desired order in the order section of the chart.
4. If the physician would not like the conversion to occur, he/she will write an order in the order section saying "**NO IV TO PO CONVERSION**". The pharmacist will discontinue the oral order and continue the IV order. The pharmacist at this time will also place a note in the comments section of the IV medication computer order with the current date and "NO IV TO PO CONVERSION", therefore identifying medications the physician does not want switched to oral.
5. If a physician has not written an order for "**NO IV TO PO CONVERSION**" within 24 hours, the pharmacist will assume that the recommendation is acceptable and will initiate the oral therapy.

All inpatient units are included in the IV to PO program.

Conversion Protocols

If the patient is on this IV medication...		Convert patient to this PO medication if they meet criteria for conversion...			
Drug	**Regimen**	**Drug**	**Regimen**	**Bioavailability**	**Month/Year Initiated**
Azithromycin (Zithromax®)	250 mg IV q24h 500 mg IV q24h	Azithromycin (Zithromax®)	250 mg PO/NG q24h 500 mg PO/NG q24h	37%	9/2000
Ciprofloxacin (Cipro®) Schedule doses to begin after HD	200 mg IV q12h 200 mg IV q24h 400 mg IV q12h 400 mg IV q24h	Ciprofloxacin (Cipro®)	250 mg PO/NG q12h 250 mg PO/NG q24h 500 mg PO/NG q12h 500 mg PO/NG q24h	60-80%	9/2000
Clindamycin (Cleocin®)	300 mg IV q6h 300 mg IV q8h 600 mg IV q6h 600 mg IV q8h 900 mg IV q6h 900 mg IV q8h	Clindamycin # (Cleocin®)	150 mg PO/NG q6h 150 mg PO/NG q8h 300 mg PO/NG q6h 300 mg PO/NG q8h 450 mg PO/NG q6h 450 mg PO/NG q8h	90%	7/2002
Fluconazole (Diflucan®)	100 mg IV q24h 200 mg IV q24h	Fluconazole (Diflucan®)	100 mg PO/NG q24h 200 mg PO/NG q24h	90%	9/2000
Linezolid (Zyvox®)	600 mg IV q12h	Linezolid (Zyvox®)	600 mg PO/NG q12h	100%	7/2002
Metronidazole (Flagyl®)	500 mg IV q6h 500 mg IV q8h	Metronidazole (Flagyl®)	500 mg PO/NG q6h 500 mg PO/NG q8h	100%	9/2000
Moxifloxacin[y]	400 mg IV	Moxifloxacin[y]	400 mg PO q24h	90%	7/2002

(Avelox®)	q24h	(Avelox®)			
Rifampin (Rifadin®)	IV q8-24h	Rifampin (Rifadin®)	Equivalent rifampin dose (same dose as IV) q8-24h	90-95%	7/2002
TMP-SMX (Bactrim®)	IV q6-12h	TMP-SMX (Bactrim®)	Equivalent TMP dose PO/NG q6-12h	90-100%	7/2002

Diarrhea at higher oral dose and frequency.

y Levofloxacin, gatifloxacin, and trovafloxacin will be subject to the automatic therapeutic interchange program for IV and PO quinolones (unless the prescriber writes "Do Not Substitue"). No dosage adjustment is necessary for renal or hepatic dysfunction. Check microbiology results for susceptibility data when appropriate.

ANTIMICROBIAL DRUG-FOOD INTERACTION CHART

Antimicrobial	Drug-Food Interaction	Type of Interaction	Patient Directions
Abacavir	None		
Acyclovir	None		
Adefovir	None		
Amantadine	None		
Amoxicillin	None		
Amoxicillin/ clavulanate	None		
Ampicillin	Food	Food may result in a decreased ampicillin concentration	Take the medicine on an empty stomach, 1 hour before or 2 hours after meals with a full glass of water
Atovaquone	Food	Food, particularly high fat, increases atovaquone exposure	Take this medicine with a full meal.
Azithromycin	None		
Cefaclor	Food	Possible decrease in cefaclor concentrations	Take this medicine with or without food
Cefdinir	None		
Cefixime	None		
Cefpodoxime	None		
Cefprozil	None		
Cefuroxime	None		
Cephalexin	None		
Ciprofloxacin	Caffeine	Possible increase in caffeine concentrations and enhanced CNS stimulation	This typically occurs in heavy caffeine users. Avoid/minimize caffeine (coffee, soda, chocolate) while using this medicine.

	Cations (aluminum, calcium, magnesium, iron), antacids, dairy products	Possible decrease in ciprofloxacin concentrations	Take without food. Do not take with milk, yogurt, or other dairy products. Take 2h before or 6h after administration of di-/tri-valent cations (aluminum, calcium, magnesium, iron) or antacids.
Clarithromycin	None		
Clindamycin	None		
Dapsone	None		
Dicloxacillin	None		
Didanosine	Food	Food may reduce didanosine exposure	Take this medicine on an empty stomach.
Doxycycline	None		
Efavirenz	Food	Food may increase absorption	Take this medicine on an empty stomach, preferably at bedtime. Swallow this medicine with water.
Entecavir	Food	Food may decrease entecavir exposure	Take this medicine on an empty stomach, at least 2 hours before or 2 hours after a meal
Erythromycin	Food	Food may result in altered erythromycin concentrations	Best taken on an empty stomach, but may be taken with a low-fat meal/snack to prevent stomach upset.
	Grapefruit Juice	Possible increase in bioavailability	Try to avoid grapefruit juice when possible.
Erythromycin/sulfisoxazole	Food	Food may result in altered erythromycin concentrations	Best taken on an empty stomach, but may be taken with food if stomach upset occurs.
	Grapefruit Juice	Possible increase in bioavailability	Try to avoid grapefruit juice when possible.
Ethambutol	None		
Famciclovir	None		

Fluconazole	None		
Flucytosine	None		
Ganciclovir	None		
Gemifloxacin	Cations (aluminum, calcium, magnesium, iron), antacids	Possible decrease in gemifloxacin concentrations	Take without food. Do not take with milk, yogurt, or other dairy products. Take 2h before or 3h after administration of di-/tri-valent cations (aluminum, calcium, magnesium, iron) or antacids.
Indinavir	Food	Food may decrease bioavailability of indinavir	Take on an empty stomach, at least 1 hour before or 2 hours after a meal. Drink water, skim or non-fat milk, juice, coffee, or tea when taking the medicine. If you need to take the medicine with food, eat a small, low-fat, low-protein meal.
Isoniazid	Tyramine-containing food	Tyramine foods may increase blood pressure	Avoid foods or drinks that contain tyramine. This includes aged cheeses, dried meats, sauerkraut, soy sauce, tap beers, or red wines.
	Food	Food may decrease isoniazid exposure	Take on an empty stomach (1 hour before or 2 hours after a meal). May be taken with food to avoid stomach upset.
	Histamine-containing foods	Possible exaggerated response to histamine-containing foods	Fish (tuna, skipjack, or other tropical fish) may cause headache, flushing, pounding heartbeat, sweating, dizziness, chills, or diarrhea. If you have these symptoms, call your doctor.
Itraconazole	Food	Food may decrease or increase bioavailability, depending on the dosage form	Take the **capsule** just after eating a full meal. Take the oral **solution** on an empty stomach.
	Grapefruit Juice	Possible decrease in bioavailability	Try to avoid grapefruit juice when possible.
Lamivudine	None		
Levofloxacin	Cations (aluminum, calcium, magnesium,	Possible decrease in levofloxacin concentrations	Take without food. Do not take with milk, yogurt, or other dairy products. Take 2h before or 2h after administration of di-/tri-valent cations (aluminum, calcium, magnesium, iron) or antacids.

	iron), antacids, dairy products		
Linezolid	Tyramine-containing food	Tyramine foods may result in a significant pressor response	Avoid foods or drinks that contain tyramine. This includes aged cheeses, dried meats, sauerkraut, soy sauce, tap beers, or red wines.
Lopinavir/ ritonavir	None		
Metronidazole	None		
Minocycline	Cations (aluminum, calcium, magnesium, iron), antacids, dairy products	Possible decrease in minocycline concentrations	Take without food. Do not take with milk, yogurt, or other dairy products. Take 2h before or 6h after administration of di-/tri-valent cations (aluminum, calcium, magnesium, iron) or antacids.
Moxifloxacin	Cations (aluminum, magnesium, iron), antacids	Possible decrease in moxifloxacin concentrations	Take without food. Take 4h before or 8h after administration of di-/tri-valent cations (aluminum, magnesium, iron) or antacids.
Nelfinavir	Food	Food may increase nelfinavir exposure	Take this medicine with food or milk.
Nevirapine	None		
Nitrofurantoin	None		
Oseltamivir	None		
Penicillin VK	None		
Posaconazole	Food	Food, particularly high fat, may increase posaconazole exposure and increase concentrations	Take this medicine with food or a liquid nutritional supplement
Primaquine	Grapefruit Juice	Possible increase in plasma	Try to avoid grapefruit juice when possible.

		concentrations	
Pyrazinamide	None		
Pyrimethamine	None		
Ribavirin	None		
Rifabutin	None		
Rifampin	Food	Food may decrease rifampin concentrations	Rifampin should be taken on an empty stomach, 1 hour before or 2 hours after a meal.
Rimantadine	None		
Ritonavir	None		
Saquinavir	Grapefruit Juice	Possible increase in bioavailability	Take this medicine within two hours after eating a full meal. The medicine may not work as well if you take it on an empty stomach. Try to avoid grapefruit juice.
Stavudine	None		
Sulfadiazine	None		
Telithromycin	None		
Tenofovir	None		
Tetracycline	Cations (aluminum, calcium, magnesium, iron), antacids, dairy products	Possible decrease in tetracycline concentrations	It is best to take this medicine on an empty stomach, 1 hour before or 2 hours after a meal. Swallow the medicine with a full glass of water. Do not take with milk, yogurt, or other dairy products. Take 2h before or 6h after administration of di-/tri-valent cations (aluminum, calcium, magnesium, iron) or antacids.
Tipranavir	None		
Trimethoprim	None		
Trimethoprim/ sulfamethoxazole	None		
Valacyclovir	None		

Valganciclovir	High Fat Food	Possible increase in ganciclovir exposure	Take this medicine with food or milk.
Voriconazole	Food	Possible decrease in voriconazole exposure	Take this medicine at least 1 hour before or 1 hour after a meal.
Zalcitabine	None		
Zanamivir	None		
Zidovudine	None		

INFECTION CONTROL

Contact Information

- Telephone – 559-5276; Campus zip code #4031
- 24 hour on-call through hospital operator 559-4000 or 552-2000
- Website – The Nebraska Medical Center Intranet → Departments → Infection Control
- Medical Director: Mark E. Rupp, M.D., 559-5276
- Manager: Nedra Marion, R.N., 559-7968

Isolation Precautions

Patients with various conditions are placed into isolation to minimize the risk of transmission to other patients and healthcare workers. A full listing of isolation precautions can be found at the Healthcare Epidemiology Website http://intranet.nebraskamed.com/nursing/healthcareepidemiology/Isolation.aspx. These recommendations are based on guidelines from the Centers for Disease Control and Prevention (CDC) http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html

There are four major classifications of isolation precautions:

Standard Precautions

All patients should be cared for using standard precautions. All patients should be considered to potentially harbor a bloodborne pathogen. Standard precautions require adherence to hand hygiene recommendations (at a minimum, hand hygiene upon entering and leaving the patient room) and use of barrier precautions (gown, gloves, eye-protection, etc.) for contact with blood or body fluids.

Contact Precautions

Contact precautions are utilized in the care of patients infected or colonized with epidemiologically important microorganisms that can be transmitted via direct contact or indirect contact with environmental surfaces and vectors. The most common bacteria requiring contact isolation are MRSA, VRE, *C. difficile*, and multi-drug resistant gram-negative bacilli. Precautions include:

- Private room (cohorting is considered at times of limited bed availability, consult the Department of Healthcare Epidemiology)
- Strict adherence to hand hygiene
- Gloves
- Gowns if contact is anticipated between the healthcare worker's clothing and the patient or patient-care environment
- Masks/eye protection if patient has respiratory infection and is coughing/being suctioned or has wound irrigation
- Dedicated patient care equipment (stethoscope, scale, etc.)

Droplet Precautions

Droplet precautions are used for a patient known or suspected to be infected with a pathogen transmitted by respiratory droplets. The most common organisms requiring use of droplet precautions are meningococcus, influenza, and pertussis. Precautions include:

- Private room (cohorting is considered at times of limited bed availability, consult the Department of Healthcare Epidemiology)
- Strict adherence to hand hygiene
- Mask (surgical) upon entering room

Airborne Precautions

Airborne precautions are utilized in the care of patients known or suspected to be infected with pathogens transmitted by airborne droplet nuclei (small particles that can

remain suspended in the air). The most common diseases/pathogens requiring airborne precautions are pulmonary tuberculosis, chickenpox, and disseminated varicella. Precautions include:

- Private room with negative pressure and special ventilation – contact infection control or access services to get room setup
- N-95 respirators are used for care of patients known or suspected to be infected with tuberculosis or other pathogens that are transmitted via an airborne route (Healthcare workers should be fit-tested before wearing N-95 respirators or caring for patients in airborne isolation).

In addition to the 4 major transmission-based isolation categories above, additional precautions are utilized in the care of certain immunocompromised patient populations. These precautions are used in OHSCU for profoundly neutropenic hosts and can be instituted in other areas of the hospital for similar patients. The specific measures are more fully described in the NMC Nursing Practice Guidelines posted on the institutional intranet under policy PG103 "Immunocompromised: risk for Infection" http://intranet.nebraskamed.com/nursing/manuals.aspx. These measures include the following:

- Private room
- Strict adherence to hand hygiene
- No persons with respiratory infections or other communicable illnesses should enter
- No live plants or flowers
- No fresh fruit or vegetables

Isolation Precautions Quick Reference

A full listing of pathogens/diseases and required isolation measures can be found at the Infection Control Intranet site:
http://intranet.nebraskamed.com/nursing/healthcareepidemiology/Policies.aspx

Disease/Pathogen	Precaution	Duration
Anthrax – Cutaneous Pulmonary	Contact Standard	Until resolved N/A
Antibiotic resistant bacteria (MRSA, VRE, multi-drug resistant gram-negative bacilli)	Contact	Varies with type of bacteria - see website
Chickenpox – Symptomatic Incubating	Airborne/Contact Airborne	Until lesions crusted From day 10-21
Clostridium difficile colitis	Contact	1 week after treatment is completed and asymptomatic (whichever is longer)
Gastroenteritis – rotavirus, norovirus, etc	Contact	Until symptoms resolved
Influenza	Droplet	Duration of illness
Measles	Airborne	Duration of illness
Meningitis – unknown Meningococci *H. influenzae*	Droplet Droplet Droplet	Until patient has received 24 hours of effective antibiotic
Pertussis	Droplet	Until patient has received 7 days of appropriate antibiotic
Respiratory Syncytial Virus	Contact	See RSV isolation pathway
Tuberculosis (pulmonary or laryngeal)	Airborne	Refer to TB control plan
Zoster/Shingles Localized Disseminated	 Standard Airborne	 Duration of illness Duration of illness

Removing a Patient from Isolation

MRSA and VRE

Patients infected or colonized with MRSA or VRE may remain colonized for prolonged periods and may continue to shed organisms into the environment, serving as a nidus for continued transmission. To document that a patient is "decolonized," obtain screening cultures (rectal swabs for VRE or nares swabs for MRSA).

-Patient should be off antibiotics for at least 48 hours

-Cultures should be obtained three times, at least one week apart

Tuberculosis

Patients with known or suspected TB can be removed from airborne isolation in the following situations:

a. Suspected TB

-Diagnosis is confirmed to be something other than tuberculosis, and tuberculosis is no longer in the differential diagnosis.

OR

-Three sputum specimens from three separate days are reported as negative for acid fast bacilli (AFB).

b. Smear positive for AFB

-Cultures or other laboratory tests reveal AFB to be other species of AFB (non-tuberculous).

c. Known Pulmonary TB

-Patient is on effective therapy

-Patient is clinically improving

-Sputum smear is AFB-negative on three separate days

Guidelines for Prevention of Central Venous Catheter-Related Infections

1. Insert the central venous catheter (CVC) at the subclavian site unless the site is unavailable or medically contraindicated.
2. Use full sterile barrier precautions in the insertion of a CVC which includes:
   - Long sleeve sterile gowns
   - Sterile gloves
   - Cap
   - Mask
   - Full-size sterile drape
   - Eye protection (bloodborne pathogen precautions)
3. Use 2% chlorhexidine with 70% alcohol for local skin antisepsis. Use repeated back and forth strokes of the applicator sponge for approximately 30 seconds. Use of chlorhexidine is contraindicated in infants less than 2 months of age.
4. If any component of the catheter or kit becomes contaminated, discard and replace with a sterile device or new kit.
5. After insertion, the site should be covered with a sterile, transparent dressing. Dressings should be changed every 7 days and as needed if the dressing becomes loose, damp, or soiled.
6. Catheters placed under emergent or non-sterile conditions should be removed and replaced at a new site when the patient's condition allows.
7. The catheter hub or connector should be scrubbed vigorously with friction with 70% alcohol for at least 5 seconds before the catheter is accessed.
8. Remove unnecessary catheters as soon as possible

Full recommendations and supporting literature are available at
http://www.cdc.gov/hicpac/pubs.html

Guidelines for Prevention of Nosocomial Pneumonia

1. Disinfect and sterilize respiratory therapy equipment and ventilator circuits per approved guidelines and recommendations.
2. Practice good standard infection control precautions. Disinfect hands when moving from a dirty area or task to a clean area or task.
3. Remove endotracheal tubes, nasogastric tubes (NG), and other devices as soon as possible.
4. Elevate the head of the bed at 30-45º.
5. Vaccinate with pneumococcal and influenza vaccines in appropriate individuals.

Full recommendations and supporting literature are available at
http://www.cdc.gov/hicpac/pubs.html

Guidelines for Prevention of Surgical Site Infections

1. Prophylactic antibiotics should be administered no more than 60 minutes prior to skin incision.
2. If the operation is prolonged, a second dose of antibiotics should be administered depending on the half-life of the antibiotic (cefazolin – administer a second dose at four hours).
3. Dose prophylactic antibiotics based on the weight of the patient (e.g. 2 grams of cefazolin for patients $\geq$ 80 kg).
4. Continue prophylactic antibiotics for no more than 24 hours after the end of the procedure.
5. Do not remove hair at the operative site unless necessary. If hair is removed, used electric clippers and remove hair in the pre-operative area just prior to the procedure. Do not use a razor blade to remove hair.
6. Thoroughly disinfect the skin at the operative site using an approved disinfectant.
7. Maintain blood glucose levels ($\leq$ 200 mg/dl), particularly in diabetic patients.
8. Maintain normothermia (temperature ≥36°C).
9. Maintain dressing on a primarily closed incision for 24-48 hours. Do not expose the wound to tap water for at least 48 hours (if healing normally) or longer (for non-intact wound).

Full recommendations and supporting literature are available at
http://www.cdc.gov/hicpac/pubs.html

Guidelines for Prevention of Urinary Tract Infections

1. Indwelling urinary catheters should be used only when absolutely necessary, should not be used solely for personnel convenience, and should be discontinued as soon as possible.
2. Hand hygiene should be done immediately before and after any manipulation of the catheter site or apparatus.
3. Use as small a catheter as possible, consistent with good drainage.
4. Secure indwelling catheters properly after insertion to prevent movement and urethral traction.
5. A sterile closed drainage system is to be used with indwelling catheters.
6. The meatal-catheter junction and the entire perineal area shall be washed with a clean washcloth and soap and water daily and as needed.
7. Indwelling catheters should not be changed at arbitrary fixed intervals. In general, if the urine is flowing freely, the catheter is not encrusted, and the drainage bag is functioning well, then there is no need to change the system.

Full recommendations and supporting literature are available at
http://www.cdc.gov/hicpac/pubs.html

Bloodborne Pathogen Exposure

The Department of Employee Health staffs a 24-hour hotline to ensure timely evaluation of bloodborne pathogen (BBP) exposures.

If you experience a potential exposure to BBP you should do the following:

1. Stop the procedure, or excuse yourself from continuation, as soon as it is feasible and safe for the patient.
2. Wash the affected area with soap and water.
3. Report your exposure to the 24-hour hotline using the Employee Health Department **888-OUCH** pager.
4. Follow the instructions regarding further evaluation and post-exposure prophylaxis

Reportable Diseases

Nebraska law requires clinical laboratory personnel and physicians to report evidence of actual communicable disease to the local health department or the State Health Department of Health. In such instances, Healthcare Epidemiology will complete a Disease Case Report and send it to the County Health Department. A copy will be sent to the attending physician of the patient. The relevant language in the Nebraska statute can be found in Nebraska Health and Human Services Title 173 – Control of Communicable Diseases or online at http://www.hhs.state.ne.us/reg/t173.htm**.** Please call Healthcare Epidemiology if you have concerns about the reporting. Diseases reportable to the health department include:

The following diseases, poisonings, and organisms must be reported **immediately**:

Anthrax (*Bacillus anthracis*^)*
Botulism (*Clostridium botulinum*)*
Brucellosis (*Brucella abortus^, B. melitensis^, and B. suis**
Cholera *(Vibrio cholerae*)
Coccidiodomycosis (*Coccidioides immitis/posadasii*)*
Diphtheria (*Corynebacterium diphtheriae*)
Eastern equine encephalitis (EEE virus)*
Food poisoning, outbreak-associated
Glanders *[Burkholderia (Pseudomonas) mallei]**
Haemophilus influenzae infection (invasive disease only)
Hantavirus pulmonary syndrome (Sin Nombre virus)
Hemolytic uremic syndrome (post-diarrheal illness)
Hepatitis A (IgM antibody-positive or clinically diagnosed during an outbreak)
Influenza due to novel or pandemic strains (includes highly pathogenic avian influenza virus)*
Measles (Rubeola)
Melioidosis [*Burkholderia (Pseudomonas) pseudomallei*]*
Meningitis (*Haemophilus influenzae or Neisseria meningitidis*)
Meningococcal disease, invasive (*Neisseria meningitidis*)
Monkeypox virus infection*
Pertussis [whooping cough] (*Bordetella pertussis*)
Plague (*Yersinia pestis*)*
Poliomyelitis, paralytic
Q *fever (Coxiella burnetii)**
Rabies (human and animal cases and suspects)
Ricin poisoning*
Rift Valley fever*
Rocky Mountain Spotted Fever (*Rickettsia rickettsii*)*
Rubella and congenital rubella syndrome
Severe Acute Respiratory Syndrome [SARS] (SARS-associated coronavirus)

Smallpox*
Staphylococcal enterotoxin B intoxication*
Staphylococcus aureus, vancomycin-intermediate/resistant (MIC ≥ 4 μg/mL)
Tick-borne encephalitis, virus complexes (Central European Tick-borne encephalitis virus, Far Eastern Tick-borne encephalitis virus, Kyasanur Forest disease virus, Omsk Hemorrhagic Fever virus, Russian Spring and Summer encephalitis virus)*
Tularemia (*Francisella tularensis*)*
Typhus Fever, louse-borne *(Rickettsia prowazekii)** and flea-borne / endemic murine (*Rickettsia typhi*)
Venezuelan equine encephalitis*
Viral hemorrhagic fever (including but not limited to Ebola virus, Marburg virus, and Lassa fever virus)*
Yellow Fever

The following diseases, poisonings, and organisms must be reported **within seven days** of detection or diagnosis:

Acquired Immunodeficiency Syndrome (AIDS)
Adenovirus infection (conjunctivitis, respiratory)
Amebae-associated infection (*Acanthamoeba* spp., *Entamoeba histolytica*, and *Naegleria fowleri)*
Arboviral infections (including, but not limited to, West Nile virus, St. Louis encephalitis virus, Western Equine Encephalitis virus, and Dengue virus)
Babesiosis (*Babesia* species)
Campylobacteriosis (*Campylobacter* species)
Carbon monoxide poisoning (use breakpoint for non-smokers)
Chancroid (*Haemophilus ducreyi)*
Chlamydia trachomatis infections (nonspecific urethritis, cervicitis, salpingitis, neonatal conjunctivitis, pneumonia)
Clostridium difficile (antibiotic-associated colitis and pseudomembranous colitis)
Creutzfeldt-Jakob Disease (subacute spongiform encephalopathy [14-3-3 protein from CSF or any laboratory analysis of brain tissue suggestive of CJD])
Cryptosporidiosis (*Cryptosporidium parvum*)
Cyclosporiasis (*Cyclospora cayetanensis*)
Ehrlichiosis, human monocytic (*Ehrlichia chaffeenis)*
Ehrlichiosis, human granulocytic (*Ehrlichia phagocytophila*)
Encephalitis (caused by viral agents)
Escherichia coli gastroenteritis (*E. coli* O157-H7^ and other Shigatoxin-positive *E. coli* from gastrointestinal infection)
Giardiasis (*Giardia lamblia*)
Gonorrhea (*Neisseria gonorrhoeae*): venereal infection and ophthalmia neonatorum
Hansen's Disease (Leprosy [*Mycobacterium leprae]*) ‡
Hepatitis B infection (positive surface antigen tests and all IgM core antibody tests, both positive and negative)
Hepatitis C infection (all positive screening tests [e.g. EIA, ELISA, etc.] are reportable; all confirmatory tests [e.g. RIBA, NAT tests such as PCR for qualitative, quantitative, and genotype testing] are reportable regardless of result [i.e., both positive and negative tests])
Hepatitis D and E infection
Herpes simplex, primary genital infection
Histoplasmosis (*Histoplasma capsulatum)*
Human immunodeficiency virus infection
Influenza deaths, pediatric (< 18 years of age)
Influenza (Antigen or PCR positive or culture confirmed)
Kawasaki disease (mucocutaneous lymph node syndrome)
Lead poisoning
Legionellosis (*Legionella* species)
Leptospirosis (*Leptospira interrogans*)
Listeriosis (*Listeria monocytogenes*)
Lyme disease (*Borrelia burgdorferi*)

Lymphocytic choriomeningitis virus infection
Lymphogranuloma venereum (LGV [*Chlamydia trachomatis*])
Malaria (*Plasmodium* species)
Meningitis, including viral, bacterial, and fungal (all such cases must be reported within seven days except those caused by *Haemophilus influenzae and Neisseria meningitidis*, which must be reported immediately)
Mumps
Mycobacterium spp. (including *M. tuberculosis* complex organisms)
Necrotizing fasciitis
Norovirus infection (laboratories only)
Poisoning or illness due to exposure to agricultural chemicals (herbicides, pesticides, and fertilizers), industrial chemicals, mercury, or radiologic exposures
Psittacosis (*Chlamydophila psittaci*)
Respiratory syncytial virus infection (laboratories only)
Retrovirus infections (other than HIV)
Rheumatic fever, acute (cases meeting the Jones criteria only)
Rotavirus infection \
Salmonellosis, including typhoid fever (*Salmonella* serogroup)
Shiga toxin-positive gastroenteritis (enterhemorrhagic *E coli* and other shiga toxin-producing bacteria)
Shigellosis (*Shigella* species)
Streptococcal disease (all invasive disease caused by Groups A and B streptococci)
Syphilis (*Treponema pallidum*) RPR and FTA reactive
Syphilis, congenital
Tetanus (*Clostridium tetani*)
Toxic shock syndrome
Toxoplasmosis, acute (*Toxoplasma gondii)*
Transmissible spongiform encephalopathies
Trichinosis (*Trichinella spiralis*)
Tuberculosis (see *Mycobacterium* spp.)
Varicella primary infections (chicken pox)
Varicella death (all ages)
Yersiniosis (*Yersinia* species not *Y. pestis*)

*Potential agents of bioterrorism

APPENDIX A. Antibiotic Abbreviations for Susceptibility Reports

ANTIBIOTIC	ABBREVIATION
Amikacin	AK
Ampicillin	AM
Ampicillin/sulbactam (Unasyn)	AS
Amoxicillin/clavulanate (Augmentin)	AUG
Azithromycin	AZI
Aztreonam	AZT
Carbenicillin	CB
Cefazolin	CFZ
Cefepime	CEP
Cefotaxime	CFT
Cefotetan	CTN
Cefoxitin	CFX
Ceftazidime	CAZ
Ceftriaxone	CTX
Cefuroxime	CRM
Chloramphenicol	CH
Ciprofloxacin	CP
Clarithromycin	CLR
Clindamycin	CD
Colistin	COLI
Daptomycin	DAP
Doxycycline	DC
Ertapenem	ERT
Erythromycin	E
Gentamicin 500 Synergy	GM500
Gentamicin	GM
Hi level Gentamicin	GMS
Hi level Streptomycin	STS
Imipenem	IMP
Levofloxacin	LVX
Linezolid	LZD
Meropenem	MERZ
Metronidazole	MTZD
Mezlocillin	MZ
Moxifloxacin	MXF
Naladixic Acid	NAL
Nitrofurantoin	FD
Norfloxacin	NXN
Ofloxacin	OFL
Oxacillin	OX
Penicillin	P
Piperacillin/tazobactam (Zosyn)	PTZ
Piperacillin	PI
Quinupristin/dalfopristin (Synercid)	SYD
Rifampin	RIF
Streptomycin 2000 Synergy	ST2000
Tetracycline	TE
Ticarcillin/clavulanate (Timentin)	TIM
Tigecycline	TGC
Tobramycin	TO
Trimethoprim-sulfamethoxazole	SXT
Vancomycin	VA