WHEN IS THE DUAL ANTIBIOTHERAPHY PREFERRED?

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The management of infected critically ill patients is a challenge for ED and ICU physicians.

Patients admitted with symptoms prior to hospitalization are considered to have community-acquired infections, and those who develop infection more than 48 hours following admission are considered to have hospital-acquired, or nosocomial infections.

Seriously ill patients presenting with fever must be quickly evaluated for possible infection because most are treatable.

However, drug fever, hypersensitivity reaction, collagen vascular disease, neoplastic disease, pulmonary embolism, trauma, burns, pancreatitis, hypothalamic dysfunction, and other non-infectious causes of fever must be considered in the differential diagnosis.

In contrast, some patients may appear to be stable but nonetheless have serious infections.

--Elderly patients,

--uremic patients,

--patients with end-stage liver disease

or those receiving corticosteroids

often will fail to mount a significant febrile response even to serious infection.

In addition, some infections are notorious for presenting with minimal symptoms—these include

- infective endocarditis,
- spontaneous bacterial peritonitis,
- intraabdominal abscess,
- endophthalmitis
- meningitis.

In the absence of other symptoms and signs, fever in the

asplenic patient,

neutropenic or immunosuppressed patient,

intravenous drug user or alcoholic,

elderly patient

requires a rapid and thorough diagnostic evaluation.

The infectious syndromes that may require direct admission and immediate therapy in the ICU:

- Sepsis
- Community acquired pneumonia
- Urosepsis
- Infective endocarditis
- Intraabdominal infections
- Necrotizing soft tissue infections

SEPSIS

Sepsis, severe sepsis, and septic shock can be considered points on a continuum describing increasing severity of a patient's individual systemic response to infection.

A prospective observational study demonstrated that among hospitalized patients meeting the criteria for SIRS, 26% subsequently developed sepsis, 18% developed severe sepsis, and 4% developed septic shock.

The interval from SIRS to severe sepsis and septic shock was inversely correlated with the number of SIRS criteria met. The mortality rates of sepsis, severe sepsis, and septic shock were 16%, 20%, and 46%, respectively.

MICROBIOLOGIC ETIOLOGY

Virtually any microorganism can cause sepsis or septic shock, including bacteria, viruses, protozoa, fungi, spirochetes, and rickettsiae.

Bacteria remain the most common etiologic agent responsible for sepsis.

Gram-negative sepsis cannot be distinguished from gram positive sepsis on the basis of clinical characteristics alone.

However, certain epidemiologic, host, and clinical factors increase the likelihood of particular organisms.

For example, *Escherichia coli is the most frequently demonstrated etiologic* agent of sepsis largely because the urinary tract is the most common source of infection.

A coordinated approach to early treatment of sepsis is associated with reduced mortality.

This “early goal-directed” therapy, targeted on the first hours of care in the emergency department and ICU, focuses on :

Adequate fluid replacement first (to achieve central venous pressure of 8–12 mm Hg) and then

Vasopressors as needed to maintain a mean arterial pressure of greater than 65 mm Hg.

ANTIBIOTICS

The next therapeutic challenge is choosing appropriate antibiotics. All available clinical, epidemiologic, and laboratory data should be considered in making this decision.

Rarely is the causative microorganism known at the time treatment for sepsis is initiated,

Table 1 Potential bacteria responsible for sepsis depending on the site of infection and suggested antibiotics for use in severe infections

Site	Bacteria	%	Suggested treatment
Urinary tract infections (severe acute pyelonephritis)	Enterobacteriaceae including	60–70	Ceftriaxone IV or ceftazidime (if suspicion of *P. aeruginosa*) ± aminoglycoside
	Escherichia coli	40	
	Pseudomonas aeruginosa	8	
	Enterococcus sp.	15	
	Staphylococcus sp.	4	
Intra-abdominal sepsis	Gram-negative bacilli including	60	Ertapenem (if no risk of *P. aeruginosa*)
	Escherichia coli	40	Piperacillin-tazobactam
	Pseudomonas aeruginosa	30	
	Gram-positive cocci including	30	Third-generation or fourth-generation cephalosporin (active against *P. aeruginosa*) + metronidazole
	Enterococcus sp.	20	Imipenem or doripenem (high-risk patients)
	Anaerobes including	30	± fluconazole
	Bacteroides sp.	20	± aminoglycoside (if shocked)
	Fungi	20	
Nosocomial pneumonia	Enterobacteriaceae	30–40	β-lactam (active against *P. aeruginosa*)
	Pseudomonas aeruginosa	17–30	± aminoglycoside
	Staphylococcus aureus	7–15	± glycopeptide or linezolid if MRSA is suspected
	Streptococcus pneumoniae	3–5	
	Haemophilus influenzae	4–6	
Pneumonia without risk factors for MRP	*Staphylococcus aureus*	45	Third-generation cephalosporin without activity against *P. aeruginosa*
	Streptococcus pneumoniae	9	± Macrolide (if intracellular bacteria are suspected)
	Haemophilus influenzae	20	
	Other Gram-negative bacilli	20	
	Anaerobes	4	
Skin infections	*Streptococcus* sp.	40	β-lactam + β-lactamase inhibitor
	Staphylococcus sp.	30	Piperacillin/tazobactam
	Anaerobes	30	Second-generation cephalosporins (such as cefoxitin)
	Gram-negative bacilli	10–20	Carbapenems
Catheter-related bloodstream infection	*Staphylococcus* sp.	50	Glycopeptide or linezolid + β-lactam with activity against *P. aeruginosa*
	Enterobacteriaceae	30	
	Pseudomonas aeruginosa	10–15	
Nosocomial meningitidis	Gram-negative bacilli including	60	Meropenem + glycopeptide or linezolid
	Acinetobacter sp.	30	
	Staphylococcus sp.	20	
	Streptococcus sp.	10	
	Neisseria meningitidis	1	

Percentages do not necessarily add up to 100, because patients may have more than one type of infection or micro-organism. MRP, multiresistant pathogen; MRSA, methicillin-resistant *Staphylococcus aureus*.

COMMUNITY ACQUIRED PNEUMONIA

The most common organisms identified in community acquired pneumonia requiring intensive care hospitalization are

S. pneumoniae, Legionella, and Haemophilus influenzae, with S. aureus included in some series.

H. influenzae usually occurs in persons with chronic obstructive pulmonary disease.

S. Aureus is seen in patients with decreased local host defenses (eg, after influenza, laryngectomy, bronchiectasis, or cystic fibrosis) or generalized decrease in immunity (eg, malnutrition or immunosuppression).

P. Aeruginosa traditionally has been considered a nosocomial pathogen, although it can cause severe community-acquired pneumonia.

The physician should consider this organism in a patient who has structural lung disease such as bronchiectasis, was hospitalized recently, or is currently receiving broad-spectrum antibiotics, or resides in a nursing home.

Atypical pathogens, especially Legionella species, can cause severe community-acquired pneumonia. More than half of such cases are caused by L. pneumophila subgroup

Chlamydia pneumoniae and Mycoplasma pneumoniae typically cause tracheobronchitis or mild pneumonia and only occasionally severe pneumonia.

In patients with episodes of altered level of consciousness caused by seizures, other neurologic diseases, and substance abuse, an aspiration syndrome should be considered.

Aspiration of gastric contents can cause a chemical pneumonitis—with or without a polymicrobial pneumonia—that can lead to an anaerobic lung abscess.

EMPIRICAL ANTIBIOTIC THERAPY IN COMMUNITY ACQUIRED PNEUMONIA

Because it is impossible to cover all pathogens empirically, the physician must use the available data to make an informed decision regarding therapy.

In most situations involving hospitalized patients, when no clues to etiologic agent can be obtained from history, physical examination, or laboratory data,

empirical antibiotic therapy should consist of a third generation cephalosporin in combination with a macrolide or a quinolone.

EMPIRICAL ANTIBIOTIC THERAPY FOR COMMUNITY-ACQUIRED PNEUMONIA IN PATIENTS REQUIRING ICU ADMISSION

Patient Category	Most Likely Causative Organisms	Empirical Antibiotic Choices[1]
ICU patient	*S. pneumoniae* *Legionella* sp. *M. pneumoniae*	Third-generation cephalosporin[2] *plus* either IV azithromycin or respiratory fluoroquinolone[3]
ICU patient with increased risk for *P. aeruginosa* (recent antibiotic use, hospitalization, or structural lung disease)	*S. pneumoniae* *Legionella* sp. *H. influenzae* *C. pneumoniae* Enteric gram-negative rods *P. aeruginosa*	Antipseudomonal, antipneumococcal β-lactam[4] *plus* ciprofloxacin or levofloxacin (750 mg/day). Or Antipseudomonal, antipneumococcal β-lactam[4] *plus* aminoglycoside and azithromycin Or Antipseudomonal, antipneumococcal β-lactam[4] *plus* aminoglycoside and respiratory fluoroquinolone[3]
ICU patient with increased risk for *S. aureus* (gram-positive cocci in clusters in a tracheal aspirate or in an adequate sputum sample, end-stage renal disease, injection drug use, prior influenza, prior antibiotic therapy, necrotizing pneumonia in absence of risks for aspiration.)	Community-acquired methicillin-resistant *S. aureus* (CA-MRSA)	*Add* vancomycin or linezolid

UROSEPSIS

The majority (70–95%) of cases of community-acquired acute urinary tract infections are caused by *E. coli*

Staphylococcus saprophyticus, enterococci, Proteus mirabilis, Klebsiella species, and Enterobacter species identified in most of the remaining cases.

The list of etiologic agents is modified by factors such as use of indwelling urinary catheters, residence, urinary tract instrumentation, immunosuppression, or recent broadspectrum antibiotic administration.

In any of these settings, multidrug-resistant gram-negative bacilli, coagulase-negative staphylococci, or C*andida species may be responsible for* infection.

TREATMENT OPTIONS OF UROSEPSIS

In all patients, initial antimicrobial therapy should target the organism seen on the Gram-stained smear of the urinary sediment.

In the absence of an identified organism on Gram stain, empirical therapy should consist of a third-generation cephalosporin, an extended-spectrum penicillin (eg, piperacillin), a fluoroquinolone, and/or an aminoglycoside depending on the severity of the infection, the patient's renal function and risk for renal insufficiency, and other factors.

If *Enterococcus is suspected, ampicillin or piperacillin with or* without an aminoglycoside is appropriate.

TREATMENT OPTIONS OF INFECTIVE ENDOCARDITIS

The spectrum of initial antimicrobial therapy in a critically ill patient with suspected infective endocarditis should be broad, directed at the pathogens implicated most commonly in this disease.

Initial therapy should include vancomycin to cover MRSA, a penicillin with activity against streptococci and enterococci, and an aminoglycoside for synergy against these organisms.

If infection with *S. aureus is highly likely, some infectious disease specialists use a semisynthetic penicillin such as nafcillin or oxacillin in conjunction with vancomycin to optimize coverage of both methicillin-sensitive and methicillin-resistant strains.*

When faced with a patient who has a history of a serious allergic reaction to penicillin, the physician should use vancomycin in stead of β-lactams.

NECROTIZING SOFT TISSUE INFECTIONS

Empirical Antibiotic Therapy

Empirical antimicrobial treatment of necrotizing fasciitis should include coverage of aerobic gram-positive cocci, aerobic gram-negative rods, and anaerobes.

Initial antimicrobial choices could include a penicillin or a first-generation cephalosporin along with an aminoglycoside and either clindamycin or metronidazole.

Given the dramatic increase in rates of community-acquired MRSA infections, empirical therapy should include clindamycin, and trimethoprim-sulfamethoxazole, or in some cases, vancomycin.

If *S. pyogenes is suspected, the treatment of* choice is high-dose penicillin.

INTRAABDOMINAL INFECTIONS

The majority of intraabdominal infections are polymicrobial in nature,

caused by Enterobacteriaceae, anaerobes, or streptococci.

The organisms isolated from a given intraabdominal infection reflect the flora native to the involved region of the GI tract.

INTRAABDOMINAL INFECTIONS: PATHOPHYSIOLOGY, MICROBIOLOGY, AND TREATMENT.

Intraabdominal Infection	Pathophysiology	Microbiologic Etiology	Diagnostic Tests	Empirical Antimicrobial Therapy
Peritonitis (spontaneous)	Translocation of bacteria across gut lumen in cirrhosis	*E. coli* (most frequent), *K. pneumoniae*, *S. pneumoniae*, streptococci, enterococci	Paracentesis (neutrophils >250/μL, positive Gram stain or culture)	Third-generation cephalosporin (preferably cefotaxime or ceftriaxone)
Peritonitis (secondary)	Perforation of viscus	Enterobacteriaceae, anaerobes, streptococci, enterococci, *Candida* species	Paracentesis (polymicrobial Gram stain or culture), plain films or CT showing free peritoneal air	β-lactam/β-lactamase inhibitor *or*
Intraperitoneal abscess	Complication of spontaneous or secondary peritonitis	Enterobacteriaceae, anaerobes, streptococci, *Candida* species	CT scan, ultrasound, perhaps radionuclide scan	Third-generation cephalosporin (or cefepime) + metronidazole *or*
Pancreatic abscess	Complication of pancreatitis (biliary, ethanol, postoperative, or posttraumatic)	Enterobacteriaceae, anaerobes, streptococci, enterococci, *Candida* species	CT scan or ultrasound	Quinolone + metronidazole *or*
Hepatic abscess	Local spread from contiguous infection or hematogenous seeding of liver	Mixed facultative and anaerobic species (most common), unless biliary tract source (enteric gram-negative bacilli and enterococci); consider *E. histolytica*	CT scan or ultrasound	Carbapenem *or* Monobactam + metronidazole

Most intraabdominal infections are caused by polymicrobial enteric flora; thus empirical therapy should be targeted toward facultative gram-negative bacilli and anaerobes.

In the past, aminoglycosides were used as first-line therapy against gram negative bacilli but are no longer used widely because newer agents have demonstrated improved penetration and reduced toxicity.

ß-lactam/ß-lactamase-inhibitor combinations, a carbapenem, a third- or fourth-generation cephalosporin, a quinolone, and a monobactam in conjunction with metronidazole are all recommended regimens.

Thanks for your patience