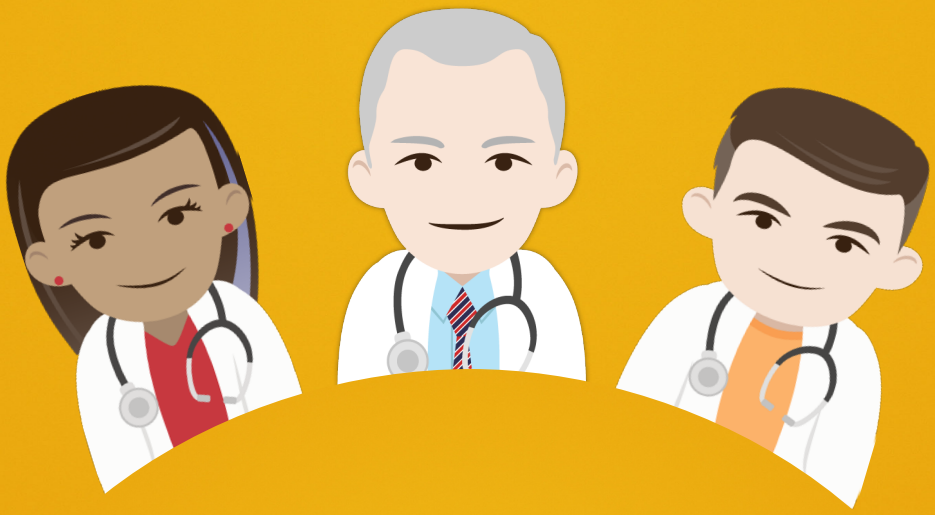
INFECTIOUS DISEASE ESSENTIALS



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Chapter 1

DIAGNOSING INFECTIOUS DISEASE

Taking a complete history

The key to medical and surgical diagnosis is to have the same orderly approach to every patient. It is well known that 70% of diagnoses can be made by excellent history-taking. Physical exam and labs make about 30% of diagnoses.

The three-paragraph approach

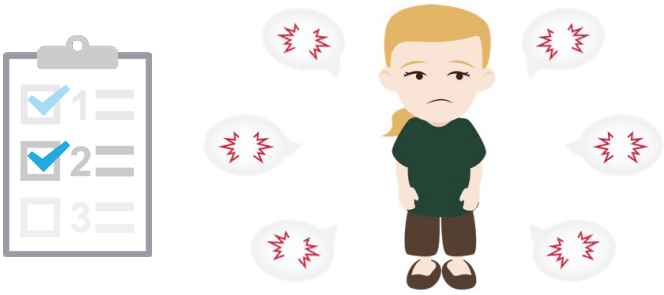
The chief complaint, or presenting complaint, is the key.

Paragraph one

Make the patient decide what is the worst of all symptoms and then allow a description in their own words without interrupting. If the patient strays from describing the chief complaint, get the patient back to it. No other symptom descriptions are allowed at this point. When the physician has a thorough understanding of this chief complaint, paragraph one is complete.

Paragraph two

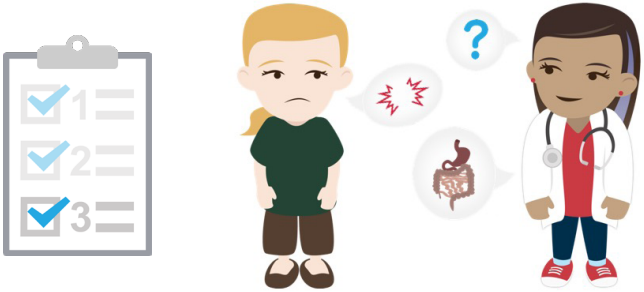
The patient may now describe all remaining symptoms associated with the chief complaint, in their own words. The physician should now have a reasonable idea of the organ system causing the trouble.



Paragraph three

The physician inquires about symptoms in the suspected organ system, which the patient did not complain of.

At this point, the history-taking of present illness is finished. The remainder of the history can be considered with the offending organ system in mind.



Remaining history

For infectious diseases, a travel history is very important. If it has not come up earlier, it should be addressed at this point, along with other relevant social factors such as occupation, smoking history, and sexual history. A comprehensive physical exam of the offending organ system must be carried out, along with at least a cursory exam of other systems. If you stick to this template with every patient, you will compose a thorough and complete history of the present illness. This will allow you to be better equipped to make a quick and accurate diagnosis for your patient.

Previously seen patients are evaluated in exactly the same way except that the medical record should be at least briefly reviewed before interviewing the patient.

Performing a world-class physical exam

It is impossible to examine every body system in detail in most patients suspected of having an infectious disease. It is possible and essential to examine the body system which is the suspected source of the infection in great detail, with at least a cursory exam of other body systems.

For example, if the history of present illness indicated a probable lung infection, it is important to maintain a systematic approach to the examination of the thorax. All other organ systems may be considered at a later time point.

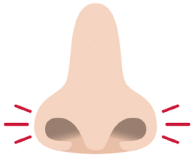
The classic medical school training of **inspection**, **palpation**, **percussion**, and **auscultation** remains a great organizational tool, and can be used to examine many organ systems.

For example, let's look in more detail at how to perform a thorough physical examination of the lungs in a person with a suspected respiratory infection.

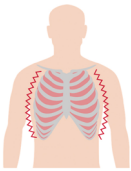
Inspection

You can observe much about a patient's condition just by looking.

- Flaring of the nostrils signifies air hunger.

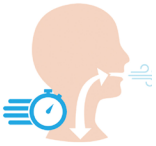


- Intercostal retractions denote increased work of breathing or stiff lungs from a consolidative process like some pneumonias.



- Stridor usually signifies upper airway obstruction (for example, croup, epiglottitis, or the presence of a foreign body).

- A fast respiratory rate is indicative of hypoxia.

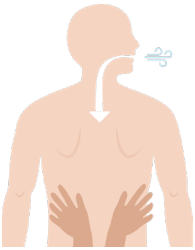


Palpation

Palpation involves actually feeling the thorax with your hands.

In some patients with chest pain the origin is a superficial structure rather than a deep organ (for example, in a patient with broken ribs); tenderness of the sternum at the junction of ribs could be mistaken for pain of myocardial origin.

Having the patient breathe in, while the hands are placed on either side of the chest posteriorly, can show the physician whether each lung is expanding during breathing.



Percussion

By using good percussion technique, it is possible to recognize the presence of a normal amount of air in the lungs, which has a resonant sound.

A dull sound will be found in patients with a large area of consolidation underlying the percussing fingers.

The percussion note has almost no resonance (i.e., *flat*) if a pleural effusion or pus in the pleural space is present.

A drum-like tympanitic sound will be present if there's too much air in the underlying lung, such as emphysema or, more urgently, a pneumothorax.

Auscultation

The entire thorax should be examined for **crackles**, which may range from fine (indicating early pneumonia or heart failure) to coarse with a Velcro-like sound (as present in pneumonia, pulmonary edema, pulmonary fibrosis) and may occur early to late in inspiration.

Wheezes are musical sounds, usually in expiration, which indicate bronchial obstruction (asthma, COPD). Overlying a consolidated lobe, large airway breathing (referred to as bronchial breath sounds) may be apparent where it is not normally found, indicating pus in most alveoli under the stethoscope.

Other consolidative sounds are **egophony** (a bleating, nasal quality imparted to the spoken voice) and **whispered pectoriloquy** (whispered words intelligible to the listener when normally whispered words are not intelligible).

In addition, the vibrations of the sound of the spoken voice are increased over an area of consolidation. This is known as increased **vocal fremitus**.

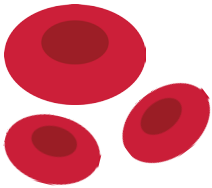
Finally, a leathery sound may be apparent over an area of pleuritis (pleural friction rub).

Based on the careful physical examination of the chest, findings suggestive of a particular pathogen or disease process may be found. However, performing a proper and thorough physical exam will provide you with important information necessary for making an accurate diagnosis.

Interpreting blood test results

When presented with the blood test results from a patient, it is important to know what to look for if you suspect an infectious disease.

Red blood cells



Erythrocytes, or red blood cells (RBCs), are normally disk-shaped with a diameter of 6.2–8.2 µm. Acute infections are generally limited in duration and do not dramatically affect RBC size. However, assessing the number and morphology of RBCs can help you recognize conditions such as anemia, dehydration, malnutrition, and leukemia.

Chronic infections

Chronic infections like tuberculosis may cause the **anemia of chronic disease**. Cytokines released as a consequence of infection drive this process by direct bone marrow suppression, by inhibition of erythropoietin production, or by disruption of iron metabolism either directly or indirectly.

Malaria

Malaria due to *Plasmodium falciparum* can cause massive hemolysis, disseminated intravascular coagulation (DIC), and microangiopathic hemolytic anemia (MAHA) because so many RBCs are affected, and the lining of small blood vessels become roughened by clots and inflammation. The other types of malaria generally don't cause massive hemolysis and cells are normocytic.

When severe hemolysis is present there is often anisocytosis (variation in cell size) because of the presence of reticulocytes. This occurs because the bone marrow is turning out young RBCs in response to the hemolysis.

Macrocytic anemia

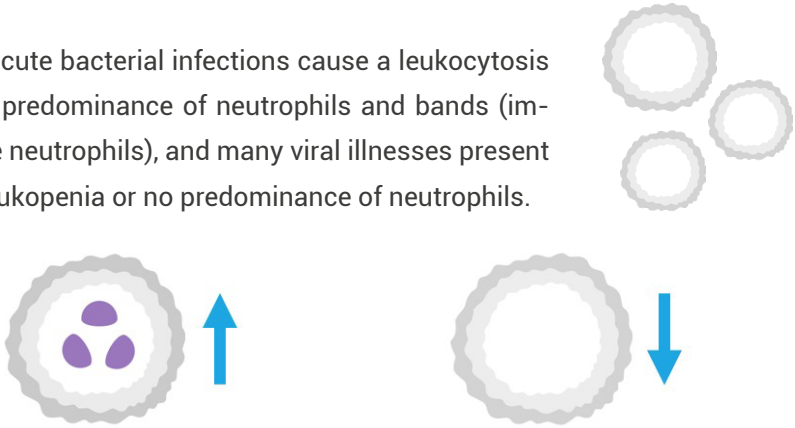
Macrocytic anemia is notoriously caused by the fish tapeworm *Diphyllobothrium latum*, which absorbs more B12 than the human host and leads to B12 deficiency.

Microcytic, hypochromic anemia

Microcytic, hypochromic anemia (MHA) is usually due to blood loss and hookworm infestation could be the cause of it. This is a result of the worms engulfing and disrupting small intestinal villi causing chronic blood loss. Microscopically reviewing the blood smears of patients with anemia is an excellent habit for the interested infectious disease diagnostician because it may lead to a direct diagnosis or to suggest infectious causes.

White blood cells

Most acute bacterial infections cause a leukocytosis with a predominance of neutrophils and bands (immature neutrophils), and many viral illnesses present with leukopenia or no predominance of neutrophils.



Bacterial infections

Viral infections

However, when faced with a sick, febrile patient there are some classic bacterial infections which can be associated with **leukopenia**, such as typhoid fever and brucellosis, which an astute physician would likely consider.

Some viral illnesses, like infectious mononucleosis, will present with an **atypical lymphocytosis**. These are actually mostly activated T cells (95%) responding to Epstein-Barr virus infection of B cells. The cytoplasm tends to be indented by surrounding RBCs. They are frequently found in the early stages of infectious mononucleosis, but are not specific for the disease.

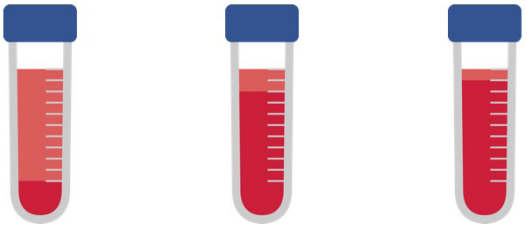
When **thrombocytopenia**, **petechiae**, and **hemorrhage** are part of the clinical picture, some hemorrhagic fevers should be considered and a careful travel history obtained.

Other tests

Erythrocyte sedimentation rate

The erythrocyte sedimentation rate (ESR) is a blood test that indirectly measures the degree of inflammation in the body.

ESR is generally elevated in the presence of acute phase reactants, like c-reactive protein and fibrinogen, which are produced in high quantities during inflammation.



≥ 100 mm / h > 20 mm / h normal

C-reactive protein

C-reactive protein (CRP) synthesis rate in the liver increases proportionally with the intensity of the inflammatory process stimulating CRP production and vice versa. In one study, an extremely high CRP elevation of more than 500 mg / L was associated with more than 80% likelihood of the presence of a bacterial infection.

This summarizes the most common blood tests used to diagnose infectious diseases. But other tests may be conducted by specialists as needed.

Deciphering culture results

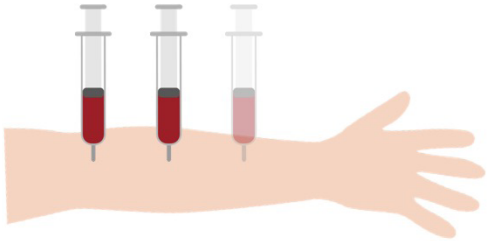
The most common cultures used to test for infectious agents

- Blood
- Sputum
- Urine
- Wound
- Cerebrospinal fluid
- Stool

Blood samples

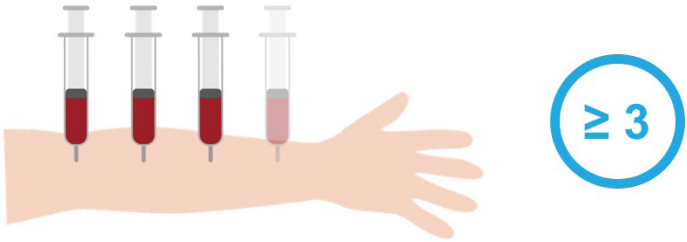
Skin contaminants in blood culture bottles are common, very costly to the healthcare system, and are frequently confusing to clinicians. However, with professional phlebotomists the incidence of contamination is lessened.

Blood from at least two venipunctures is ideal to help confirm the results. Common skin contaminants include coagulase-negative staphylococci, *Bacillus* spp, and diphtheroids.



When only one of two samples yields such organisms, skin contamination is probable. However, when virulent organisms are isolated, such as *Staphylococcus aureus* or beta-hemolytic streptococci, skin contamination is unlikely and results should be considered genuine. Isolation of aerobic gram-negative bacilli should be considered valid results, since these organisms are not natural residents of human skin.

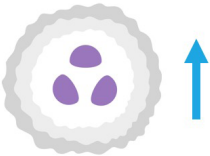
For suspected endocarditis, at least three separate blood cultures should be done. This is because an infected heart valve will shed bacteria into the blood continuously, therefore, all or almost all blood cultures will be positive.



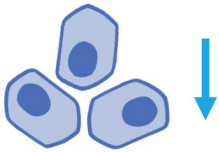
Sputum samples

The vast majority of microbiology labs perform Gram stains of sputum specimens to determine the quality of the sample before processing. Even before examining under oil immersion, technicians will review the smear under low magnification (10x) because human cells can be recognized at this power, whereas most bacteria cannot.

An adequate sputum sample has innumerable white blood cells (neutrophils) and little to no other cell types, especially squamous epithelial cells.



Many neutrophils



Few epithelial cells

The presence of high levels of squamous epithelial cells indicates potential contamination with saliva, and necessitates obtaining another sample.

If the sputum sample is reviewed before antibiotic therapy, it will usually contain the culprit bacteria. Such a sample is worthy of review under oil immersion and can be used for further culture.

A sample that is contaminated by saliva will contain mixed flora reflecting the oral microbiome. It should not be cultured and will be rejected by most labs.

Although many patients are not able to cough up an adequate sputum sample, the Gram stain of an adequate specimen is generally helpful in identifying the probable cause of pneumonia, such as the gram-positive *Streptococcus pneumoniae*, or the gram-negative *Klebsiella pneumoniae*.

A smear which shows many neutrophils but no organisms can also be valuable because is suggests the cause is an organism which does

not stain well with Gram's method or that the cause of the pulmonary process is not infectious at all. Thus a negative Gram stain will lead the prudent physician to look for another cause like tuberculosis, fungus, *Legionella* or another cause of inflammation of the lung.

Urine samples

A urine culture which contains more that 100 000 colony-forming units (cfu) / mL is considered indicative of bacteriuria in adult patients.

Less than 100 000 cfu / mL is considered a contaminant unless the sample comes from a female patient with symptoms of a urinary tract infection (UTI). In such a situation even 1000 cfu / mL is considered significant if the culture yields a known uropathogen like *E. coli*. Note that many older women have asymptomatic bacteriuria which does not require treatment.

Likewise, patients with indwelling urinary catheters acquire bacteriuria at the rate of about 8% per day. Thus, at the end of two weeks most will have significant bacteriuria. Catheterized patients should not be treated for UTI in the absence of symptoms indicating a urinary source of infection.

Wound samples

An open wound will become colonized by multiple organisms but may not actually be infected. Thus, a careful evaluation of the patient and the cleaned and debrided wound is essential. Secondary infections are often extensions of preexisting lesions like traumatic or surgical wounds or pressure ulcers, which serve

as the primary portal of entry for microbial pathogens and are often polymicrobial involving subcutaneous tissue.

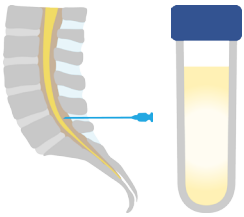
Wound cultures should not be done unless infection is suspected.

Signs of infection

- Increased pain
- Warmth
- Erythema
- Drainage
- Systemic symptoms

When infection is diagnosed clinically, deep tissue specimens retrieved via biopsy or needle puncture with semi-quantitative bacterial counts are preferred to guide antibiotic therapy.

Cerebrospinal fluid samples

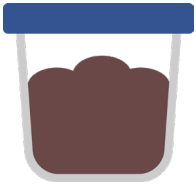


During a lumbar puncture, a minimum of 0.5–1 mL of cerebrospinal fluid (CSF) should be sent immediately after collection to the microbiology laboratory in a sterile container for bacterial testing. Larger volumes (5–10 mL) increase the sensitivity of culture and are required for optimal recovery of mycobacteria and fungi.

> 0.5–1 mL 5–10 mL

A Gram stain should be done when bacterial meningitis is suspected. The sensitivity of the Gram stain for the diagnosis of bacterial meningitis is 60%–80% in patients who have not received antimicrobial therapy and 40%–60% in patients who have received treatment. For the most common cause of fungal meningitis, *Cryptococcus neoformans*, the sensitivity of CSF culture is > 70%.

Stool samples



The specimen of choice to diagnose diarrheal illness is the diarrheal stool, not a formed stool or a swab.

Most laboratories will have the ability to culture for *Salmonella*, *Shigella*, and *Campylobacter* and test for Shiga toxin-producing *E. coli.*

In studies of adult patients who submitted more than one specimen, the enteric pathogen was detected in the first sample 87%–94% of the time, with the second specimen bringing the positive rate up to 98%. In pediatric patients, the first specimen investigated in the laboratory detects 98% of the enteric pathogens.

Chapter 2

RESPIRATORY INFECTIONS

Overcoming the common cold

Causes

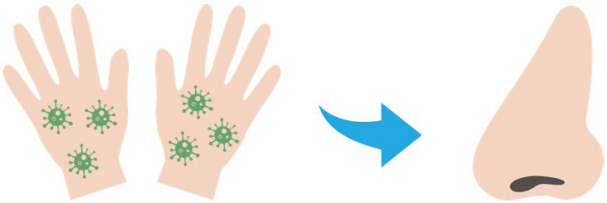
Most upper respiratory infections are caused by viruses.

The most frequent type of infection is the common cold. Many of these infections are acquired through contact with children from the ages of six months to five years, who average more than seven colds per year. In children, colds cause eustachian tube dysfunction and often are accompanied by middle ear infections.

Pathogenesis

The symptoms of sinus congestion and runny nose are not due to the virus itself but are instead a result of our own immune cytokine response, with kinins causing much of the congestion.

Virus particles present on the hands of an infected person enter the nasal epithelial cells and replicate. Some are able to disrupt and shed the nasal cells and cilia in the process but with control of the infection, the mucosa normalizes in two weeks or less. This also means that symptoms can linger for more than a week making some patients seek antibiotics unnecessarily.



The common cold is complicated by bacterial sinusitis in < 10% of people, so antibiotic treatment is generally unnecessary.

Clinical management

Management of the common cold essentially involves managing symptoms.

For malaise, myalgias, and arthralgias, **acetaminophen or a nonsteroidal antiinflammatory drug (NSAID)** is usually sufficient.

Blowing the nose should be done gently, since forceful blowing can drive secretions up into the sinuses possibly predisposing to acute bacterial sinusitis.

Patients should be advised to **limit the use of nasal sprays**, as rebound vasodilation can occur after just 2–3 days of use, exacerbating the symptoms.

Aspirin should not be given to children because of concern for Reye syndrome, which is characterized by increased intracranial pressure and acute fatty liver.

Dozens of studies using **vitamin C and / or echinacea** products have **shown no reduction** in severity or duration of disease. In a meta-analysis of 16 studies, zinc products were shown to reduce the duration of symptoms by approximately one day.

Prevention

Cold victims should **refrain from shaking hands** with others until symptoms have subsided.

The best prevention is **thorough hand washing** after potential contact with patients with cold symptoms.

Soft tissues for gentle nose blowing are far better than a dirty handkerchief.

When present, coughing should be done properly, by **coughing into the arm / sleeve**, rather than into the hands, to decrease spread to others.

Handling pharyngitis

Pharyngitis is the inflammation of the pharynx, most commonly referred to as a *sore throat*. It can be either viral or bacterial in origin. About 70% of pharyngitis is caused by viruses.

Viral pharyngitis

Pathogenesis

The symptoms and signs of viral pharyngitis are not distinctive unless there is accompanying conjunctivitis, which is most commonly caused by adenoviruses.

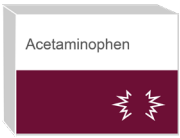
Common symptoms

- Oral ulcers
- Nasal congestion
- Cough

Herpangina (mouth blisters) is characterized by ulcers and vesicles in the posterior pharynx and is usually due to a coxsackie virus. The most common cause of hand-foot-mouth disease is coxsackie A 16. It causes painful lesions in the mouth and on the hands and feet.

Clinical management

Over-the-counter pain relievers, such as acetaminophen or a nonsteroidal antiinflammatory agent, like ibuprofen or naproxen have been shown to provide fast and effective relief of sore throat pain.



Salt-water gargles are an old standby for throat pain. It is not clear that salt water works to relieve pain but it is unlikely to be harmful.

Sprays containing topical anesthetics, such as benzocaine or phenol are available to treat sore throat. However, such sprays are no more effective than sucking on hard candy.

A variety of **lozenges or cough drops** containing topical anesthetics are available to treat throat pain or relieve dryness. Lozenges may persist longer in the throat than sprays or gargles and thus may be more effective for symptom relief.

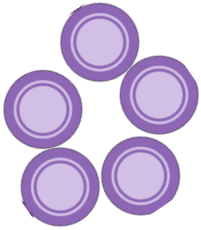
Other treatments that may help with throat pain include sipping cold or warm beverages, or eating cold or frozen desserts, such as ice cream or popsicles.

Bacterial pharyngitis

Bacterial pharyngitis is less common than viral pharyngitis.

Pathogenesis

Except for relatively rare infections like diphtheria or peritonsillar abscess, bacterial pharyngitis most commonly results from a group A streptococcal infection. About 30% of pharyngitis in children and 15% in adults is due to this organism.



Group A *Streptococcus*

30%

15%

Common symptoms of group A streptococcal pharyngitis

- Fever
- Severe sore throat with tonsillar exudates
- Tender anterior cervical lymphadenopathy
- Absence of a cough

Clinical management

Rapid streptococcal antigen testing has a sensitivity of 70–90% and a specificity of 95%.

This infection is ordinarily treated with ten days of penicillin V or amoxicillin.

For patients with a beta-lactam allergy, ten days of cephalexin or a five-day course of azithromycin may be used.

10 days | 10 days | 5 days

Diagnosing upper respiratory infections

Acute bacterial sinusitis

Acute bacterial sinusitis is an unusual complication of viral sinusitis from the common cold. It is more likely to occur in patients with anatomic abnormalities of the nose and sinuses, for example, a deviated nasal septum or obstruction of ostea.

Causes

The principal cause is *Streptococcus pneumoniae* and less commonly *Haemophilus influenzae*, or *Moraxella catarrhalis*.

Pathogenesis

Patients often present with

- Fever
- Focal sinus pain
- Toothache in maxillary sinusitis (possible)
- Purulent nasal secretions
- Opacification of one or more sinuses on CT scan

Clinical management

In addition to promoting drainage with decongestants for 48 hours, amoxicillin-clavulanate is a good choice because of the possible presence of beta-lactamase-producing pathogens like *Moraxella catarrhalis*.

For patients with a penicillin allergy, an oral third-generation cephalosporin like cefpodoxime is an acceptable choice.

If the patient has a history of anaphylaxis to penicillin, a respiratory quinolone like levofloxacin will cover most of the common pathogens.

Acute otitis media

Middle ear infections are the most common cause of office visits in children six months to two years of age. They are a frequent complication of viral upper respiratory infections. It is an uncommon infection in adults and when present suggests anatomical obstruction of the eustachian tube, like allergy or a nasopharyngeal tumor.

Pathogenesis

Common symptoms in children

- Fever
- Fussiness
- Ear pain (indicated by tugging at one or both ears)
- Cough

On exam, the tympanic membrane is bulging, immobile, and has a diminished light reflex.

The most common pathogen is again the gram-positive *Streptococcus pneumoniae*, followed by gram-negatives *Haemophilus influenzae* and *Moraxella catarrhalis*.

Clinical management

If patients have not received antibiotics recently, amoxicillin is preferred. If given recent antibiotics, resistant organisms should be suspected and amoxicillin-clavulanate is a better choice.

For patients with a penicillin allergy, cefpodoxime is recommended.

Fluoroquinolones are relatively contraindicated in children because of the effect on growing cartilage and tendons.

Acute epiglottitis

Acute epiglottitis is a life-threatening infection, which can be complicated by sudden asphyxiation. It is most common in children between two and six years of age.

Pathogenesis

In the past, the most common cause was *Haemophilus influenzae* type b (Hib) but in developed countries most children receive Hib vaccine making this pathogen rare. However, it is still a problem in the developing world.

Other causes are group A *Streptococcus* (GAS), *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (MRSA), and *Streptococcus pneumoniae*.

Common symptoms

- Acutely ill
- Fever
- Sitting forward in classic *tripod* position (to keep airway open)
- Hoarseness
- Inspiratory stridor

Clinical management

The oropharynx should be examined with extreme caution by having the patient open the mouth and trying to observe a swollen epiglottis without the use of a tongue depressor, which may cause sudden occlusion of the airway by the inflamed epiglottis.

When the diagnosis is suspected, emergency consultation with an ear, nose, and throat specialist should be obtained.

The airway may then be visualized by nasopharyngoscopy and the trachea intubated if necessary.

Blood cultures are often positive for the pathogen. Empirical therapy should be given with ceftriaxone plus vancomycin, adjusting after the results of cultures are available.

Coping with bronchitis

Bronchitis is the inflammation of the bronchi.
It can be either acute or chronic.

90%

Acute bronchitis

Acute bronchitis is frequently treated by physicians with antibiotics despite the fact that 90% of cases are viral in etiology.

Most cases of acute bronchitis occur in wintertime.

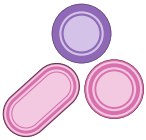
Common symptoms

- Cough
- Low-grade fever
- Physical findings limited to rhonchi or wheezes

Clinical management

Chest x-ray is usually not helpful in diagnosing acute bronchitis.

Albuterol has been shown to be helpful in decreasing the severity and duration of the cough.



If symptoms are unusually severe at the outset, or bronchitis fails to resolve gradually, a bacterial infection might be considered. The presence of a cough that is repetitive and exhausting, followed by an

audible inhalation sound, like a *whoop*, or cough followed by vomiting (in a child) should make a doctor consider pertussis.

Acute exacerbation of chronic bronchitis

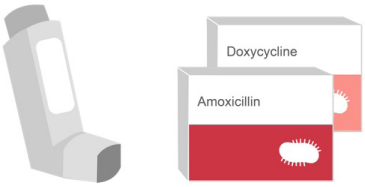
Pathogenesis

The most common cause of acute exacerbation of chronic bronchitis (AECB) is a viral infection. This is characterized by a period of unstable lung function with worsening airflow and productive cough.

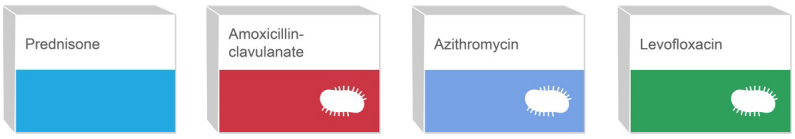
Continued smoking and air pollution most likely contribute to severe acute exacerbations. *Chlamydophila pneumoniae* is responsible for about 5% of mild or moderate AECB.

Clinical management

For mild exacerbations, a case could be made for increasing use of bronchodilators without antibiotics or with amoxicillin or doxycycline.



For severe exacerbations, most authorities recommend a five-day course of prednisone plus amoxicillin-clavulanate. Azithromycin or levofloxacin could serve as alternatives, for patients with a beta-lactam allergy.



Determining where to treat community-acquired pneumonia

Tests to consider for optimal evaluation of patients with community-acquired pneumonia

- Pulse oximetry
- Complete blood count with differential white blood cell count
- Chest x-ray
- Metabolic panel
- Sputum Gram stain and culture
- Blood cultures (for ICU patients)
- Urine antigen tests (for ICU patients)

For very severe pneumonia, *Klebsiella* should be considered among the causes.

Where should I treat my patient with community-acquired pneumonia?

CURB-65

Most emergency departments employ the CURB-65 criteria. In this scoring system, a point is given for the presence of each of the following criteria.

- Confusion or altered mental status
- Blood urea nitrogen greater than 20 mg / dL
- Respiratory rate of over 30 breaths per minute
- Blood pressure < 90 mmHg systolic or diastolic blood pressure < 60 mmHg
- Age 65 years or older

0–1 points: consider management as an outpatient after an observation period.
1–3 points: can be managed on the medical ward.
> 3 points: should be initially treated in the intensive care unit (ICU).

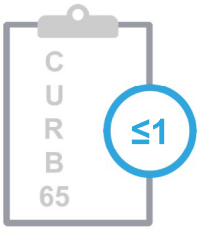
≤ 1 point

1–3 points

≥ 3 points

Managing community-acquired pneumonia

Outpatients



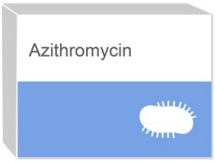
Pathogenesis

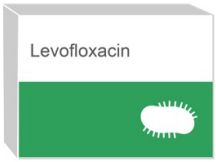
Major pathogens to consider

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*
- *Legionella pneumophila*

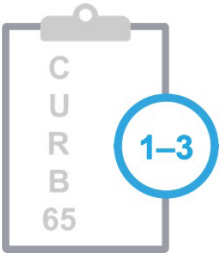
Clinical management

Azithromycin has good efficacy against these organisms. Alternatively, a respiratory fluoroquinolone, such as levofloxacin should be sufficient.





Inpatients



Pathogenesis

Many patients admitted to the medical wards will be able to produce an adequate sputum specimen for culture and Gram stain. The smear, if classic for *Streptococcus pneumoniae* or *Staphylococcus aureus*, will dictate more specific antibiotic therapy until culture results are available.

Clinical management

IV antibiotics are generally necessary for inpatients with community-acquired pneumonia.

Typically, vancomycin or ceftaroline is used to treat *Staphylococcus aureus* or ceftriaxone for *Streptococcus pneumoniae*. However, in the absence of a good sputum sample, it is necessary to treat empirically for several possible pathogens. Therefore, a cephalosporin like ceftaroline, which covers gram-negative and gram-positive pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA), can be given.

In addition, azithromycin should be added to cover atypical pathogens like *Chlamydophila pneumoniae, Legionella pneumophila*, and *Mycoplasma pneumoniae*. Alternatively, a respiratory quinolone should be sufficient to treat these atypical causes.

A patient who has experienced influenza prior to becoming sick again would be a classic story for a complicating staphylococcal pneumonia since influenza infection damages the lining of the bronchi and predisposes the lung to infection by a virulent organism like *S. aureus*, which may colonize the upper respiratory tract. Other virulent organisms may also be involved in patients with preceding influenza.

Intensive care unit

Patients with severe, lobar pneumonia may be so hypoxic that mechanical ventilation is required. Organisms to consider in such a scenario include *Klebsiella pneumoniae*. These patients often have bloody sputum, the Gram stain of which classically shows thick, gram-negative bacilli. Patients can be treated safely with ceftriaxone for suspected *Klebsiella pneumonia*.

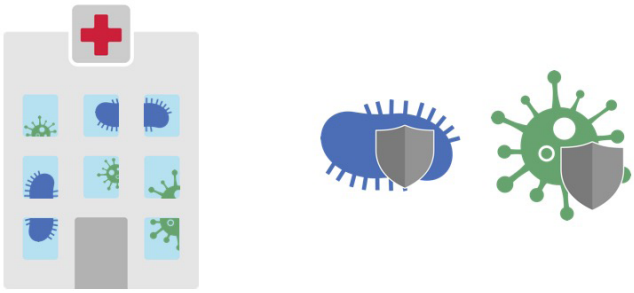
If the patient is producing no sputum, many pulmonologists would perform a **bronchoalveolar lavage** to obtain immediate microbiologic samples before treating empirically. Such a strategy would be superior to treating empirically and observing the patient for 24–48 hours because if the patient worsens, bronchoalveolar lavage may then be too dangerous and the results of cultures and smears altered by the empirical therapy.

Agents which would cover possibly resistant gram-negative bacilli like *Pseudomonas,* such as piperacillin-tazobactam, cefepime, or meropenem, along with a respiratory quinolone like levofloxacin to cover *Legionella* could be chosen empirically while awaiting the results of lavage specimen testing.

Health-care-associated pneumonia

When treating patients with pneumonia who arrive in the clinic or emergency department, it is important to watch out for patients who frequent hospitals regularly, either as inpatients or outpatients. When pneumonia develops in these persons, we call it health-care-associated pneumonia (HCAP).

Because of their frequent exposure to the hospital, they may be exposed to the hospital's *bugs*. Many of these organisms are multidrug-resistant (MDR).



With respect to treatment, they are a unique group of patients if they are diagnosed with pneumonia when they arrive at the hospital. However, the workup of these patients, including CURB-65 evaluation, would generally be the same as for those with community-acquired pneumonia.

Treating hospital-acquired pneumonia

As the name suggests, hospital-acquired pneumonia occurs when a patient develops pneumonia while hospitalized with another illness.

Far and away, the most common type of hospital-acquired pneumonia is ventilator-associated pneumonia (VAP), which can be defined as pneumonia developing 48 hours or more after mechanical ventilation has begun.

The incidence of getting pneumonia by coming into the hospital is less than 10% unless the patient requires a ventilator for more than a day, in which case the incidence rises to greater than 25%.

< 10%

> 25%

The overall mortality from VAP is greater than 30%. In most intensive care units, 10–35% of the patients already have VAP and this increases with time. More than 50% of patients who have been on a ventilator for ten days have VAP.

Risk factors that increase mortality from VAP

- Male gender
- Organ dysfunction
- Central nervous system (CNS) disorders
- Emergency surgery

Risk factors for developing VAP

- Blood transfusion
- Nasogastric (NG) tube
- Tracheostomy
- Required to remain in supine position (e.g., because of low blood pressure)

Pathogenesis

80% of VAP is caused by the organisms summarized by the acronym, ESKAPE.

E*nterococcus* spp
S*taphylococcus aureus*
K*lebsiella pneumoniae*
A*cinetobacter baumannii*
P*seudomonas aeruginosa*
E*nterobacter* spp

70% are gram-negative bacilli, with *Pseudomonas* being the most common pathogen. *Staphylococcus aureus* is the most common organism among the gram-positive causes.

Many of these organisms are more prone to becoming multidrug-resistant, which is important to keep in mind, since patients with prolonged stays in intensive care units (ICUs), like trauma patients who might develop VAP more than once, are at an increased risk of developing infections caused by multidrug-resistant organisms. This severely limits the choice of antibiotics that can be used to treat these infections.

Unusual causes of VAP

- *Legionella*
- *Aspergillus*
- Respiratory syncytial virus (RSV) or other viruses

Organisms like these should be suspected when empirical therapy is not working or when Gram stain and routine cultures haven't revealed the cause, and the patient is deteriorating.

For these bugs, special cultures and stains or even wet mounts of secretions may allow the physician to stumble onto the diagnosis. VAP has such a high mortality that it is important to obtain appropriate pulmonary secretions for culture.

Clinical management

Most pathogens will be identified by either endotracheal suction, bronchoalveolar lavage or, if necessary, video-assisted thorascopic surgery to obtain lung tissue for culture.

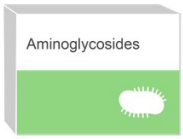
Since diagnosis is at times difficult, a physician should adopt the Sherlock Holmes attitude by performing a world-class exam of the lungs, both anteriorly and posteriorly, reviewing all imaging, and reviewing the Gram stain of the secretions in the microbiology lab.

If the Gram stain is negative, an acid-fast smear for tuberculosis should be ordered and reviewed, followed by a Wright's or Giemsa stain of secretions. If still no cause is apparent but evidence for pneumonia is solid, a wet mount of pulmonary secretions may reveal a fungal cause long before fungal culture results are available.

Since the most common cause of VAP is a gram-negative rod, and *Pseudomonas* is most likely, it is reasonable to begin an empiric antipseudomonal beta-lactam plus or minus an aminoglycoside. The beta-lactams will cover upwards of 90% of *Pseudomonas*, and the aminoglycosides should cover as many as possible of the other resistant 10%.

Pseudomonas

90%

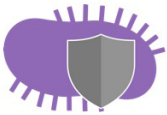


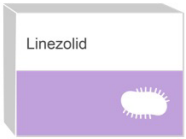
10%

Although the aminoglycoside is nephrotoxic, short-term therapy until culture results are available will likely not affect renal function substantially.

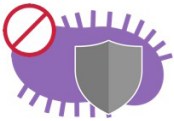
For patients with a beta-lactam allergy, aztreonam or ciprofloxacin (possibly with an aminoglycoside) is a good option.

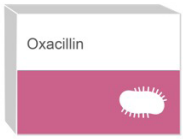
When *S. aureus* is suspected by Gram-stained smears, empirical therapy should cover MRSA (e.g., vancomycin or linezolid) at least until culture results are available.





If the isolate is not MRSA, very narrow-spectrum drugs, such as nafcillin or oxacillin are preferred. Alternatively, cefazolin or clindamycin may be used in patients with a penicillin allergy.





At least one study has shown no significant difference in outcome between eight or 14 days of antibiotic treatment. Therefore, it is best to discontinue effective antimicrobial therapy after eight days of treatment to decrease the likelihood of inducing antibiotic resistance.

Chapter 3

GASTROINTESTINAL TRACT AND ABDOMINAL INFECTIONS

Differentiating intraabdominal infections

Peritonitis

The normal peritoneal cavity contains less than 100 mL of sterile fluid and contains less than 250 cells / µL, all macrophages and lymphocytes.

Pathogenesis

Spontaneous bacterial peritonitis (SBP) almost always arises without explanation in patients with ascites due to hepatic dysfunction or nephrotic syndrome. Bacteria may enter the ascitic fluid from bacteremia or by translocation across the bowel wall.

Causes of spontaneous bacterial peritonitis

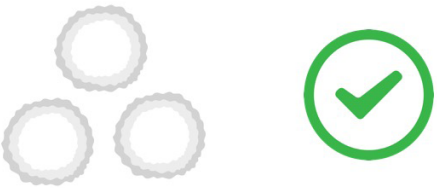
- *Escherichia coli* (50%)
- *Streptococcus pneumoniae* and other streptococci (15–20%)
- *Klebsiella* (10%)
- Anaerobic bacteria like *Clostridium* (5%)

Common symptoms

- Patients may be asymptomatic or have only mild diffuse abdominal pain
- Abdominal tenderness (50% of patients)
- Fever (80% of patients)

A high index of suspicion for peritonitis is important in a patient with fever or deterioration in liver or kidney function.

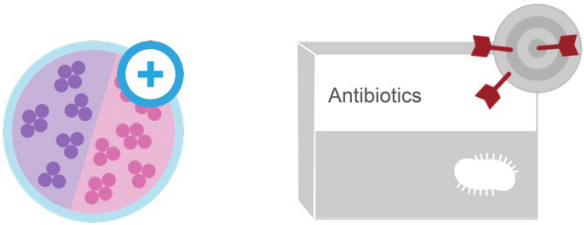
The diagnosis of SBP is confirmed by examining the peritoneal fluid for the presence of more than 250 neutrophils / µL.



> 250 cells / µL

Clinical management

Gram staining is frequently negative, but when positive, the morphology of the organism can determine appropriate empirical antibiotics.



When Gram staining is negative, antibiotics should be chosen which cover a mixed microbial flora including anaerobes. This might include piperacillin-tazobactam or a carbapenem like ertapenem.

Intraabdominal abscess

Intraabdominal abscesses are ordinarily complications of other processes.

Biliary tract disease is the most common predisposing factor of liver abscesses.

Bacteremia, especially from infective endocarditis is the most likely source of a splenic abscess.

Previous acute pancreatitis from alcoholism, gallstones or trauma can be complicated by pancreatic abscess.

Often, the actual cause of the abscess remains unknown.

Common symptoms

- Fever
- Chills
- Right or left upper quadrant pain
- Pain radiating to the shoulders (usually liver or spleen abscesses)
- Worsening epigastric pain radiating to the back (pancreatic abscess)
- Septic-like picture (pancreatic abscess)

Clinical management

The most sensitive imaging for intraabdominal abscess is abdominal computed tomographic (CT) scan, but ultrasound may be used for the initial study.

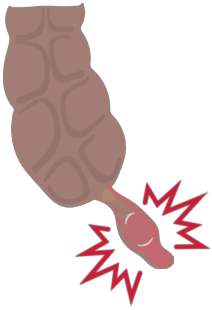
Blood cultures should be routinely done and in the case of splenic abscess, an echocardiogram might be necessary to rule out endocarditis as the source of the abscess.

CT-guided drainage is required for most abscesses. The fluid should be processed with Gram stain and aerobic and anaerobic cultures.

Since mixed infections are characteristic of all three types of abscess, antibiotics like piperacillin-tazobactam or in the case of a life-threatening pancreatic abscess a carbapenem like meropenem, should cover the involved aerobic and / or anaerobic organisms.

Recognizing appendicitis and diverticulitis

Acute appendicitis



Acute appendicitis usually begins with vague, often colicky epigastric or periumbilical pain, which localizes to the right lower quadrant over the next 12 hours.

Pathogenesis

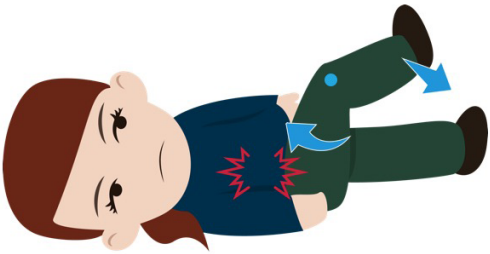
Common symptoms

- Moderate fever
- Right lower quadrant tenderness
- Guarding
- Rebound tenderness
- Positive obturator sign
- Moderately elevated white blood cell count

The technique for detecting the obturator sign, called the **obturator test**, is carried out on each leg in succession. The patient lies on their back with the hip and knee both flexed at ninety degrees. The examiner holds the patient's ankle with one hand and knee with the other hand. The examiner internally rotates the hip by moving the patient's ankle away from the patient's body while allowing the knee to move only inward.

When acute appendicitis is suspected, the inflamed and enlarged appendix may come into physical contact with the obturator internus

muscle, which will be stretched when this maneuver is performed on the right leg. This causes pain and is evidence in support of an inflamed appendix.

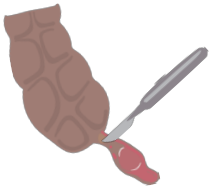


Obturator sign

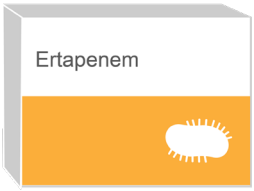
Clinical management

Rectal exam should be done in virtually all patients who present with abdominal pain, and in the case of appendicitis, tenderness in the high right rectal region is suggestive of the diagnosis.

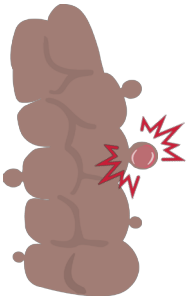
The diagnosis can be confirmed with a CT scan and in uncomplicated cases laparoscopic appendectomy is curative.



Antibiotics play a lesser role, however, and are only given once the diagnosis is apparent. Ertapenem, with its long half-life in a single daily dose, has been shown to be effective.



Diverticulitis



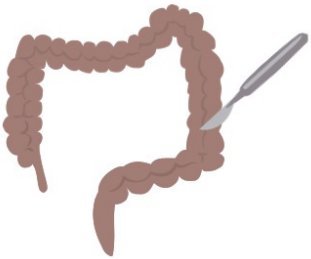
Diverticulitis is inflammation of a diverticulum. Diverticula are small pouches that can develop in the wall of the intestine.

Pathogenesis

Common symptoms

- Mild to moderate left lower quadrant abdominal pain (lasting days)
- Diarrhea
- Nausea
- Vomiting
- Fever
- Slight increase in white blood cell count
- Left lower quadrant abdominal tenderness
- Phlegmon (an inflammatory mass)

Clinical management

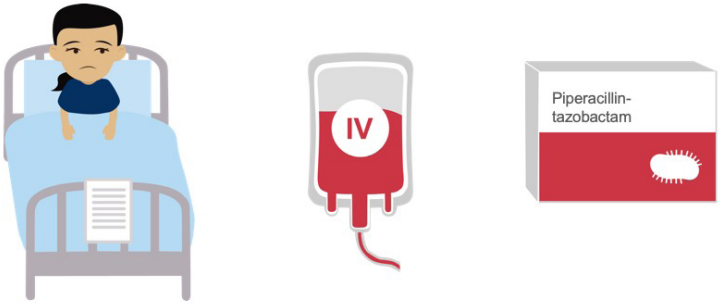


For most patients surgical resection of the involved sigmoid colon is ultimately required.

However, in order to reduce inflammation and infection, treating with antibiotics that cover the mixed flora of the colon prior to surgery is highly recommended.

For mildly ill patients, amoxicillin-clavulanate or a fluoroquinolone plus metronidazole should be effective.

For sick patients, hospitalization and IV antibiotics, such as piperacillin-tazobactam or ertapenem are required.



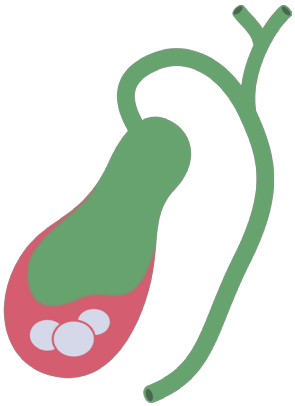
Managing cholecystitis and colitis

Cholecystitis

Cholecystitis refers to the inflammation of the gall bladder.

Pathogenesis

Gallstones are present in more than 90% of patients who develop acute cholecystitis. The stones slow down the normal flow of bile in a similar way that sluggish urine flow predisposes to urinary tract infection. Bacteria from the gut colonize the partially obstructed biliary tract and eventually cause acute cholecystitis.



Common symptoms

- Abrupt onset of steady right upper quadrant (RUQ) abdominal pain
  - often after a large, fatty meal
- Pain may radiate to the right shoulder region
- Nausea and vomiting (70% of cases)
- Abdominal tenderness
  - often in the RUQ upon inspiration (Murphy's sign)

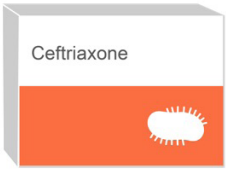
Common laboratory findings

- Elevated white blood cell counts
- Bilirubin
- ALT (alanine aminotransferase)
- Alkaline phosphatase

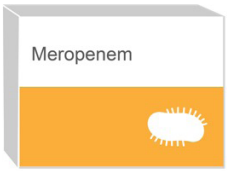
Clinical management

The imaging of choice is ultrasound and when the probe is placed in the RUQ and the patient inspires, the associated pain / tenderness constitutes a positive sonographic Murphy's sign.

For mild to moderate disease, ceftriaxone is recommended. For severe disease, a carbapenem like meropenem is preferred.



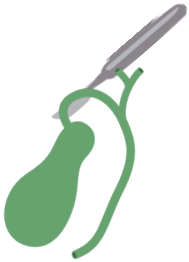
Mild / moderate



Severe

For patients with a beta-lactam allergy in severe disease, the combination of a fluoroquinolone plus metronidazole should cover the mixed aerobes and anaerobes expected.

After the acute inflammation subsides, an elective laparoscopic cholecystectomy is recommended in most patients.



Antibiotic-associated colitis

The vast majority of cases of antibiotic colitis are caused by *Clostridium difficile*, an anaerobic gram-positive bacillus, which is resistant to many antibiotics.

Pathogenesis

C. difficile is also a member of the normal colonic flora in many individuals. Thus, when patients receive antibiotics, the bacteria may survive or transition to spores, which may later germinate and produce toxins that injure the bowel and cause diarrhea.

When the injury is severe, the mucosa may be studded with pseudomembranes made up of sloughed epithelial cells and inflammatory cells. The diarrhea may be mild or severe and is rarely bloody, although stools may test positive for occult blood.

Characteristics of severe disease

- Fever
- Abdominal tenderness or distention
- Hyperactive or hypoactive bowel sounds
- Hypertension
- Septic shock

In critically ill patients, the only clue to the colitis may be otherwise unexplained leukocytosis. Stools are usually positive for leukocytes and *C. difficile* toxin. Alternatively, pseudomembranes can be recognized by colonoscopy if the diagnosis cannot be confirmed by toxin assay.

Clinical management

The initial treatment of choice in a patient who is toxin-positive and mildly to moderately ill would be oral vancomycin for ten days. Alternatively, oral fidaxomicin, a macrocyclic lactone antibiotic with activity versus *C. difficile*, could also be given for ten days. Fidaxomicin has a lower rate of recurrence than vancomycin. If neither of these drugs

is available, metronidazole, which was once considered first-line therapy, can be used.

For recurrent disease, fecal transplants from uninfected persons are more effective than vancomycin. If unrecognized and untreated, *C. difficile* colitis may lead to the development of toxic megacolon, which sometimes requiring lifesaving colectomy for hope of cure.

Handling food poisoning

There are many potential causes of food poisoning or food-borne illnesses and many different presentations. Most food poisoning is not caused by the presence of the bacterium itself, but by the presence of a toxin produced by bacteria which can linger in food. There are two basic categories of toxins that cause food poisoning: heat-stable toxins, which remain active at high temperatures, and heat-labile toxins, which are inactivated by high temperatures such as through cooking food.

Heat-stable toxins

Staphylococcus aureus

Staphylococcus aureus food poisoning is commonly seen at picnics.

Common sources of preformed toxin

- Sandwich spreads
- Packaged meats
- Cream-filled pastries
- Foods left unrefrigerated for extended periods

The syndrome produced has the fastest onset of any food poisoning.

Common symptoms

- Abrupt onset of nausea and vomiting (4–8 hours)
- Usually resolves in 24–48 hours

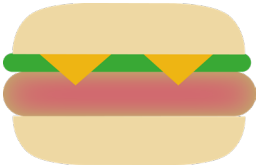
Management is primarily supportive.

Hemolytic uremic syndrome

Enterohemorrhagic *Escherichia coli* (EHEC) is an organism possessing a toxin originally found in *Shigella dysenteriae* known as Shiga toxin 2. Shiga toxin 2 causes widespread endothelial damage, which in turn disrupts and distorts RBCs and results in a microangiopathic hemolytic anemia.

The endothelial damage includes the renal vasculature and can cause acute kidney injury. Thus, the process is known as the hemolytic uremic syndrome (HUS).

The food source most commonly associated with HUS is undercooked hamburger meat. Patients are usually infants and toddlers.



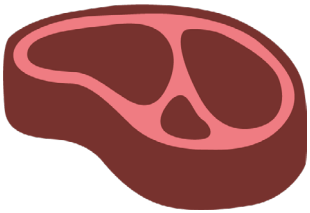
Common symptoms

- Abdominal cramps
- Nausea and vomiting
- Non-bloody diarrhea (becomes bloody within 3 days)
- High fever not typical
- Elevated blood urea nitrogen and creatinine levels

Ironically, treatment with antibiotics may result in increased toxin levels, especially with bactericidal antibiotics, which may result in the release of preformed toxin and worsen the process. Thus, antibiotics are reserved only for patients with documented bacteremia.

Heat-sensitive toxins

Alpha toxin



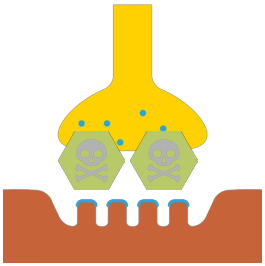
Clostridium perfringens is a gram-positive anaerobic organism, which is the second most common cause of food-borne illness in the United States and the United Kingdom. It produces a heat-labile, preformed alpha toxin and can be found in undercooked beef. The toxin damages the small intestinal membrane producing pores in the mucosa.

Common symptoms

- Abdominal cramps
- Mild or severe watery diarrhea

The disease is self-limited and only supportive care is required.

Botulinum toxin



Clostridium botulinum produces a toxin which blocks acetylcholine release from the synapses of neurons at the neuromuscular junction, resulting in life-threatening flaccid paralysis when it involves muscles of respiration.

When spores of the organism contaminate canned foods in an acidic environment, the spores germinate and become toxin-producing gram-positive bacilli.

Common symptoms

- Diplopia (within hours)
- Difficulty breathing (becomes more obvious later)

Treatment involves antitoxin administration and respiratory support with mechanical ventilation if necessary.

Before 1950, the fatality rate associated with food-borne botulism was 60–70%, while currently it is 5–10% in developed countries.

Heat-stable and heat-labile toxins

Some bacteria produce both heat-stable and heat-labile toxins, which contribute to food poisoning.

Bacillus cereus

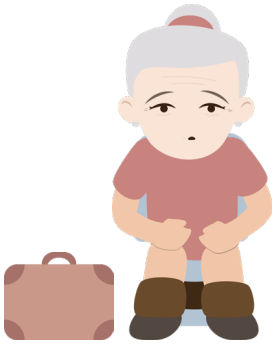
Like staphylococcal food poisoning, *Bacillus cereus* makes a heat-stable toxin in foods (notoriously fried rice), which when reheated and ingested, causes the abrupt onset of vomiting. The organism also makes a heat-labile toxin, which causes watery diarrhea lasting one to two days.

Treatment of food poisoning due to *B. cereus* consists of supportive care; antibiotics are not indicated.

Enterotoxigenic Escherichia coli

The most common cause of traveler's diarrhea is Enterotoxigenic *Escherichia coli* (ETEC).

The infection is transmitted via contaminated drinking water sometimes obvious and at other times in unsuspected sources like salads and even salsa in restaurants.



Unlike the *E. coli* of normal fecal flora, ETEC produces both a heat-stable and a heat-labile toxin. The heat-stable toxin causes cells to secrete chloride into the intestinal lumen—water and sodium would follow. The heat-labile toxin also causes electrolytes and water to be secreted into the lumen through a similar mechanism.

Common symptoms (abrupt onset)

- Cramps
- Watery diarrhea
- Sometimes fecal incontinence

Travelers diarrhea can be treated with a single dose of ciprofloxacin or azithromycin.

Coping with diarrhea

Infectious diarrhea can originate in either the large or small bowel, with distinguishing characteristics typical of each type.

Invasive large bowel diarrhea

Common routes of transmission

- Food handlers
- Unpasteurized dairy products
- Undercooked eggs (potentially carrying *Salmonella*)
- Seafood (potentially harboring *Vibrio* spp)
- Exposure to wild and domestic animals
- Consumption of contaminated water (most common)

Invasive diarrhea most often causes colitis. Thus, patients have the abrupt onset of variable fever, hypogastric cramps, and small-volume diarrhea with tenesmus, which describes the severe urgency to defecate with or without anal discomfort.

Stool exam shows the presence of white and red blood cells indicating an invasive process. Stool and blood cultures are recommended for sick patients.

Many infections are self-limited with symptoms resolving within a week. If symptoms are mild, no antibiotics need to be given unless there is danger of exposing others to organisms like *Salmonella* and *Shigella*. However, when in doubt, it's generally best to treat. It is noteworthy that

for severe disease ciprofloxacin is the primary or alternative treatment, although doxycycline is recommended for *Yersinia enterocolitica* infections.

Antidiarrheal agents should not be used because slowing peristalsis may result in a buildup of the enteric pathogen, leading to complications like toxic megacolon.

Small bowel diarrhea

Viruses cause 30–40% of infectious diarrhea. Two viruses in particular are notorious—*Rotavirus* and *Norovirus*.

Rotavirus

Rotavirus is the leading worldwide cause of dehydrating, diarrheal illness in very young children, and causes 400 000 deaths per year. By age five, virtually all children have been infected.

The onset of disease begins with two to three days of fever and vomiting followed by watery diarrhea producing up to 20 stools / day.

The disease is ordinarily self-limiting and does not require antibiotic treatment.

Norovirus

Norovirus is the leading cause of foodborne diarrhea in the United States and is responsible for 20% of all cases of diarrhea in adults and children.

It is often transmitted via food handlers in mass settings like cruise ships but is also common in daycare centers and classrooms.

Since dehydration can be life-threatening in severe viral diarrhea, it can be avoided with oral rehydration solutions containing sucrose and sodium chloride, or with IV normal saline in sicker patients.

How can we distinguish small from large bowel diarrhea?

Small bowel diarrhea

- Usually caused by viruses
- Watery diarrhea
- Large-volume diarrhea
- Sometimes results in fecal incontinence

Large bowel diarrhea

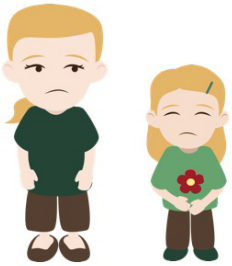
- Usually caused by non-viral pathogens
- Colitis
- Small-volume diarrhea
- Fecal urgency
- Tenesmus

Chapter 4

UROGENITAL INFECTIONS

Resolving urinary tract infections

Acute cystitis



Acute cystitis, or bladder infection, is ordinarily an infection of women and of girls over two years of age. Cystitis can occur in newborn boys but is extremely rare in older boys or men.

Pathogenesis

Common symptoms (acute onset)

- Dysuria
- Frequent urination

Urinalysis typically shows

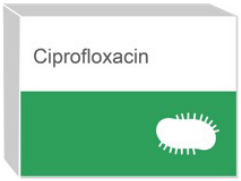
- Red blood cells
- White blood cells
- Positive leukocyte esterase
- Nitrites

Clinical management

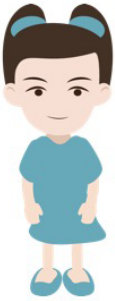
E. coli is the most common cause of bacterial cystitis and antibiotic resistance is increasing owing to the frequent use of trimethoprim-sulfamethoxazole and ampicillin over many decades.

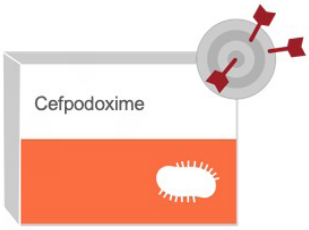
Three days of therapy has been shown to be as good as two weeks of treatment when treating acute cystitis.

Single-dose therapy may be considered in women and a fluoroquinolone, such as ciprofloxacin is often the best choice.



In prepubescent girls, however, a third-generation cephalosporin like cefpodoxime (or cefixime) should be given empirically pending the results of cultures, and urinary tract ultrasound is recommended to rule out anatomical abnormalities. Seven to 14 days of therapy is recommended.





A negative urine culture in a patient with dysuria should raise the possibility of chlamydial urethritis, which can be diagnosed with nucleic acid amplification tests. This would be treated with seven days of doxycycline.

Acute pyelonephritis

Acute pyelonephritis refers to infection of the kidney.

Pathogenesis

Common symptoms

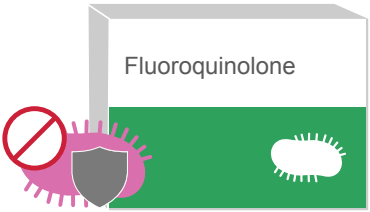
- Fever
- Chills
- Pyuria
- Flank pain
- Costovertebral angle tenderness over the affected kidney

Urinalysis typically shows

- Numerous white blood cells
- Gram stain showing neutrophils and gram-negative rods
- At least 100 000 colonies of *E. coli* (or other gram-negative bacillus)

Clinical management

If there is a low risk of multidrug-resistant gram-negative bacilli in the region, seven to 14 days of a fluoroquinolone will likely be effective.



For concern of multidrug-resistant gram-negative bacteria, seven to 14 days of a carbapenem like meropenem is recommended pending culture results.

Imaging should be used sparingly in young women and is not generally necessary for a straightforward case. However, if stones or ureteral obstruction are suspected or for recurrent pyelonephritis, imaging should be done beginning with ultrasound followed by CT scan.

Acute prostatitis

Acute bacterial prostatitis is typically a disease of men over 35 years of age and is usually caused by *E. coli* or more rarely, *Enterococcus* spp. When it occurs in men under 35 years of age, *Neisseria gonorrhoeae* should be suspected.

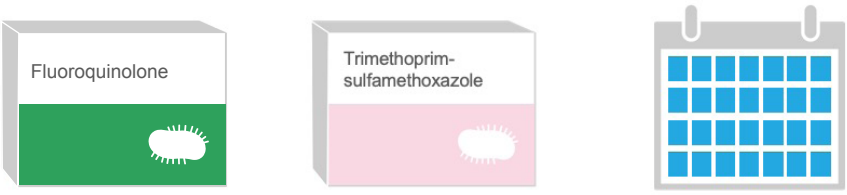
Common symptoms

- Fever
- Chills
- Dysuria
- Increased urinary frequency
- Lower back or pelvic pain (sometimes)
- Pyuria

Clinical management

Recommended treatment is with a fluoroquinolone or trimethoprim-sulfamethoxazole for a minimum of ten to 14 days. However, if necessary, some authorities recommend four weeks of treatment because of the relatively poor concentrations of most antibiotics achievable in the prostate.

Chronic bacterial prostatitis



In contrast, chronic bacterial prostatitis is a disease of men with enlarged prostates.

Common symptoms

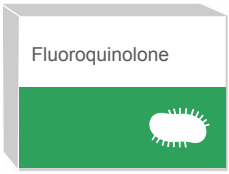
- Patients are not acutely ill
- Intermittent dysuria
- Increased urinary frequency
- Pelvic pain (sometimes)

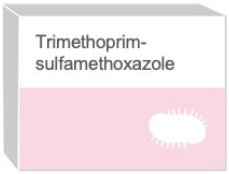
Clinical management

A bacterial cause can be determined by a comparison of pre- and post-prostate massage urinalysis and cultures of prostate secretions.

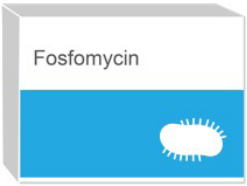
Because the prostate is not inflamed in chronic prostatitis, most antibiotics do not penetrate the gland sufficiently to treat the infection. Fluoroquinolones and to a lesser extent trimethoprim-sulfamethoxazole

(TMP-SMX) treatment does result in adequate tissue levels, but at least four to six weeks of a fluoroquinolone or up to 12 weeks of TMP-SMX is generally necessary to fully eradicate the infection.



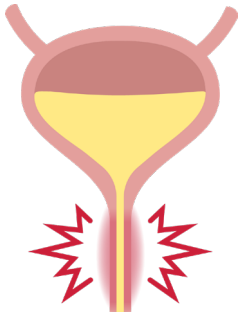


A newer antibiotic, fosfomycin, penetrates the prostate gland and was reportedly successful in the treatment of chronic prostatitis with 12–16 weeks of treatment.



Diagnosing urethritis and pelvic inflammatory disease

Urethritis



Urethritis refers to infections involving the urethra.

Pathogenesis

Common causes

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*

Gonorrhea

Common symptoms of gonorrhea in men

- Urethral gonnorhea
- Severe dysuria
- Urethral discharge
- Symptoms one to ten days after exposure from sexual encounter

Common symptoms of gonorrhea in women

- More subtle than symptoms in men
- Vaginal discharge
- Dysuria
- Intermenstrual bleeding

A Gram stain of the urethral discharge will show gram-negative, intracellular diplococci. This test is very sensitive in men but not in women.

Chlamydia

Most non-gonococcal urethritis is caused by *Chlamydia trachomatis*.

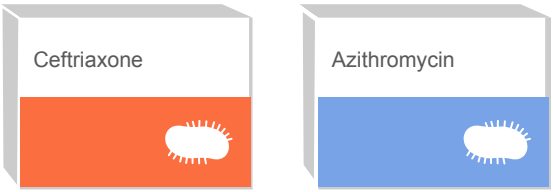
Common symptoms

- Urethral (men)
- Vaginal discharge (women)

In men, Gram stain may be helpful in distinguishing the two pathogens. In *Chlamydia* infections, neutrophils are present, but no bacteria are seen. The Gram stain is not helpful in women because of the mixed flora in vaginal secretions. PCR tests have very good sensitivity and specificity for both pathogens.

Clinical management —gonorrhea and chlamydia

The treatment recommended by the Centers for Disease Control and Prevention (CDC) for urethral or vaginal gonorrhea is dual therapy with a single dose of ceftriaxone plus azithromycin.



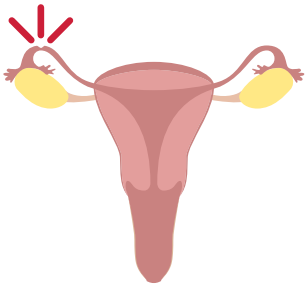
The use of combination therapy involving two antimicrobials with different mechanisms of action aims at improving treatment efficacy and potentially slowing the emergence and spread of resistance to cephalosporins. Use of azithromycin as the second antimicrobial is preferred to doxycycline because of the convenience and compliance

advantages of single-dose therapy and the substantially higher prevalence of resistance of *N. gonorrhoeae* isolates to tetracyclines than to azithromycin. It should be noted that 40–50% of patients with proven gonorrhea are coinfected with *Chlamydia*. Accordingly, azithromycin in a single dose or ten days of doxycycline should be included even if tests are negative for *Chlamydia*.

Pelvic inflammatory disease

Pelvic inflammatory disease (PID) is a disease that affects the female reproductive organs.

Pathogenesis



Common causes

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*

PID can result from previous tubal injury and partial obstruction from one of these pathogens. In that case, a mixed microbial flora resembling fecal flora can be present with or without *N. gonorrhoeae* or *C. trachomatis*. The disease ordinarily occurs in sexually active young women.

Common symptoms

- Pelvic pain
- Vaginal discharge
- Dyspareunia
- Fever (often but not always)
- Uterine or adnexal tenderness
- Cervical motion tenderness

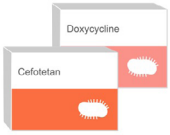
Common laboratory findings

- Elevated white blood cell count
- Elevated erythrocyte sedimentation rate (ESR)
- Increased c-reactive protein

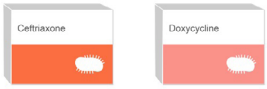
Ultrasound may reveal a dilated fallopian tube or even a pyosalpinx, a condition in which the fallopian tube fills up and swells with pus.

For patients who require hospitalization, the combination of cefotetan and doxycycline has been popular for many years.

Unlike cephalosporins of most generations, cefotetan (a second-generation cephamycin) has useful activity against anaerobes which might be part of the infectious process.



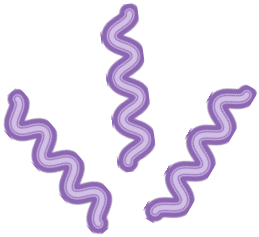
For patients who can be treated as outpatients, a single dose of ceftriaxone plus a 14-day course of doxycycline is usually effective.



Single dose 14 days

Discerning primary and secondary syphilis

Syphilis is a sexually transmitted disease caused by the spirochete, *Treponema pallidum*. These spirochetes have a characteristically helical shape and are transmitted from a person with an active syphilitic skin lesion, through mucosal lesions or microperforations, which are breaks in the skin or mucosal sites.



Syphilis presents in four stages

- Primary
- Secondary
- Tertiary
- Latent

Primary syphilis

Ten to 90 days after sexual exposure, the first signs of a primary syphilis infection appear.

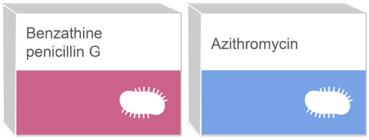
Common symptoms

- Chancre (circumscribed, painless ulcer with rounded, firm borders and a clean base)
  - usually asymptomatic
  - easily transmitted to uninfected persons
- Lymphadenopathy (painless, *rubbery*)

Serology may be negative in up to 30% of individuals with primary syphilis.

Clinical management

Treatment is a single dose of benzathine penicillin G (2.4 million units intramuscular [IM]) or azithromycin (2 g orally).



Secondary syphilis

Secondary syphilis results when many organisms from the primary lesions gain access to the bloodstream. This typically occurs two to eight weeks after the chancre appears. In some patients the chancre is still present.

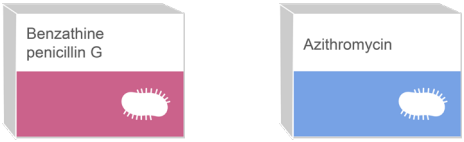
Common symptoms

- Diffuse papulosquamous rash on hands and feet
- Chancre may still be present
- Mucous membrane lesions in mouth or genitals
- Exophytic lesions in genital area
- Aseptic meningitis-like picture with cerebrospinal fluid pleocytosis
- Fever
- Malaise
- Sore throat
- Myalgias

At this stage, nearly 100% of patients will have a positive serologic test for syphilis.

Clinical management

The treatment for secondary syphilis is the same as for primary syphilis (single dose of benzathine penicillin G [2.4 million units IM] or azithromycin [2 g orally]).



If not treated, the symptoms of secondary syphilis will eventually subside, but the infection will remain and develop into tertiary or latent syphilis.

Treating tertiary and latent syphilis

Tertiary syphilis

Tertiary syphilis may clinically manifest in many ways and may involve the cardiovascular system, brain, spinal cord, and any deep organ.

Common presentation

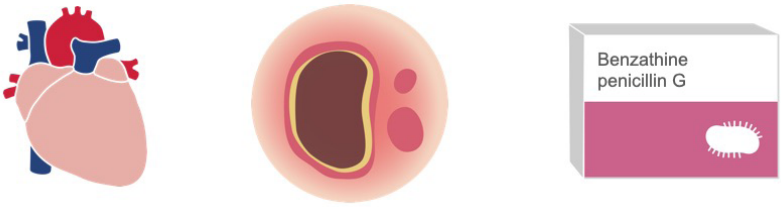
- Some patients are asymptomatic
- Cardiovascular syphilis
  - aortitis (70–80% of untreated patients)
  - aortic aneurysms
  - aortic insufficiency
  - narrowing of coronary ostea
- Tabes dorsalis (classic spinal cord lesion)
  - loss of vibratory and position sense
  - peripheral neuropathy
  - unstable gait
- Syphilitic gummas (macroscopic or microscopic granulomatous reactions)
  - can appear in any infected organ (including skin)
- Neurosyphilis

Neurosyphilis can manifest as a stroke or as gradual deterioration in cognitive ability. It can manifest as emotional lability, paranoia, carelessness in appearance, delusions or hallucinations, confabulation, decreased memory, and slurred speech.

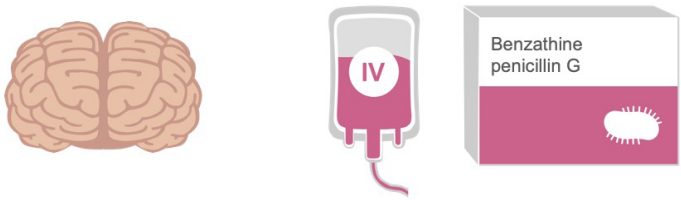
Neurosyphilis should be considered in patients with unexplained dementia, and serology and cerebrospinal fluid (CSF) analysis should be carried out in these patients. CSF findings include a pleocytosis, elevated protein, and a positive CSF VDRL, which is a non-treponemal test that detects antibodies to cardiolipin antigen.

Clinical management

Cardiovascular syphilis and gummas can be treated with benzathine penicillin G (2.4 million units IM) once a week for three weeks



but neurosyphilis requires two weeks of high-dose, intravenous penicillin G (18–24 million units / day).



With treatment, many patients show some improvement in neurological function and ongoing aortitis may be halted. Patients with aortic aneurysms and aortic insufficiency need to be carefully evaluated by cardiologists and cardiovascular surgeons for definitive therapy.

Latent syphilis

Patients with latent syphilis have a positive serology for *Treponema pallidum* without manifest disease.

Early latent syphilis

The initial infection occurred within the past 12 months.

Late latent syphilis

The infection occurred more than 12 months previously.

Diagnosing early latent syphilis

- Positive syphilis serology

  and
- Four-fold increase in non-treponemal titers compared to first serological measurement

  or
- Experienced symptoms suggestive of primary or secondary syphilis in past year

  or
- Had sexual partner with primary, secondary, or latent syphilis within last year

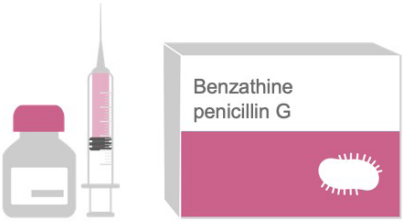
Clinical management

Treatment of early latent syphilis involves a single intramuscular dose of 2.4 million units of benzathine penicillin G.

Diagnosing late latent syphilis

All other patients with a positive serology are considered to have late latent syphilis.

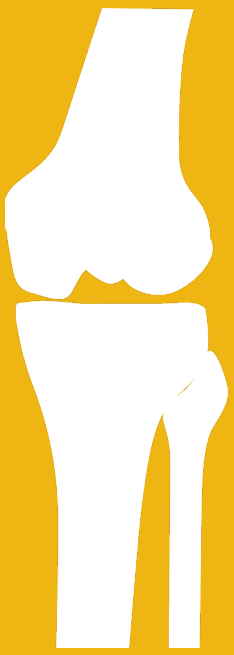
These patients could have occult neurosyphilis and cerebrospinal fluid analysis is recommended. If the cerebrospinal fluid (CSF) does not reveal white blood cells or increased protein, patients can be treated with 2.4 million units of benzathine penicillin G IM once a week for three weeks.



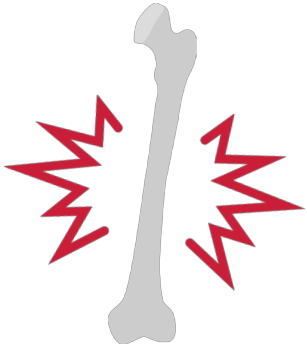
However, if their CSF contains more than five white blood cells per microliter (µL) and CSF protein is greater than 45 mg / dL, they should be assumed to have neurosyphilis and should be treated as such.

Chapter 5

BONE, JOINT, AND SKIN INFECTIONS



Treating osteomyelitis



Osteomyelitis refers to infection of the bone.

Osteomyelitis can arise from

- Bacteria circulating in the bloodstream (hematogenous)
- Organisms in infections present near bones (contiguous infections)
- Traumatic inoculation
- A complication of joint replacement

Common causes

- *Staphylococcus aureus*
  - 80% of cases
- *Kingella kingae*
  - children under two
- *Staphylococcal, Salmonella* or gram-negative rod bacteremia
  - older persons
  - persons with frequent IV infusions, bladder and intravascular catheters
- *Pasteurella mulocida*
  - dog and cat bites

Acute osteomyelitis

Acute osteomyelitis is most common in infants and children and is hematogenous in origin.

Pathogenesis

Staphylococcus aureus is the most common organism involved but streptococci or *Haemophilus influenzae* can cause the disease as well.

In infants the nearby joint is often involved because the joint capsule surrounds the epiphysis and diaphysis. Concomitant joint infections are not common in older children and adults because the joint capsule is outside the epiphysis.

Common symptoms

- Fever with or without chill
- Focal pain
- Redness
- Tenderness

Laboratory and imaging findings

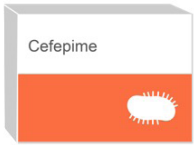
- Moderately elevated white blood cell count
  - predominance of neutrophils and bands
- Rapid erythrocyte sedimentation rate (ESR)
- Elevated c-reactive protein
- Radiolucencies and elevated periosteum (occasionally) on x-ray
- Areas of enhancement in bone marrow on MRI

Vertebral osteomyelitis, like acute osteomyelitis in children, is usually hematogenous in origin and may result from an infected intravenous access, urosepsis or from dental abscesses. Thus, the microbiology often involves *S. aureus*, enteric bacteria or mixed mouth flora. Fewer than half of the patients are febrile but focal pain and tenderness of the spine is characteristic.

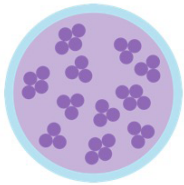
Clinical management

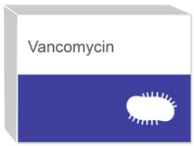
Bone infections are difficult to eradicate and antimicrobial therapy is necessarily prolonged. Therefore, it is crucial to biopsy involved bone to make an exact microbiologic diagnosis to tailor antimicrobial therapy to the best regimen. Biopsies must be performed prior to antimicrobial treatment and can be done via needle or open biopsy.

For acute osteomyelitis in infants, empirical therapy with vancomycin to cover gram-positive organisms including MRSA, plus cefepime to cover gram-negatives, is preferred.



For older children, the bone biopsy should be sent for cultures and Gram's stain. If gram-positive organisms are present, vancomycin should be commenced empirically.





If cultures yield methicillin-susceptible *Staphylococcus aureus*, intravenous nafcillin or oxacillin should be substituted for vancomycin.

In children, three weeks of antibiotic treatment is usually sufficient. Debridement of bone is rarely necessary unless there is antibiotic failure. Moreover, once the infection is clearly improved, therapy may be switched to oral antibiotics.

Chronic osteomyelitis

Chronic osteomyelitis often follows a traumatic wound with fractures requiring open reduction and internal fixation.

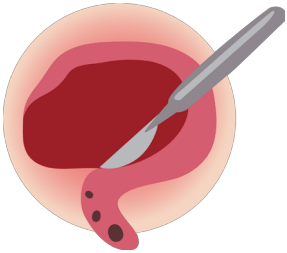
Pathogenesis

Symptoms may be subtle since patients are left with residual chronic symptoms from the original injury. Signs of infection may come and go with overlying redness, pain, increased warmth, and tenderness over the underlying bone. Purulent drainage through fistulous tracts may emerge from the area.

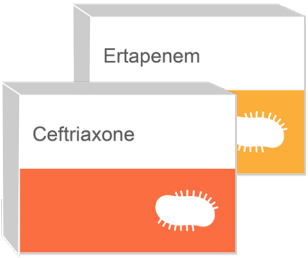
Overall, *Staphylococcus aureus* is the most common cause in upper or lower extremities, but gram-negative organisms may be found, especially in lower extremity infections. Imaging of bone often shows lucencies

and periosteal elevation and a frank abscess in bone may occur, called Brodie's abscess.

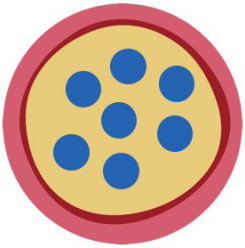
Clinical management



Treatment of chronic osteomyelitis first involves surgical debridement of all dead bone and, if the remaining defect is large, covering of the wound with skin and / or muscle flaps.



Four to six weeks of antibiotic therapy is usually required and is based upon the results of cultures from the debrided tissue. Drugs with long half-lives, such as ceftriaxone and ertapenem, are often chosen because they can often be given once daily as outpatients. However, broad-spectrum agents used for a long time when not absolutely necessary increase the risk of multidrug-resistant bacteria, so it's best to de-escalate treatment based on the culture results when possible.



Many surgeons place antibiotic-impregnated polymethylmethacrylate beads into the wound as part of local therapy, especially if the wound contains large areas of dead space after surgery. Procedures are mainly a surgical decision and antibiotics have to be adapted to cultures and to remaining defects in the infected bone.

Conquering septic arthritis

Septic arthritis is usually the result of a hematogenous (blood-borne) infection.

Pathogenesis

Common causes

- *Staphylococcus aureus* (~ 50% of cases)
- Other streptococci (20% of cases)
  - *Streptococcus pneumoniae*
  - *Streptococcus gallolyticus*
    - suggests intestinal lesion like colon cancer
    - consider colonoscopy in these patients
- *Neisseria gonorrhoeae* (3% of cases)
  - most common in sexually-active young adults

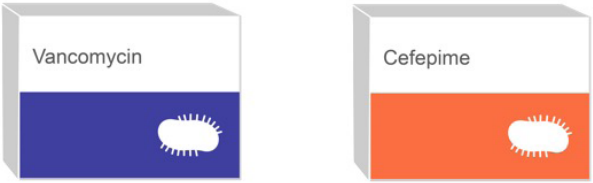
The knee is the most common joint involved in persons over 15 years of age and the hip in infants and children. Septic arthritis is also more frequent in persons with prosthetic joints and rheumatoid arthritis.

The infection can be rather subtle in patients with rheumatoid arthritis because they may have redness and tenderness of joints due to the underlying disease. An infected joint may go unrecognized before major joint destruction has occurred.

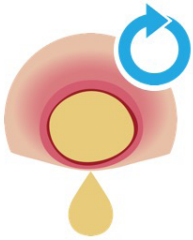
The diagnosis of septic arthritis requires joint aspiration, fluid analysis, fluid culture and Gram stain. Infected joint fluid will generally show increased white blood cell count, increased protein, and has a decreased viscosity and glucose. Gram stains are positive for the causative organism in half of the patients and joint fluid culture is positive in more than 80%. Blood cultures are positive in half the patients. Because of the possible negative results of these studies, empirical treatment is often needed.

Clinical management

A good combination for empirical therapy is vancomycin (for suspected MRSA) plus cefepime, which would cover the vast majority of pathogens expected.



Repeat drainage by arthrocentesis is needed until cultures are negative and WBC counts decrease. The hip joint is difficult to drain percutaneously and usually requires open drainage. Drainage is urgent because infection can destroy a joint in a short period of time.



Recognizing common skin and soft tissue infections

There are many common skin and soft tissue infections. None are highly contagious. However, precautions should be taken when changing open wound dressings with increased attention to regular handwashing and hygiene as well as the avoidance of direct contact with even small skin breakdown to help curtail spread.

Impetigo

Impetigo is a vesiculopustular or crusted, superficial skin infection usually caused by *Streptococcus pyogenes* with or without *Staphylococcus aureus*.

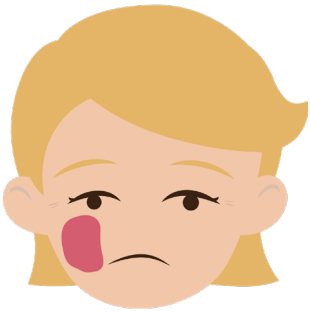
Common symptoms

- May be slightly itchy
- Pain and constitutional symptoms absent

The crusts are typically honey-colored and the undersurface contains abundant gram-positive cocci.

To hasten resolution, the infected crusts should be gently scrubbed off with a soft cloth or soft brush. For patients with few lesions, topical mupirocin, fusidic acid or retapamulin antibiotics work well, but if many lesions are present, systemic therapy with penicillin V or trimethoprim-sulfamethoxazole for a five-day course is usually sufficient. Healing occurs without scarring.

Erysipelas



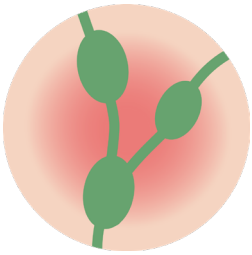
Erysipelas is a spreading infection, which involves the epidermis and more superficial layers of the skin and is almost always caused by *Streptococcus pyogenes* but *Staphylococcus aureus* can mimic it.

The lesions are characteristically sharply demarcated and the skin follicles are easily visible because of the superficial edema giving the surface of the skin a peau d'orange, or orange peel, appearance. The lesions are most commonly on the lower extremities and less often the face.

Common symptoms

- Skin lesion
- Pain
- Fever
- Systemic toxicity

Lymphangitis



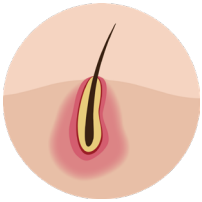
Lymphangitis is inflammation of the lymphatic system. Lymphangitis and lymphadenitis are usually caused by *Staphylococcus aureus* or beta-hemolytic streptococci, alone or in combination. They are generally a complication of an infected wound, traumatic or otherwise.

Common symptoms

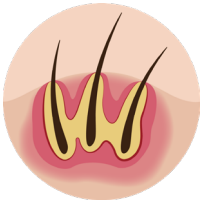
- Characteristic red streak (overlying inflamed lymphatic channels)
- Tender, engorged lymphatic channels
- Fever
- Chills
- Malaise
- Infection may progress rapidly to bacteremia and sepsis

After obtaining blood cultures, empirical vancomycin to cover possible methicillin-resistant *Staphylococcus aureus* should be given pending the culture results.

Furuncles and carbuncles



Furuncles, or boils, originate from a staphylococcal folliculitis and are deep-seated infections involving the entire hair follicle and adjacent soft tissue.



A carbuncle consists of several furuncles developing in adjoining hair follicles and coalescing to form a large, deeply situated mass with multiple drainage sites.

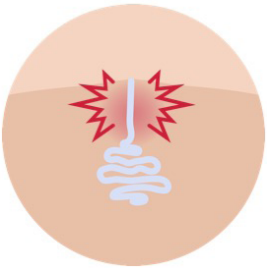
Because of increased carriage of *Staphylococcus aureus*, diabetes mellitus is a risk factor.

Patients may or may not have fever and other systemic symptoms but the lesions are generally very painful. Incision and drainage are the mainstays of treatment.

Most patients are given antibiotics before manipulation of the abscess. Because of concern for community-acquired MRSA, outpatients are generally given trimethoprim-sulfamethoxazole or doxycycline.

Inpatient therapy would begin with intravenous vancomycin prior to incision.

Hidradenitis suppurativa



Hidradenitis suppurativa is secondarily an infectious disease but primarily a congenital keratinous follicular plugging of apocrine sweat gland ducts. The obstruction leads to infection by innate and colonizing skin flora and is thus usually a mixed infection. *S. aureus* can be a part of the pathologic process.

This diagnosis should always be considered in patients with a history of recurrent boils.

Antibiotics for mixed infection which include anaerobes are most effective, such as amoxicillin-clavulanate or a fluoroquinolone plus metronidazole, along with incision and drainage of any obvious abscess. Definitive therapy requires excision of areas where apocrine sweat glands are found, such as axillae or groin.

Controlling life-threatening skin and soft tissue infections

While some skin infections are rather innocuous, there are others you will need to identify and treat quickly, as they can be life-threatening.

Cellulitis

Staphylococcal or streptococcal causes

Cellulitis is commonly caused by staphylococci or streptococci. It is mainly superficial but extends into subcutaneous tissue.

Because cellulitis and erysipelas can be serious infections, blood cultures should be drawn before antibiotics are given.

Vancomycin is the prudent empirical choice pending susceptibility studies. Warm soaks and elevation of extremities may hasten recovery by improving circulation in the involved areas.

Other causes

Cellulitis can also be caused by less common organisms. For example, *Aeromonas hydrophila* is a gram-negative rod, which is an ubiquitous inhabitant of fresh water. *Vibrio vulnificus* is a curved gram-negative rod, which is likewise part of normal sea water flora.

Both organisms can cause life-threatening cellulitis and bacteremia with fever, pain, tenderness, erythema, and swelling of skin usually after traumatic injury and exposure to these bodies of water.

These types of cellulitis are notorious for rapid progression because of their virulence and can lead to necrotizing fasciitis.

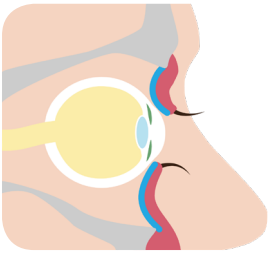
Fluoroquinolones are preferred for *Aeromonas hydrophila* and the combination of ceftriaxone and doxycycline for *Vibrio vulnificus*.

Periorbital cellulitis

Cellulitis can also involve the orbit. The orbital septum is a membranous sheet forming the anterior boundary of the orbit.

Preorbital cellulitis

Infection of the skin anterior to the septum are known as preorbital cellulitis.

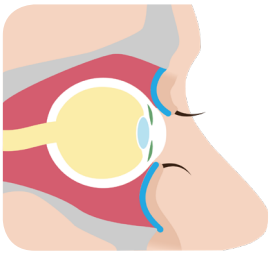


Common symptoms

- Fever
- Swelling, redness, and tenderness of periorbital tissues
- Orbit itself is not involved
- Extraocular muscle movements intact

Infections are usually due to respiratory pathogens like *Haemophilus influenzae* and *Streptococcus pneumoniae*.

Postseptal cellulitis



Patients with postseptal orbital cellulitis have deep involvement of the orbit itself.

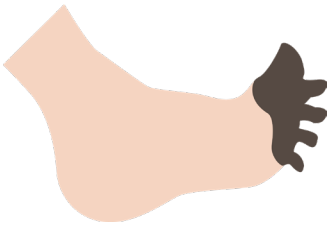
Common symptoms

- Extraocular palsy
- Visual disturbance
- Redness
- Tenderness
- Swelling

The usual pathogen in postseptal orbital cellulitis is *Staphylococcus aureus*.

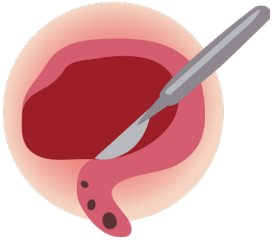
Emergency debridement and drainage are usually needed for postseptal cellulitis because of the possibility of multidrug-resistant bacteria. Vancomycin should be given along with a beta-lactam like ceftriaxone.

Necrotizing fasciitis



Necrotizing fasciitis is a life-threatening form of deep skin infection, which involves all layers plus muscle fascia beneath. Early on, the infection may resemble cellulitis with fever, erythema, tenderness, and warmth. However, antibiotic therapy would fail, owing to deep collections of purulent material beneath the skin. The overlying skin is very indurated and feels hard with little indentation of the skin with palpation.

Later, cutaneous anesthesia may be present, reflecting involvement of sensory nerves as they emerge through fascia en route to the skin. In late stages bullae may form.



Emergency imaging will reveal fasciitis and an emergent surgical consultation should be requested. Cure requires wide debridement of all involved tissue including resection of fascia.

Antibiotic therapy should be based upon Gram stain of pus and tissue resected at surgery, plus historical clues.

Five types of necrotizing fasciitis have been identified

- Type I—infection by at least one anaerobe (e.g., *Bacteroides* or *Peptostreptococcus* **and** one or more facultative anaerobic species, e.g., *E. coli, Streptococcus* spp [not group A])
- Type II—*S. pyogenes* + / - other organisms (especially *S. aureus*)
- Type III—infection caused by marine organisms (e.g., *Vibrio vulnificus, Aeromonas hydrophila*)
- Type IV—community-acquired MRSA
- Type V—*Klebsiella pneumoniae* as monomicrobial cause

The evaluation and surgical management are the same for all types, only the choice of antimicrobial will differ.

Fournier's gangrene

Fournier's gangrene is a unique form of Type I necrotizing fasciitis involving male genitalia. Found most commonly in diabetics, the infection can also be related to local trauma, paraphimosis, periurethral

extravasation of urine following urologic surgery or perirectal surgery. It is a rapidly spreading cellulitis and fasciitis often characterized by cutaneous crepitus from gas-producing gastrointestinal flora.

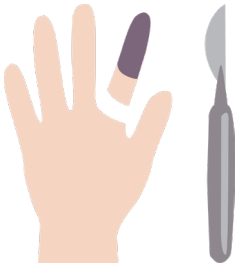
Emergent wide debridement is indicated and broad coverage with piperacillin-tazobactam or a carbapenem are reasonable choices of antimicrobial agents.

Gas gangrene

Gas gangrene is a life-threatening, deep infection through fascia down to muscle, which develops following a traumatic wound or recent surgical procedure. The infection is caused by toxin-producing *Clostridium* spp, usually *Clostridium perfringens*.

Initially the overlying skin is pale, but rapidly becomes bronze, then purplish-red with the formation of bullae on the skin. Within 24 hours, a rapid development of shock and multi-organ failure occurs.

Widespread debridement may not be sufficient. Rather, amputation of an extremity may be required to achieve a margin around the process. At surgery, the dead muscle is brick-red and fails to contract when stimulated by electrocautery.

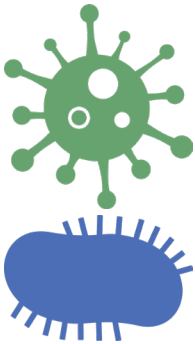


Antibiotic therapy with high-dose IV penicillin G (to kill the organisms) plus clindamycin (to shut down toxin production) is only adjunctive to surgery. Prognosis for patients with gas gangrene is poor.

Chapter 6

CENTRAL NERVOUS SYSTEM INFECTIONS

Identifying acute meningitis



Meningitis is inflammation of the meninges—the membranes that surround the brain and spinal cord.

Meningitis can be viral or bacterial in origin and can present acutely or more chronically.

Viral meningitis

Acute viral meningitis typically occurs in warmer months of the year.

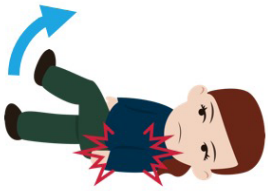
Common causes

- *Enteroviruses* (46%)
- Herpes simplex virus (HSV) 1 or 2
- Varicella zoster virus

Common symptoms (abrupt onset)

- Headache
- Nausea
- Vomiting
- Neck pain or stiffness
- Photophobia (< 30% of patients)
  - high predictive value
- Kernig's sign
  - strong pain in back (when knee extended and hip flexed)
  - high predictive value

- Brudzinski's sign
  - involuntary hip flexion (when neck is flexed)
  - high predictive value



Kernig's sign

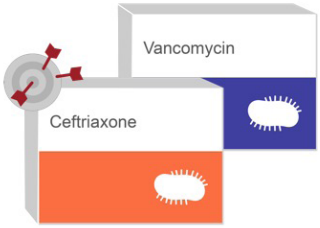
Brudzinski's sign

All patients with suspected meningitis should undergo a lumbar puncture for cerebrospinal fluid (CSF) studies.

Common laboratory findings (CSF)

- Lymphocytic pleocytosis
- Normal protein
- Normal glucose
- Negative Gram stain and culture

Clinical management



In classic cases when the patient is mildly to moderately ill with no confounding features, such as being immunocompromised or prior antibiotic therapy, a case can be made for withholding empirical antibiotic therapy for bacterial meningitis with close observation. This includes rest, analgesia, and anti-nausea medication. However, most authorities recommend administering empirical antibiotics until the final results of cultures are available. One common empirical regimen is the combination of ceftriaxone and vancomycin.

Most patients with HSV2 meningitis receive IV acyclovir when the PCR is positive for viral DNA. Whether it results in faster resolution or prevention of long-term sequelae is uncertain. Most people with mild viral meningitis usually get better on their own within seven to ten days.

Bacterial meningitis

The most common cause of bacterial meningitis is *Streptococcus pneumoniae*. However, this can differ with the age of the individual. In newborns, group B *Streptococcus* is most common because of the high vaginal colonization rate of pregnant women but *Listeria* and *E. coli* must also be considered. *Neisseria meningitidis* become common after the age of two years and is most common among teens and young adults, especially those living in dormitories or military barracks. In older people, *Streptococcus pneumoniae* and *Listeria* infections are the most likely cause of acute bacterial meningitis.

Group B Streptococcus

Neisseria meningitidis

S. pneumoniae/ Listeria

Common symptoms

Newborns

- Listless or fretful
- Poor feeders with weak sucks
- Labile temperatures
- Vomiting
- Diarrhea

Toddlers

- Fever
- Vomiting
- Stiff neck

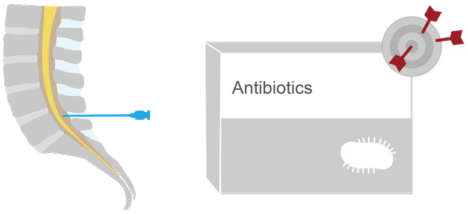
Older children / adults

- Fever
- Altered mental status (80% of cases)
- Neck stiffness
- Kernig's sign (may be present)
- Brudzinski's sign (may be present)
- Petechial or purpuric rash (when *N. meningitidis* is the cause)

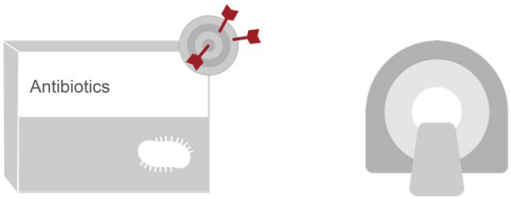
Clinical management

Since acute bacterial meningitis is among the causes of sudden death, empirical antibiotics need to be given as soon as possible. Patients whose picture is suggestive of bacterial meningitis should be quickly examined for focal neurologic deficits like cranial nerve palsy because, if present, there is greater danger of uncal herniation following a lumbar puncture.

If no focal findings are apparent on neurologic exam, an immediate lumbar puncture should be done, CSF collected, and empirical antibiotics given. The CSF is then immediately sent to the laboratory for analysis (cell count, protein, glucose, cultures, and Gram's stain) to save time and possibly mortality.



When there are focal neurologic signs, empiric antibiotics should be given before the patient is sent off for a brain CT scan, because a delay in providing antibiotics may affect mortality.



If imaging shows no focal abnormalities, an immediate lumbar puncture should be done and CSF sent to the lab for analysis.

Common laboratory findings (CSF)

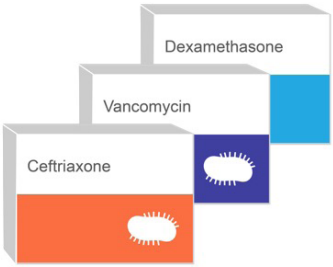
- High WBC count (> 90% neutrophils)
- High protein (> 100 mg / dL)
- High glucose (< 2/3 of corresponding blood glucose obtained immediately before lumbar puncture)

Normal CSF contains no neutrophils, so any amount is significant.

Specific therapy can often be guided by Gram stain results, which are positive in 60–90% of cases, and bacterial antigens in 50–100% of cases. If patients have received antibiotics before CSF was obtained, the Gram stain will be less often positive. Bacterial antigen testing may still be useful.

When there is an antecedent history of swimming and especially diving in fresh water lakes, free-living amoeba can cause a picture identical to acute bacterial meningitis. Thus, it is prudent to take that history and consider a wet mount of freshly obtained CSF where the motile amoebae can usually be seen.

In most patients, the combination of ceftriaxone, vancomycin, and dexamethasone is given empirically. Ceftriaxone and vancomycin should cover the vast majority of pathogens and dexamethasone has been shown to lower the incidence of complications from the inflammatory reaction in the subarachnoid space.



The empirical therapy is directed at the most likely organisms to cause meningitis in various age groups. However, the Gram stain may reveal a specific organism, which may make a physician modify treatment.

Ceftriaxone is a mainstay for most types of meningitis in older children and adults and is usually not de-escalated. Importantly, ceftriaxone is to be avoided in newborns but ampicillin is added to empirical therapy in newborn or elderly patients, because of the risk of *Listeria* infections.

Managing chronic meningitis

Chronic meningitis has a slower onset than the acute forms. Patients have often had symptoms for one month or longer.

Common causes

- Typically slower growing pathogens
- *Mycobacterium tuberculosis*
- *Cryptococcus* spp
- *Histoplasma capsulatum*
- *Coccidioides immitis*
- *Borrelia burgdorferi*

Tuberculous meningitis

Common symptoms (gradual onset)

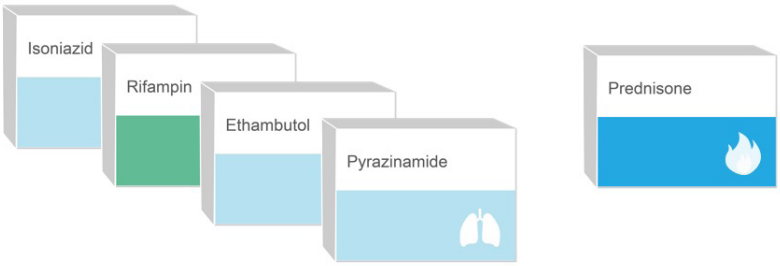
- Listlessness
- Irritability
- Anorexia
- Fever
- Headache
- Vomiting
- Seizures
- Coma
- Stiff neck
- Cranial nerve palsies

Common laboratory findings (CSF)

- Yellowish
- Increased pressure
- Lymphocytic pleocytosis
- High protein
- Low glucose

Cultures are negative in 15–25% of cases and the tuberculin skin test is usually, but not always, positive.

If a strong clinical case can be made for tuberculous meningitis, four-drug therapy with a combination of isoniazid, rifampin, ethambutol, and pyrazinamide should be given, along with tapering doses of prednisone to diminish inflammation, while awaiting the results of confirmatory studies.



Cryptococcal meningitis

Cryptococcal meningitis is the most common fungal cause of meningitis. It is usually due to *Cryptococcus neoformans* serogroup A or D, which is frequently isolated from pigeon and other bird excreta.

Common symptoms

- Slowly progressive headache
- Confusion
- Mild-moderate meningismus
- Visual disturbances

Common laboratory findings (CSF)

- Elevated opening pressure
- Low glucose
- High protein
- High leukocyte count (> 20 / µL) with lymphocyte predominance

India ink mount is positive about half the time but cryptococcal antigens are present in CSF and blood in most patients.

Clinical management

Induction treatment with two weeks of liposomal amphotericin B plus flucytosine is followed by three months of fluconazole (or longer in patients with HIV infection).

In AIDS patients who have cryptococcal meningitis and have just begun antiretroviral therapy, symptoms of meningitis may transiently worsen as their immune function improves. This is referred to as the immune

reconstitution inflammatory syndrome (IRIS), which is treated with tapering corticosteroids while continuing antifungal therapy. Close monitoring of intracranial pressure is indicated if initial pressures were elevated or borderline. Daily lumbar punctures until pressures have decreased or symptoms have resolved are indicated, as this can be a life-threatening complication.

Histoplasma meningitis

Histoplasma meningitis occurs almost exclusively in immunocompromised patients.

Common symptoms (slow progression)

- Fever
- Headache
- Confusion
- Cranial nerve defects

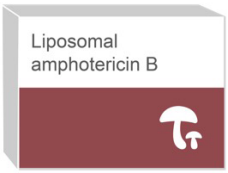
Common laboratory findings (CSF)

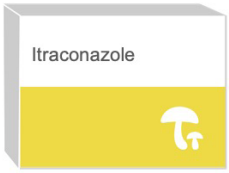
- Lymphocytic pleocytosis
- High protein
- Low glucose

Clinical management

Diagnosis is made in a patient from an endemic area and since positive cultures are the exception, diagnosis is confirmed by the presence of Histoplasma antigens and anti-Histoplasma IgM antibodies.

Treatment is with liposomal amphotericin B for four to six weeks, followed by itraconazole for 12 months.





Coccidioides meningitis

Coccidioides spp can produce a chronic meningitis much like that of histoplasmosis.

Common symptoms

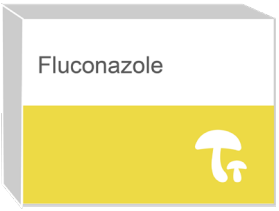
- Headache
- Vomiting
- Stiff neck
- Confusion
- Diplopia

Common laboratory findings (CSF)

- Lymphocytic pleocytosis
- High protein
- Low glucose

Testing of CSF for anti-Coccidioides antibodies complimented by cultures and antigen testing yields the diagnosis with high sensitivity and specificity.

Coccidioides meningitis is presently incurable because of high relapse rates.



In the 20th century, patients with this infection had to endure monthly intraventricular injections of amphotericin B through devices such as Ommaya reservoirs. The development of fluconazole revolutionized treatment, since it has excellent penetration into CSF and has good activity against *Coccidioides* spp; however, it still only controls the infection, rather than curing it, so lifelong therapy has been recommended because relapses are so common.

Lyme meningitis

Chronic meningitis due to Lyme borreliosis usually begins within approximately one month of the tick bite.

Common symptoms

- Headache
- Stiff neck
- Photophobia
- Bell's palsy (occasionally)
- Negative Kernig's sign
- Negative Brudzinski's sign

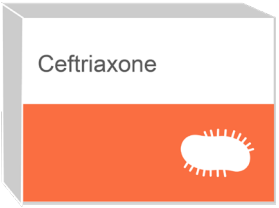
Common laboratory findings (CSF)

- Lymphocytic pleocytosis (< 100 cells / µL)
- Normal glucose
- High protein

Serology for Lyme disease will ordinarily be positive for antibodies to *Borrelia burgdorferi* at this stage. Immunotesting of CSF will usually show a positive IgG or IgM.

Clinical management

Treatment with ceftriaxone should be given for 14–28 days depending upon the response to therapy.



Eliminating encephalitis

Encephalitis is characterized by diffuse inflammation and swelling of the brain.

Arboviruses

The most common causes of epidemic encephalitis are the arboviruses, of which West Nile virus is most common in the United States. Most arboviruses are transferred via mosquito bites.

Common causes

Older adults

- West Nile Virus
- St. Louis encephalitis

Infants and young children

- Western equine encephalitis
- Eastern equine encephalitis

Common symptoms (appear 5–15 days after mosquito bite)

- Fever
- Lethargy
- Stiff neck
- Stupor (severe cases)
- Seizures (severe cases)

Common laboratory findings (CSF)

- Lymphocytic pleocytosis
- High protein
- Normal glucose

These infections can be diagnosed by employing PCR to identify specific viral causes.

Clinical management

These are not chronic infections and the immune system gradually deals with the virus. Some tend to be more severe than others with mortality rates ranging from 4–33%. Treatment can only be supportive.

Herpes encephalitis

Herpes encephalitis is the most common cause of sporadic encephalitis.

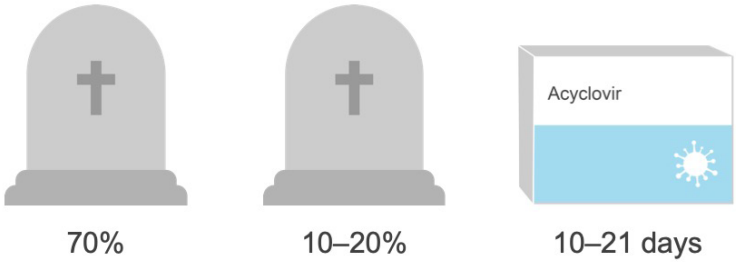
Common symptoms (abrupt onset)

- Headache
- Fever
- Behavioral and speech changes

Imaging usually reveals abnormalities in the temporal lobe.

Clinical management

Without treatment, mortality is 70%. This can be reduced to 10–20% with intravenous acyclovir for 10–21 days.



Chapter 7

LIFE-THREATENING SYSTEMIC INFECTIONS

Recognizing sepsis

Sepsis can best be defined as a systemic, deleterious host response to infection. When severe, it can lead to acute organ dysfunction or septic shock, which is not easily reversed with fluid resuscitation.

Septic shock carries a mortality of 40–70%. Many cases of sepsis are associated with bacteremia but a focus of infection outside the bloodstream can cause the entire process.

Common sources of infection

- Pulmonary infections (~ 50% of cases)
- Unspecified source (~ 20% of cases)
- Genitourinary or gastrointestinal tract infections (most remaining cases)

Sepsis can be caused by either gram-positive or gram-negative bacterial infections, although the latter are slightly more common.

The presence of gram-positive or gram-negative organisms stimulates an immune system cascade, which leads to the production of both pro-inflammatory and antiinflammatory cytokines. When an over response occurs in this process, sepsis develops.

Common symptoms

Early manifestations

- Confusion
- High fever
- Chills
- Hypotension

Late manifestations

- Extreme hypotension
- Rash or other skin lesions
- Gangrenous changes in extremities
- Acute respiratory distress syndrome

In babies

- Fever or hypothermia
- Respiratory distress
- Gastrointestinal problems
- Poor feeding
- Weak suck
- Vomiting
- Abdominal distension
- Worsening jaundice

In elderly patients

- Vomiting
- Diarrhea
- General weakness
- Oliguria

The physician must maintain a high index of suspicion for sepsis in patients who present to emergency facilities or in hospitalized patients who develop some of the following unexplained signs or symptoms.

- Hypothermia
- Tachycardia
- Tachypnea or hyperpnea
- Abdominal pain
- Pelvic pain
- Vaginal discharge
- Abnormal blood clotting
- Altered mental status

The **quick Sequential Organ Failure score (qSOFA)** was developed to prompt physicians to look for organ dysfunction, initiate early antibiotic treatment (within one hour), and refer the patient to an ICU.

Three parameters to quickly assess for sepsis

1. Glasgow coma score < 14
2. Systolic blood pressure < 100
3. Respiratory rate > 21

A qSOFA score of > 2 is highly suggestive of organ dysfunction and a poor outcome of sepsis.

Sepsis is most common and most dangerous in pregnant women, older adults, children under one year old, people with chronic health conditions (e.g., diabetes, kidney disease, lung disease or cancer), and immunocompromised individuals. So it is important to quickly and efficiently diagnose sepsis, especially in these patient populations, so that treatment can be initiated immediately.

Clinical management

The management of sepsis can be complicated. Emergently, the patient's oxygenation and organ perfusion needs treatment. Oxygenation is satisfactory if the central venous O_2 saturation is above 75%.

Fluid resuscitation is necessary to maintain a central venus pressure (CVP) of 8–13 mmHg and a mean arterial pressure of at least 65 mmHg. If fluids fail to reach these targets, norepinephrine is the pressor of choice.

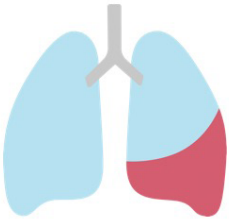
Antimicrobial failure is likely in the presence of a large abscess. Thus, an abscess must be located and adequately drained. When adequate history and physical signs are available, identifying the offending organ system is crucial to the selection of antimicrobial agents.

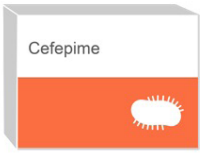
In many instances, microscopy and recent culture results will direct appropriate antibiotic choices but if not, empirical therapy is necessary.

When no history is available and there are no physical signs suggesting the offending organ system, several blood cultures should be obtained and very broad antimicrobial coverage (e.g., a carbapenem) should be given.

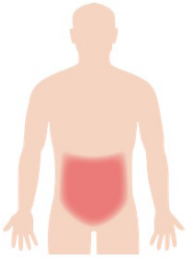
Empirical treatment should be based on the suspected source of infection.

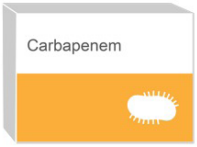
For pneumonia—a fluoroquinolone or azithromycin plus an anti-pseudomonal beta-lactam like piperacillin-tazobactam or cefepime should be given.

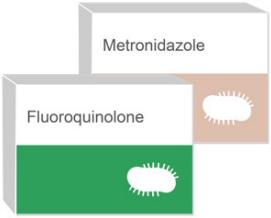




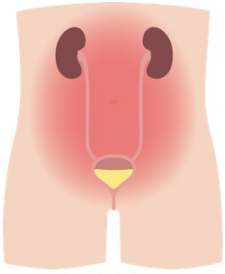
For intraabdominal infection—piperacillin-tazobactam or a carbapenem are excellent choices for mixed aerobic and anaerobic infections. For patients with a beta-lactam allergy a fluoroquinolone plus metronidazole is a good alternative.



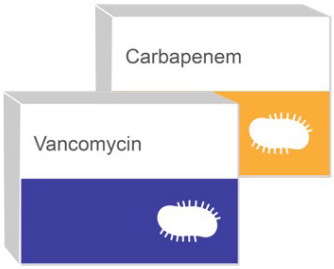




For urosepsis—a fluoroquinolone is a good choice.



For sepsis of unknown source—vancomycin plus a carbapenem like meropenem is warranted.



Defeating infective endocarditis

Pathogenesis

The pathogenesis of infective endocarditis begins with damaged heart valves from congenital heart disease, rheumatic fever, IV drug abuse or the placement of intracardiac devices, such as implantable defibrillators and pacemakers.

Valve damage leads to sterile deposits of platelets, red blood cells, white blood cells, and fibrin called nonbacterial thrombotic endocarditis, or NBTE (a non-infected vegetation).

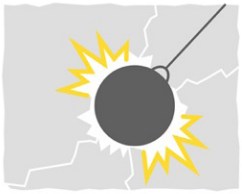
If a sufficiently virulent organism is present in the bloodstream in sufficient amounts it may colonize the damaged valve and its associated NBTE and now the mass of bacteria and NBTE (an infected vegetation) becomes infective endocarditis.

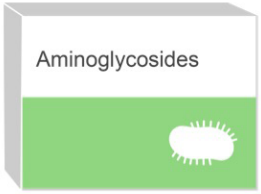
Eighty percent of infective endocarditis is caused by gram-positive cocci of which *Staphylococcus aureus* is most common.

The HACEK group of organisms consists of fastidious gram-negative bacteria that are unusual causes of infective endocarditis. They are, together with fungal infections, notoriously associated with large, friable, vegetations, which can easily break off and cause emboli to vital organs.

Enterococcus causes about 10% of infective endocarditis. *Enterococcus* is a notorious problem if it causes endocarditis because agents that interfere with the organism's cell wall can inhibit these organisms but

cannot kill them. However, bactericidal therapy is essential to prevent recurrence of endocarditis of any cause. Thus, for enterococcal endocarditis, potentially toxic aminoglycosides must be added to cell wall agents for the entire period of treatment to eradicate the infection.





Diagnosis is confirmed by multiple positive blood cultures and visible vegetations noted on echocardiography.

Clinical management

Definitive management of patients with infective endocarditis is best accomplished by an infectious disease specialist and the nuances of antimicrobial therapy are beyond the scope of this lesson.

However, while awaiting culture results, empirical therapy of native valve infective endocarditis with vancomycin plus ceftriaxone is recommended.

For prosthetic valve endocarditis, the combination of vancomycin plus gentamicin plus oral rifampin is recommended because of the possibility of methicillin-resistant *Staphylococcus aureus* (MRSA). This combination is also recommended for methicillin-resistant *Staphylococcus epidermidis* (MRSE). Adjustment of antibiotics can be made by an infectious disease specialist when available.

In some cases of endocarditis, valve replacement early in the course of endocarditis should be considered. It is associated with a lower mortality than elective valve replacement after prolonged antimicrobial treatment.

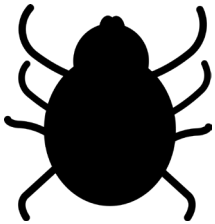
Candidates for urgent valve replacement

- Congestive heart failure
- Infections caused by difficult-to-treat organisms
  - *Enterococcus* (especially on prosthetic valves)
  - *S. aureus*
  - aerobic gram-negative bacilli
  - fungi
- Previous cerebral embolism
- Presence of large vegetations

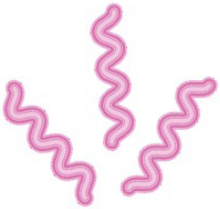
If surgery is inevitable, early surgery has a better prognosis than delaying surgery.

An endocarditis team consisting of a cardiologist, a cardiac surgeon, an infectious disease physician, a microbiologist, and an intensivist who discuss patients in the hospital with infective endocarditis weekly and make decisions about surgery has been shown to reduce mortality substantially. To complete the picture as an outpatient, follow up by a cardiology and infectious disease specialist at one, three, six, and 12 months after surgery, is optimal.

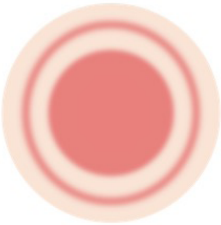
Spotting Lyme disease



Ticks are capable of transmitting many diseases, from viral to parasitic. There is good treatment for only bacterial and parasitic diseases. The most prevalent tick-borne infection in North America, Asia, and Europe is Lyme disease.



Lyme disease is caused by the spirochete, *Borrelia burgdorferi*, and usually transmitted by the bite of the nymphal stage of the hardshell tick *Ixodes scapularis*.



The earliest manifestation is an expanding, target-like lesion which may be slightly pruritic and begins to appear within a month of the tick bite. The skin lesion usually precedes fever and other signs of infection, although myalgias and arthralgias may appear in the early stages, when the skin lesion is still present.

Early disseminated disease can involve the joints, the heart, or the central nervous system (CNS). Arthritis that mostly affects the knee joint may occur when the infection remains untreated. It may be accompanied by effusion but fever is rarely present. A cranial nerve VII palsy is the most common central nervous system manifestation but an aseptic meningitis-like picture can also occur. Varying types of heart block are indicative of carditis.

Who should be screened for Lyme disease?

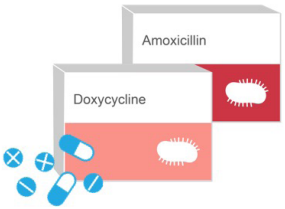
Screening serology is not necessary in patients without any disease after simply being exposed to a tick. Observation is best in these cases.

Screening is also not necessary in patients who present with the classic skin lesion—these patients should be treated.

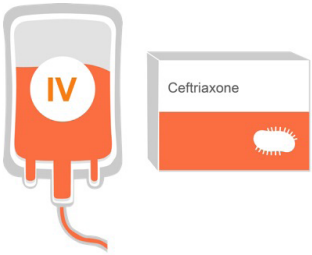
Screening should be carried out in patients with confirmed tick exposure, who show clinical findings such as facial palsy, meningitis or frank arthritis.

Clinical management

Oral therapy with doxycycline or amoxicillin for 14–21 days is usually sufficient for early Lyme disease and mild degrees of cranial nerve VII palsy, but must be continued for 30–60 days in patients with associated arthritis.



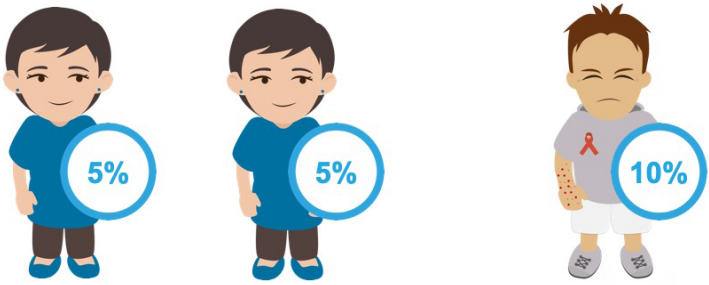
The more serious manifestations are managed with intravenous ceftriaxone.



Characterizing primary and post-primary tuberculosis

Mycobacterium tuberculosis has infected almost two billion individuals worldwide. There are 7–8 million new infections each year, with two million deaths from tuberculosis (TB) worldwide every year, partly due to the epidemic of HIV infection in sub-Saharan Africa and other developing countries. Globally, TB incidence is falling at about 2% per year and the World Health Organization (WHO) aims at ending the epidemic by 2030.

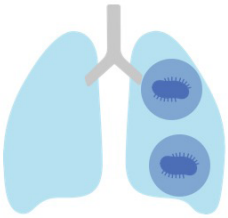
If a previously healthy individual is exposed to TB, there is a 5% chance of developing clinical disease in the first year and another 5% over a lifetime. Patients with HIV infection have a 10% annual risk of developing active disease.



First year Lifetime Annual risk

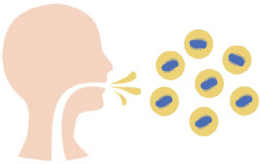
An overview of disease progression

1. After the initial infection in the lower lobes, the organisms circulate to all organs including other areas of the lung.

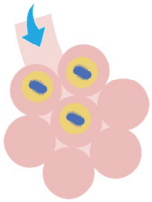


2. After cell-mediated immunity develops, they may persist in the upper lobes and eventually cause a chronic infection, which keeps a person alive long enough to develop a lung cavity and chronic cough, that causes them to transmit the infection to others.

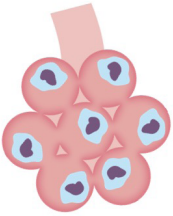
3. The infected patient coughs macroscopic droplets containing *Mycobacterium tuberculosis* into the air.



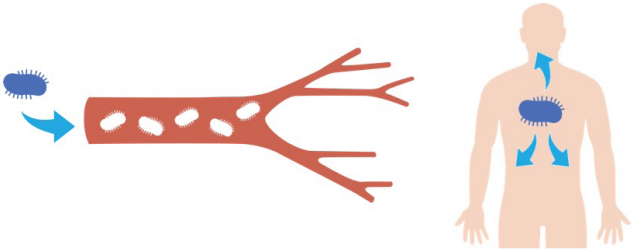
4. These macroscopic droplets evaporate into microdroplets containing one or more organisms and are small enough to be deposited into the alveoli of an unaffected individual.



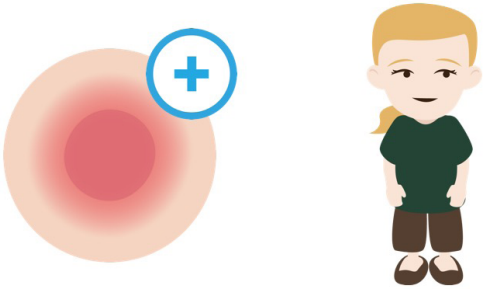
5. In the lower lobes of the lungs where they are usually inhaled, alveolar macrophages engulf the organisms, but cannot kill them, resulting in a low-grade inflammatory response in the region within the first week after infection. This is referred to as **primary tuberculosis**.



6. Organisms can also enter the bloodstream and spread everywhere during this primary infection. In the first two weeks after infection, immature granulomas begin to develop wherever organisms have been carried in the bloodstream to any organ. However, cell-mediated immunity has yet to develop fully and the patient generally remains asymptomatic. For this reason, this dissemination is referred to as a period of **silent bacillemia**.



7. At three to nine weeks after the initial infection, the immune system begins to react to the infection. Development of granulomas that contain activated T cells begins and activated macrophages, which have settled around foci of *Mycobacterium tuberculosis* emerge. If a skin test were done at this point, it would likely be positive, even though most patients do not show symptoms at this stage. The mature response to TB antigens wherever they are present is known as **post-primary tuberculosis.**



A **Ghon complex** is a radiographic phenomenon that appears after the cell-mediated immune response has matured. This represents granulomas in the region where the primary lung infection initially occurred, as well as in neighboring lymph nodes. Presence of the Ghon complex confirms past infection with TB but does not indicate an active infection.

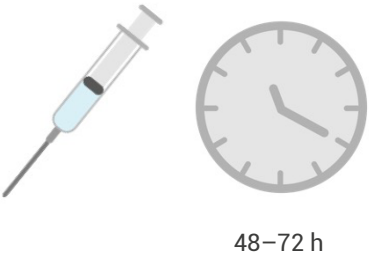
Evaluating latent tuberculosis

Remember that post-primary tuberculosis (TB) occurs after the development of a mature cellular immune response to the TB antigen. At this stage, the patient is generally still asymptomatic. At this point in time, TB in most patients will remain latent.

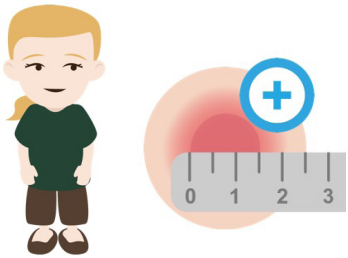
Patients with latent TB have been exposed, developed mature granulomas, and already have post-primary TB, but they are asymptomatic and likely don't know they have the disease.

Diagnosis

Latent TB is diagnosed in most of the world with a **tuberculin skin test**, which involves intradermal injection of a purified protein derivative of *M. tuberculosis* (PPD), then monitoring the site for the presence of a reaction within 48–72 hours after injection.

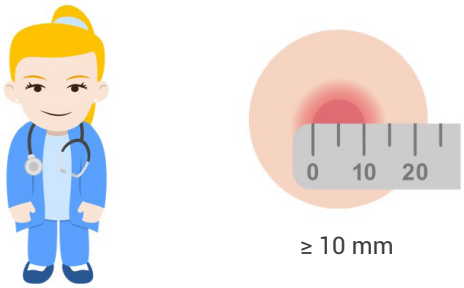


In healthy individuals, a skin test is considered positive if a 15 mm induration (a bump) is present at the site of injection 48–72 hours later.

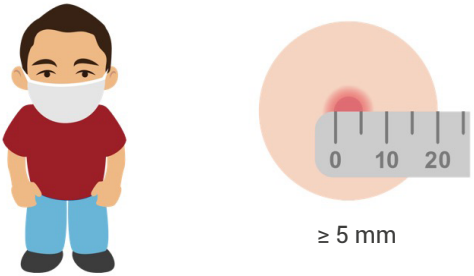


Healthcare workers are understandably at greater risk of exposure and certain others may be predisposed to contracting TB, including children

under four years of age, diabetics, prisoners, and IV drug users. Thus, the skin test in these individuals is considered positive with 10 mm induration.

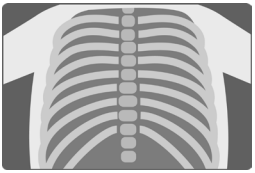


Immunosuppressed persons may not have a vigorous response to tuberculin, thus they should be assumed to have a positive test if the response measures greater than 5 mm.

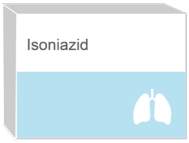


Recently, newer tests known as **interferon-gamma release assays** have become available. They come at a considerably increased cost, but avoid the necessity of returning to have the skin test read by a professional. The principle behind these tests is to incubate the patient's own T cells in the presence of tuberculosis antigens and determine whether interferon-gamma has been released by the T cells. They are reasonably sensitive and specific.

Clinical management



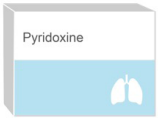
Patients with latent tuberculosis should have a screening chest x-ray to rule out active tuberculosis.

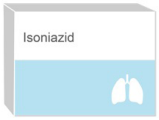


For persons with a negative chest x-ray but a positive TB skin test (or interferon-gamma release assay), nine months of isoniazid is recommended.

Since hepatitis is a known adverse effect associated with isoniazid, it is important to also obtain a single alanine aminotransferase (ALT) level after one month of therapy. Thereafter, if ALT is normal, monitoring for hepatitis symptoms is sufficient.

For patients with HIV, a combination of pyridoxine plus isoniazid is recommended to treat latent TB.



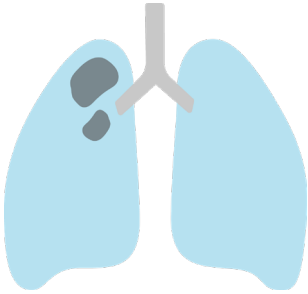


Interestingly, patients with latent TB may not reveal any abnormality on chest x-ray, but sometimes a Ghon complex or apical scarring is present.

If the skin test or interferon-gamma release assay is truly positive, the patient has been infected with TB and should be offered therapy.

Managing active tuberculosis

Active or clinical TB can develop in any organ system; however, pulmonary TB is the most common type of clinical TB. Living organisms in the lungs (usually in the apices) may cause a caseous pneumonia, which can cavitate, resulting in what is known as cavitary disease. The caseous pneumonia also results in granuloma formation.



Common symptoms of cavitary disease

- Chronic illness
- Low-grade fever
- Fatigue
- Weight loss
- Productive cough (may be blood-streaked)
- Hemoptysis

Common imaging and laboratory findings

- Apical infiltrates and cavities (chest x-ray)
- Hypoalbuminemia
- Anemia of chronic disease
- Hyponatremia
- Hypercalcemia
- High calcium

While sputum cultures are usually positive, acid-fast stains are positive in less than 50% of patients. PCR of body fluids is available in three to four hours but false-positive test results are frequent.

Clinical management

To treat active tuberculosis a nine-month treatment course is necessary. Pyrazinamide, ethambutol, isoniazid, and rifampin are given together initially. Pyrazinamide is dropped after two months and ethambutol is dropped after three months. Isoniazid and rifampin are continued for the full nine months.

2 months 3 months 9 months

Handling multidrug-resistant bacterial infections

Many organ-specific infections can be caused by multidrug-resistant (MDR) organisms. When this is the case, the arsenal of antibiotics with which you can potentially treat the infection is generally limited.

It is important to remember that infections acquired in the hospital environment are more likely to be caused by more antibiotic-resistant bacteria. This requires empirical treatment with a broad-spectrum agent. De-escalation to a more narrow-spectrum agent hopefully can be done after the results of cultures and susceptibility testing become available.

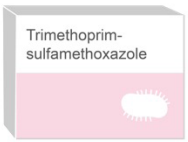
Staphylococcus aureus

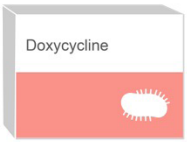
Methicillin-resistant *Staphylococcus aureus* (MRSA) was one of the first MDRs recognized, and is a common pathogen, particularly in the hospital environment. In addition to methicillin, MRSA is resistant to a host of beta-lactam antibiotics which were previously staples for treating *S. aureus* infections.

Risk factors for MRSA

- Recent hospitalization or surgery
- Nursing home residence
- Indwelling vascular catheter

The community-acquired MRSA is usually susceptible to trimethoprim-sulfamethoxazole, clindamycin or doxycycline, but cultures and susceptibility testing of drainage should be done (when possible) to best target the infection.

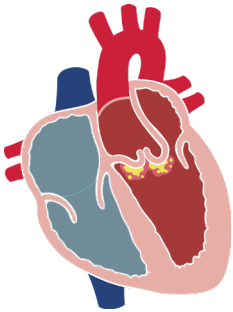




The hospital-acquired MRSA is susceptible to fewer antibiotics. The fifth-generation cephalosporin, ceftaroline, does have activity against MRSA, and provides the safety of a beta-lactam antibiotic, so in hospitalized patients, either ceftaroline or a glycopeptide like vancomycin should be used.

Enterococcus faecium

Enterococcus spp are normal inhabitants of the gastrointestinal tract that cause about 10% of cases of infective endocarditis. They are difficult to treat on native valves and especially on prosthetic valves because enterococci are only inhibited but not killed by cell wall agents. Thus, the relapse rate for enterococcal



endocarditis is high. Moreover enterococci, especially *E. faecium*, have increasingly developed resistance to antibiotics over many years of antibiotic use. Vancomycin- and ampicillin-resistant *E. faecium* are now commonplace. The susceptibility results for ampicillin and vancomycin will automatically appear on the lab report along with the culture results.

For infections without bacteremia, alternative therapy for these resistant bacteria, such as daptomycin, can be used. However, for enterococcal endocarditis, the organisms must be tested for gentamicin susceptibility. If the organism is susceptible to ampicillin, then the combination of ampicillin plus gentamicin may be used.

However, organisms like *E. faecium* are often resistant to ampicillin, vancomycin, and gentamicin. For native valve endocarditis due to this organism, rather unexpectedly, the combination of ampicillin plus ceftriaxone has been shown to have some efficacy. Failing that, the valve may need to be replaced, as it almost always does for infection on a prosthetic valve.

Linezolid or daptomycin cannot be used for a resistant enterococcal endocarditis.

Acinetobacter baumannii

Acinetobacter baumannii is actually a complex of gram-negative coccal organisms resembling *Neisseria,* which are environmental contaminants found in hospitals. Almost 20% of the isolates are multidrug-resistant.

Infection with these organisms is often in the form of ventilator-associated pneumonia (VAP). Because of antimicrobial resistance along with serious illness, which prolongs hospital stays, the mortality from VAP due to *A. baumannii* approaches 70%.

Antibiotic therapy for this infection would be the combination of ampicillin-sulbactam and colistin. Of interest, the sulbactam component, which ordinarily functions only as a beta-lactamase inhibitor, actually has activity against these organisms adding to the effect of the ampicillin.

Pseudomonas aeruginosa

P. aeruginosa has been a notorious hospital pathogen since the mid-20th century and is the single most common cause of ventilator-associated pneumonia (VAP).

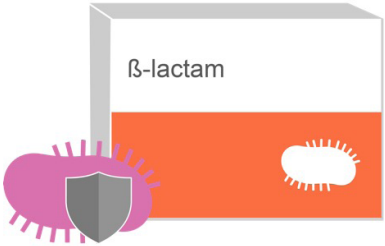
In addition to the capability of acquiring multidrug resistance genes, the organism also has several intrinsic properties that allow it to persist in the presence of many antibiotics. Moreover, unlike many enteric organisms, it has an arsenal of toxins targeting immune cells in the lung, such as a phospholipase, which can destroy the cell membrane of white blood cells.

A reasonable treatment choice for proven or suspected multidrug-resistant *P. aeruginosa* VAP would be the combination of meropenem plus colistin.

Enterobacteriaceae

Even enteric organisms can become MDR. Organisms belonging to the family *Enterobacteriaceae* are residents of the human gastrointestinal tract. As a result, this group is responsible for infections in many organ systems, such as wound infections, urinary tract infections, gastrointestinal tract infections, and pneumonia (both community-acquired and VAP).

Some of these organisms have developed resistance to many beta-lactam antibiotics, including commonly used extended-spectrum cephalosporins, such as third-generation compounds like ceftriaxone, cefotaxime, and the fourth-generation cephalosporin, cefepime.



Risk factors for infection

- Diabetes mellitus
- Prior quinolone use
- Recurrent urinary tract infection
- Prior hospital admissions
- Older age

Many of these bacteria are susceptible to carbapenems, which are the drugs of choice for treating infections resulting from these organisms. However, as might be expected, the high use of these broad-spectrum drugs has increased the rates of carbapenem resistance among these organisms.

If there is resistance to all carbapenems, colistin is one of the last options. However, it has major side effects like nephrotoxicity and neurotoxicity, and so should only be used as a last resort.

APPENDIX

Basic characteristics of common pathogenic bacteria

Short name	Full name	Gram stain	Shape	Characteristics
A. hydrophila	*Aeromonas hydrophila*	Negative	Rod	
A. baumannii	*Acinetobacter baumannii*	Negative	Cocco-bacillus	Aerobic
B. cereus	*Bacillus cereus*	Positive	Rod	Anaerobic
B. burgdorferi	*Borrelia burgdorferi*	Neither	Spirochete	Primarily extracellular
C. trachomatis, Chlamydia	*Chlamydia trachomatis*	Negative	Elementary bodies	Intracellular
C. pneumoniae	*Chlamydophila pneumoniae*	Negative	Elementary bodies	Intracellular
C. botulinum	*Clostridium botulinum*	Positive	Rod	Anaerobic, produces botulinum toxin
C. difficile	*Clostridium difficile*	Positive	Rod	Anaerobic
C. perfringens	*Clostridium perfringens*	Positive	Rod	Anaerobic
E. coli	*Escherichia coli*	Negative	Rod	Aerobic
	Enterobacter spp	Negative	Rod	Aerobic
E. faecium	*Enterococcus faecium*	Positive	Coccus	Aerobic
H. influenzae	*Haemophilus influenzae*	Negative	Cocco-bacillus	Aerobic

K. kingae	*Kingella kingae*	Negative	Cocco-bacillus	Aerobic
K. pneumoniae	*Klebsiella pneumoniae*	Negative	Rod	Aerobic
L. pneumophila	*Legionella pneumophila*	Negative	Rod	Aerobic
M. catarrhalis	*Moraxella catarrhalis*	Negative	Coccus	Aerobic
M. tuberculosis	*Mycobacterium tuberculosis*	Positive	Rod	Aerobic, intracellular
N. gonorrhoeae	*Neisseria gonorrhoeae*	Negative	Coccus	Aerobic
N. meningitidis	*Neisseria meningitidis*	Negative	Coccus	Aerobic
P. multocida	*Pasteurella multocida*	Negative	Cocco-bacillus	Aerobic
P. aeruginosa	*Pseudomonas aeruginosa*	Negative	Rod	Aerobic
S. agalactiae	*Streptococcus agalactiae*	Positive	Coccus	Anaerobic, group B strep
S. gallolyticus	*Streptococcus gallolyticus*	Positive	Coccus	Aerobic
S. pneumoniae	*Streptococcus pneumoniae*	Positive	Coccus	Aerobic
S. pyogenes	*Streptococcus pyogenes*	Positive	Coccus	Aerobic, group A strep
S. aureus	*Staphylococcus aureus*	Positive	Coccus	Aerobic
S. saprophyt-icus	*Staphylococcus saprophyticus*	Positive	Coccus	Aerobic, coagulase-negative

T. pallidum	*Treponema pallidum*	Neither	Spirochete	Aerobic
	Vibrio spp	Negative	Rod (comma-shaped)	Aerobic
Y. enterocolitica	*Yersinia enterocolitica*	Negative	Cocco-bacillus	Aerobic

Multidrug-resistant bacteria

Short name	Full name	Gram stain	Shape	Characteristics
ESBL-producing *Enterobacteriaceae*	***Extended-spectrum, beta-lactamase-producing*** *Enterobacteriaceae*	Negative	Rods	Aerobic, includes *E.coli*, *Klebsiella*, *Salmonella*, *Shigella*, and *Yersinia*
MRSA	***Methicillin-resistant*** *Staphylococcus aureus*	Positive	Coccus	Aerobic
MRSE	***Methicillin-resistant*** *Staphylococcus epidermidis*	Positive	Coccus	Aerobic
VRE	***Vancomycin-resistant*** *Enterococcus faecium*	Positive	Coccus	Aerobic

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