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AWaRe

WHO Essential Medicines List Antibiotic Book

Infographics

Draft for public comment

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Acute Cholecystitis & Cholangitis

Intra-abdominal Infection

Definition

Acute Cholecystitis: Acute inflammation of the gallbladder
• A gallstone obstructing the cystic duct for prolonged periods of time is the most frequent cause

Acute Cholangitis: Acute inflammation in the bile duct system
• A gallstone obstructing the common bile duct and malignant obstruction by tumours are the most common causes

Classification based on complexity:
• *Uncomplicated:* No involvement of the peritoneal cavity and no abscess
• *Complicated:* Involvement of the peritoneal cavity and/or abscess

Severity:
• *Mild:* Not critically ill with no signs of sepsis or septic shock
• *Severe:* Critically ill with signs of sepsis or septic shock

Most Likely Pathogens

Infections are often polymicrobial

Bacteria:
• Enterobacterales (mostly *E. coli*) and other Gram-negative bacilli (including multidrug-resistant strains)
• *Streptococcus* spp. (e.g. of the *S. anginosus* group)
• *Enterococcus* spp.
• Anaerobes (mostly *Bacteroides* spp.)

Fungi (consider if recent course of antibiotics):
• Mostly *Candida albicans*

Parasites (consider in endemic settings):
• *Ascaris lumbricoides*
• *Fasciola hepatica*

Diagnosis

Clinical Presentation

Acute Cholecystitis:
• Acute abdominal pain especially in the right upper quadrant with nausea and vomiting; fever (>38.0°C) may be absent

Acute Cholangitis:
• Abdominal pain with fever (>38.0°C) and jaundice +/- nausea and vomiting

Important:
• Consider peritonitis if there is severe pain, diffuse rebound tenderness upon sudden release of pressure on the abdomen and abdominal muscular tensing
• Hypotension and signs of organ hypoperfusion (e.g. reduced urine output) are potential signs of sepsis /septic shock that need urgent treatment

Imaging

• Abdominal ultrasound to confirm the diagnosis

• Consider doing a CT scan of the abdomen if complications suspected or diagnosis uncertain

Other Laboratory Tests

Determine disease severity and help identify a bacterial infection: White blood cell count, C-reactive protein and/or procalcitonin

Assess liver function: AST, bilirubin and alkaline phosphatase

• If sepsis is suspected consider additional laboratory tests (see sepsis infographic)

Microbiology Tests

Mild Uncomplicated Cases:
• Not usually needed

Severe Cases:
• Blood cultures (ideally before starting antibiotics)
• Microscopy and culture of abdominal fluid material and bile (if they can be drained) to adjust empiric antibiotic treatment

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Acute Cholecystitis & Cholangitis

Treatment

Antibiotic Treatment Duration

Acute Cholecystitis:
• ***Uncomplicated Cases:*** Antibiotics can be stopped once gallbladder is removed
• ***Complicated Cases:*** **5 days** is adequate in most cases with good clinical recovery and source control

Acute Cholecystitis:
• ***All Cases:*** Give antibiotics until biliary drainage procedures are performed and continue for a total of **5 days** after successful source control

Mild Cases

First Choice

ACCESS Amoxicillin+clavulanic acid 875 mg + 125 mg q8h **ORAL**

OR

WATCH Ceftriaxone 2 g q24h **IV**

OR

WATCH Cefotaxime 2 g q8h **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV/ORAL**

Second Choice

WATCH Ciprofloxacin 500 mg q12h **ORAL**

Ciprofloxacin has excellent oral bioavailability and the IV route should be reserved for patients with impaired gastrointestinal function

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV/ORAL**

Clinical Considerations

• **Cholecystectomy (for acute cholecystitis) and biliary drainage (for acute cholangitis) remain the main approaches to eliminate the source of infection**

In both conditions empiric antibiotic treatment should be guided by: The severity of symptoms, considering local prevalence of resistance (particularly of isolates of Enterobacterales producing ESBL) and individual risk factors for resistant pathogens

Important for both conditions:
• **Simplify** empiric treatment to a more narrow-spectrum antibiotic based on culture results or rapid clinical improvement if culture results unavailable
• **Step down to oral treatment** is based on improvement of symptoms, signs of infection and the ability to take oral antibiotics
• **If signs and symptoms persist**, abdominal imaging is suggested or an alternative extra-abdominal source of infection should be considered

Severe Cases

First Choice

WATCH Piperacillin+tazobactam 4 g + 500 mg q6h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

OR

WATCH Cefotaxime 2 g q8h **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV/ORAL**

Second Choice

WATCH Meropenem 2 g q8h **IV**

Consider meropenem only in complicated cases if there is a high risk of infection with ESBL-producing Enterobacterales

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Exacerbation of Chronic Obstructive Pulmonary Disease

Definition

Acute worsening of patient's respiratory symptoms beyond normal day-to-day variations that results in additional therapy in patients with underlying chronic obstructive pulmonary disease (COPD). COPD refers to a group of diseases that block airflow and impair breathing and includes emphysema and chronic bronchitis

Diagnosis

Clinical Presentation

• Recent and sustained worsening of dyspnea and cough with increased sputum production compared to the baseline in a patient with COPD

Important: symptoms can overlap with pneumonia (pneumonia more likely if tachycardia, tachypnea at rest and crepitations that persist after coughing are present)

Microbiology Tests

Usually not needed but to be considered in severe cases; the respiratory tract of people with COPD may be colonized with bacteria (e.g. *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *P. aeruginosa*, *S. maltophilia*) and a positive culture may indicate colonization rather than acute infection

Other Laboratory Tests

Consider C-reactive protein and/or procalcitonin, complete blood count, and blood pH and gases

Imaging

Consider a chest radiograph in patients requiring hospitalization to exclude other diagnoses and in outpatients if pneumonia suspected

Most Likely Pathogens

Respiratory viruses (most cases):
• Influenza virus (A and B)
• Respiratory syncytial virus
• Parainfluenza virus
• Rhinovirus
• Coronavirus (including SARS-CoV-2)

Bacteria (more rarely):
• *Haemophilus influenzae*
• *Moraxella catarrhalis*
• *Streptococcus pneumoniae*
• Gram-negative bacteria including *Pseudomonas aeruginosa* (including multidrug-resistant strains)

Prevention

Recommend smoking cessation, reduced indoor air pollution, use of long-acting inhaled β_2-agonists (± anticholinergics) and vaccination (e.g. against influenza, *S. pneumoniae* and SARS-CoV-2)

Treatment

No Antibiotic Care

• Details of COPD exacerbations management are not discussed here, refer to specific guidelines
• Supplementary oxygen and short-acting inhaled β_2-agonists (± anticholinergics)
• Systemic steroids are usually recommended (improve lung function and favour faster recovery)

Clinical Considerations

Antibiotics are not needed for most cases

• Their use could be considered in patients with dyspnea and an increased volume of purulent sputum
• In case of frequent exacerbations consider risk of infections caused by multidrug-resistant pathogens and previous colonization of the respiratory tract

Mild to Moderate Cases

Antibiotic treatment is not required in the great majority of cases (see "Clinical Considerations" when antibiotics may be indicated)
All dosages are for normal renal function

First Choice

ACCESS Amoxicillin 500 mg q8h **ORAL**

Second Choice

ACCESS Cefalexin 500 mg q12h **ORAL**

OR

ACCESS Doxycycline 100 mg q12h **ORAL**

Severe Cases

ACCESS Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL**

Antibiotic Treatment Duration

5 days

Acute Infectious Diarrhoea & Gastroenteritis

This guidance excludes Clostridioides difficile infection or enteric fever (see separate chapters)

Definition

New (<14 days) onset of diarrhoea (≥3 unformed/liquid stools in 24 hrs or more than normal for individual). Diarrhoea can be watery or bloody (dysentery)

Important: Non-infectious causes are also possible and must be considered (e.g. adverse effects of medicines including antibiotics, bowel and endocrine diseases)

Most Likely Pathogens

Most cases have a viral origin

Always consider these risk factors as they may influence the most likely etiologic agents:
- History of recent travel
- Recent consumption of potentially unsafe food
- Recent antibiotic exposure (risk of *C. difficile*)
- Immunosuppression
- Severe malnutrition

Watery diarrhoea:
- Most likely cause is viral (mostly norovirus and rotavirus)
- Consider cholera in endemic settings or in the context of outbreaks

Bloody diarrhoea (dysentery):
- Most likely cause are bacteria, mostly:
  - *Shigella* spp.
  - *Salmonella* spp.
  - *Campylobacter* spp.
  - Enterotoxigenic *Escherichia coli*

Consider parasites if symptoms do not resolve:
- Usually parasites are responsible for persistent (14-29 days duration) or chronic (>30 days duration) rather than acute diarrhoea
  - *Entamoeba histolytica*
  - *Giardia intestinalis*
  - *Schistosoma* (intestinal species)

Prevention

- Access to safe drinking-water, use of improved sanitation, hand washing with soap, good food hygiene, health education about how these infections spread
- Vaccination against cholera in endemic areas and during outbreaks

Diagnosis

Clinical Presentation

- Diarrhoea, nausea, vomiting, bloating, abdominal pain and cramping; fever may be absent
- Most cases are self-limiting in a few days
- Patients may present with varying degree of dehydration and can present with severe malnutrition (both a risk factor and a consequence of diarrhoea)

Important:
- Rapidly evaluate the degrees of dehydration (especially in the elderly)
- Signs of severe dehydration (two or more must be present):
  - Lethargy and/or unconsciousness
  - Sunken eyes
  - Inability to drink
  - Skin pinch goes back very slowly (≥2 seconds)

Microbiology Tests

Usually not needed

Consider testing if:
- Bloody diarrhoea
- Immunosuppressed patients (to exclude parasitic infections)
- Recent antibiotic use (to exclude *C. difficile*)
- Suspected cholera outbreak

Tests to consider:
- Stool culture
- Stool microscopy (for parasites)
- Vibrio cholerae antigen (e.g. in outbreaks)
- Test for *C. difficile* (if recent antibiotic exposure)

Other Laboratory Tests

Usually not needed but consider in severe cases (e.g. check electrolytes)

Imaging

Usually not needed

Acute Infectious Diarrhoea & Gastroenteritis

Treatment

No Antibiotic Care

Important: Rehydration is the main treatment for acute infectious diarrhoea
- An oral rehydration solution (ORS) is composed of clean water, sugar and salt ('make-at-home' ORS: 1L water, 6 tspn sugar, 1/2 tspn salt)
- In addition to ORS, zinc tablets (10-20 mg/day) for 10-14 days can shorten duration and severity of symptoms

- Antidiarrhoeal and antiemetic drugs are not routinely needed (they do not prevent dehydration or improve nutritional status)

Antibiotic Treatment Duration

Since treatment duration varies according to the antibiotic used, please refer to the corresponding antibiotic section for treatment duration

Cholera Antibiotic Treatment

Treat with antibiotics only in the context of an outbreak and not based on the degree of dehydration

All dosages are for normal renal function

First Choice

WATCH
Azithromycin 1 g **ORAL**
Treatment duration: single dose

Azithromycin preferred because of the decreasing susceptibility of cholera to tetracyclines and fluoroquinolones

OR

ACCESS
Doxycycline 300 mg single dose **ORAL**
- If single dose is not tolerated: 100 mg q12h

Treatment duration: 3 days

Second Choice

WATCH
Ciprofloxacin 1 g **ORAL**
Treatment duration: single dose

Clinical Considerations

- **Antibiotics usually not needed**, including in cases with severe dehydration
- Consider antibiotic treatment ONLY if:
  - Significant bloody diarrhoea
  - Severely immunosuppressed patients
  - Cholera outbreak (to limit transmission see Cholera Antibiotic Treatment)

- If symptoms do not resolve within 24-48 hours of treatment, consider giving metronidazole for treatment of *Entamoeba histolytica* and *Giardia intestinalis*

Antibiotic Treatment

All dosages are for normal renal function

First Choice

WATCH
Ciprofloxacin 500 mg q12h **ORAL**
Treatment duration: 3 days

Second Choice

WATCH
Azithromycin **ORAL**
- Day 1: 500 mg q24h
- Day 2-4: 250 mg q24h

Treatment duration: 4 days

Azithromycin is preferred in case of high prevalence of ciprofloxacin resistance among bacteria frequently associated with acute infectious diarrhoea (e.g. Salmonella spp., Shigella spp.)

OR

WATCH
Cefixime 400 mg q24h **ORAL**
Treatment duration: 3 days

OR

ACCESS
Sulfamethoxazole+trimethoprim 800 mg + 160 mg q12h **ORAL**
Treatment duration: 5 days

Use only if local data suggest susceptibility

OR

WATCH
Ceftriaxone 1 g q24h **IV/IM**
Treatment duration: 3 days

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Bacterial Meningitis

Definition

- Acute inflammation of the meninges, the membranes lining the brain and spinal cord
- The cause can be infectious or non-infectious in origin (e.g. associated with autoimmunity)

Most Likely Pathogens

Non-Immunosuppressed patients:

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*

Immunosuppressed patients or >50 years:

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Listeria monocytogenes* (consider also in pregnant women)

Consider in specific situations:

- Viral infections (especially Enteroviruses, Herpesviridae and Arboviruses)
- *Mycobacterium tuberculosis* (mostly in endemic settings and/or in HIV positive patients)
- Cryptococcal meningitis and cerebral toxoplasmosis in severely immunosuppressed patients (HIV)
- Cerebral malaria (in patients living or travelling to endemic settings)
- *Staphylococcus aureus* or Gram-negative bacteria, including multidrug-resistant strains after neurosurgical interventions or (for Gram-negative bacteria) in the context of Strongyloides hyperinfection syndrome

Prevention

- Vaccination against meningococcal, pneumococcal and *Haemophilus influenzae* type b disease
- Post-exposure antibiotic prophylaxis with ciprofloxacin or ceftriaxone for close contacts (only for meningococcal meningitis)
- https://www.who.int/health-topics/meningitis#tab=tab_3

Diagnosis

Clinical Presentation

- Acute onset (<48 h) of:
  - Fever (>38.0°C) and/or
  - Headache and/or confusion and/or
  - Neck stiffness
- All three signs and symptoms are present in only around half of patients but 95% of patients usually have at least two and the absence of all three symptoms significantly reduces the probability of meningitis
- Haemorrhagic rash may be present (especially in case of meningococcal infection)

Microbiology Tests

Ideally before starting antibiotic treatment:

- Microscopy and culture of cerebrospinal fluid (CSF)
- Cryptococcal antigen in CSF and blood (patients with HIV)
- Blood cultures
- *Note: if lumbar puncture not possible immediately start antibiotics after blood cultures. Testing should not delay giving antibiotics*

Other Laboratory Tests

- Cerebrospinal fluid (CSF) examination (leukocyte count and differential leukocyte count, protein and glucose
- Complete blood count
- Blood glucose
- CRP and/or procalcitonin
- Blood lactate

CSF findings suggestive of bacterial etiology:

- High opening pressure (normal range 80-200 mm H_2O or 8-20 cm H_2O)
- Turbid aspect
- Elevated white blood cell count (often several hundred to several thousand WBC/mm^3 or >0.1 to >1 X 10^9/L)
- Elevated % of neutrophils (>80%)
- Elevated protein (>45 mg/dL or >0.45 g/L)
- Low glucose (<40 mg/dL or <2.2 mmol/L)
- CSF/Serum glucose ratio ≤0.4

Imaging

Consider doing a head CT scan before doing the lumbar puncture in patients with focal neurological signs, decreased level of consciousness/coma or a history of central nervous system disease or recent seizures (<1 week)

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Bacterial Meningitis

Treatment

Clinical Considerations

Important:

- Due to the severity of this condition all suspected cases of meningitis should be treated as soon as possible as bacterial meningitis until this has been excluded/viral cause has been clearly identified
- *Listeria* is not covered by ceftriaxone or cefotaxime therefore when *Listeria* is suspected, ampicillin should be used

- **Empiric treatment is based on:**
  - Age of the patient
  - Immune status of the patient
  - Local prevalence of *S. pneumoniae* isolates resistant to third-generation cephalosporins (rare but can occur especially in patients with prolonged or multiple exposures to β-lactam antibiotics in the previous three months)
- If a pathogen is isolated and its susceptibilities are known, review and modify antibiotics accordingly

Use of Corticosteroids

Dexamethasone 0.15 mg/kg q6h

- Recommended **only in high-income settings** (no evidence of benefit in other settings)
- Give with the first dose of antibiotic to attenuate the inflammatory response and reduce the risk of neurological complications and death
- Continue only if *S. pneumoniae* is confirmed

Antibiotic Treatment Duration

Pathogen not identified: **10 days**

Confirmed pneumococcal meningitis: **10-14 days**

Confirmed meningococcal meningitis: **5-7 days**

Confirmed *Listeria* meningitis: **21 days**

Antibiotic Treatment

All dosages are for normal renal function

First Choice

WATCH Ceftriaxone 2 g q12h **IV**

OR

WATCH Cefotaxime 2 g q6h **IV**

Second Choice

ACCESS Ampicillin 2 g q4h **IV**

OR

ACCESS Amoxicillin 2 g q4h **IV**

OR

ACCESS Benzylpenicillin 4 million IU (2.4 g) q4h **IV**

OR

ACCESS Chloramphenicol 1 g q6h **IV**

Use chloramphenicol only when no other option is available because of toxicity

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Community-Acquired Pneumonia

Definition

An acute illness affecting the lungs usually presenting with cough, sputum production, and rapid and difficult breathing with a new or worsening pulmonary infiltrate on a chest radiograph

Most Likely Pathogens

"Typical" Bacteria:

- ***Streptococcus pneumoniae*** (most cases)
- *Staphylococcus aureus* (often associated with influenza)
- *Haemophilus influenzae* (chronic lung diseases, smoking)
- *Moraxella catarrhalis* (chronic lung diseases, smoking)
- *Enterobacterales* (severe comorbidities, e.g. chronic lung diseases, dementia, stroke)

"Atypical" Bacteria:

- *Mycoplasma pneumoniae* (more frequent in young adults)
- *Chlamydia pneumoniae* and *psittaci* (more frequent in young adults)
- *Legionella* spp. (chronic lung diseases or other underlying illness, travel, exposure to hot tubs)
- *Coxiella burnetii* (rural areas, exposure to livestock)

Respiratory Viruses:

- Influenza viruses (A and B)
- Parainfluenza virus
- Respiratory syncytial virus (RSV)
- Adenovirus
- Metapneumovirus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)

Bacteria to consider in Specific Settings:

- *Burkholderia pseudomallei* (SE Asia, Australia)

Investigating for Tuberculosis (TB)

- Consider specific investigations for TB in endemic settings especially in high-risk patients (e.g. HIV)
- A rapid molecular test performed on a single sputum specimen is the preferred first line diagnostic test for pulmonary TB and to detect rifampicin resistance

Diagnosis

Clinical Presentation

- New onset (<2 weeks) or worsening cough with fever (≥38.0°C), sputum production, dyspnea, tachypnea, reduced oxygen saturation, crepitations on lung auscultation, chest pain/discomfort without alternative explanation
- Extrapulmonary features (i.e. confusion, disorientation) may predominate in elderly, and immunosuppressed patients and fever may be absent

Microbiology Tests

Mild cases: usually not needed

Severe cases (to guide antimicrobial treatment): blood cultures, urinary antigens for *L. pneumophila* and *S. pneumoniae*

Selected cases (depending on epidemiology and risk factors): sputum rapid molecular test for *M. tuberculosis*, nasopharyngeal swab for influenza viruses and SARS-CoV-2, HIV testing in settings with high HIV prevalence and in case of recurrent and/or severe pneumonia

Other Laboratory Tests

Determine disease severity: blood urea nitrogen (see CURB-65 Scoring System box), blood pH and gases, white blood cell count

Differentiate bacterial and viral (taking into account pre-test probability): C-reactive protein and/or procalcitonin

Note: tests depend on availability and clinical severity (e.g. blood gases will only be done in severe cases)

Imaging

- Chest X-ray not necessary in mild cases
- Infiltrate may not always be evident (e.g. dehydration) and non-infectious etiologies may mimic infiltrates (e.g. lung edema, pulmonary embolism)
- Radiologic appearance cannot be used to accurately predict pathogen

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Community-Acquired Pneumonia

CURB-65 Severity Scoring System

Signs & Symptoms (1 point each)

- ○ Presence of **C**onfusion (new onset)
- ○ **U**rea > 19 mg/dL (or > 7 mmol/L)*
- ○ **R**espiratory rate > 30/min
- ○ Systolic **B**P < 90 mmHg (<12 kPa) or Diastolic BP ≤ 60 mmHg (<8 kPa)
- ○ Age ≥ **65** years

Score 0-1
• Consider outpatient treatment

Score 2
• Consider inpatient treatment
• **Consider adding clarithromycin to beta-lactam for atypical coverage**
• Perform microbiology tests

Score ≥3
• Inpatient treatment (consider ICU)
• **Consider adding clarithromycin**
• Perform microbiology tests

Other considerations such as severe comorbid illnesses or inability to maintain oral therapy should be taken into account. CURB-65 has not been extensively validated in low-income settings.

The **CRB-65 score, which does not require laboratory values for its calculation, can also be used, the score value interpretation is the same as for CURB-65*

Mild to Moderate Cases

All dosages are for normal renal function

First Choice

ACCESS Amoxicillin 1 g q8h **ORAL**

OR

ACCESS Phenoxymethylpenicillin 500 mg (800 000 IU) q6h **ORAL**

Second Choice

ACCESS Amoxicillin+clavulanic acid 875 mg+125 mg q8h **ORAL**

OR

ACCESS Doxycycline 100 mg q12h **ORAL**

Treatment

Antibiotic Treatment Duration

Treat for **5 days**

If severe disease, consider longer treatment and look for complications such as empyema, if patient not clinically stable at day 5

Severe Cases

All dosages are for normal renal function

First Choice

WATCH Ceftriaxone 2 g q24h **IV** (1 g q24h **IM***)

**A larger volume would be painful to give as intramuscular injection*

OR

WATCH Cefotaxime 2 g q8h **IV/IM**

IF CURB-65 ≥2, CONSIDER ADDING

WATCH Clarithromycin 500 mg q12h **ORAL** (or **IV**)

Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function

Second Choice

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV**
• A higher dose can be considered: 1 g+200 mg q6h

IF CURB-65 ≥2, CONSIDER ADDING

WATCH Clarithromycin 500 mg q12h **ORAL** (or **IV**)

Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function

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Hospital-Acquired Pneumonia

Definition

Hospital acquired pneumonia (HAP): Acute illness affecting the lungs caused by pathogens in the hospital setting and presenting 48 hours or more after admission

Ventilator-associated pneumonia (VAP): Acute illness affecting the lungs caused by pathogens in the hospital setting and presenting 48 hours or more after admission while the patient is on a ventilator

Important: the cut-off of 48 hours is arbitrary and chosen for convenience and surveillance purposes

Most Likely Pathogens

• HAP may be caused by the same pathogens found in CAP or by multidrug-resistant (MDR) pathogens

• Majority of data on the microbiologic etiology of HAP is derived from ventilated patients in the intensive care setting

Bacteria most frequently associated with HAP:

• *Streptococcus pneumoniae*
• *Haemophilus influenzae*
• *Staphylococcus aureus* (including MRSA)
• Gram-negative bacteria including *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (including multidrug-resistant strains)
• Anaerobes (mostly associated with large aspiration of secretions)
• *Legionella pneumophila*

Respiratory Viruses:

• Influenza viruses (A and B)
• Other respiratory viruses (including SARS-CoV-2)

Risk factors for infection with MDR pathogens:

• Previous treatment with antibiotics
• Prolonged hospital stay (particularly in the ICU)
• Prior colonization with MDR pathogens
• High local prevalence of resistant pathogens (e.g. among *S. aureus* and Gram-negative bacteria, including *P. aeruginosa*)

Diagnosis

Clinical Presentation

Non-ventilated patients: New or worsening cough +/- sputum production, difficult and rapid breathing, reduced oxygen saturation, crepitations on lung auscultation, or chest pain/discomfort with no alternative explanation; fever ≥38.0°C usually present (may be absent, especially in the elderly)

Ventilated patients: Increased respiratory secretions, reduced oxygen saturation and a new lung infiltrate on a chest-radiograph

Note: the clinical presentation is non-specific and other diseases (e.g. pulmonary embolism) can mimic HAP. HAP/VAP may progress to sepsis

Microbiology Tests

All cases:
• Blood cultures (ideally before starting antibiotics)
• Microscopy and culture of respiratory samples (ideally before starting antibiotics)
• Urinary antigens for *L. pneumophila* and *S. pneumoniae*

Selected cases (depending on epidemiology and risk factors): nasopharyngeal swab for influenza viruses and SARS-CoV-2

Important: a positive respiratory culture may indicate colonization rather than acute infection

Other Laboratory Tests

Determine disease severity: blood pH and gases, white blood cell count

Differentiate bacterial and viral (taking into account pre-test probability): C-reactive protein and/or procalcitonin

Note: tests depend on availability and clinical severity (e.g. blood gases will only be done in severe cases)

• If sepsis is suspected consider additional laboratory tests (see sepsis infographic)

Imaging

• Chest radiograph needed because other conditions have similar clinical features and antibiotics may be avoided if bacterial pneumonia is not suggested

Important:
• Chest radiographs can be difficult to interpret and correlate with the clinical presentation; many other conditions mimic infectious infiltrates (especially in the elderly)
• The radiographic pattern cannot be used to accurately predict the microbial cause

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Hospital-Acquired Pneumonia

Prevention

Key principles:

- Vaccination against pathogens that can commonly cause pneumonia
- Good hand hygiene
- Maintain mobility
- Maintain good oral and dental care
- Maintain nutrition in hospital
- Elevate the head of the bed to reduce the chances of aspirating respiratory secretions into the lungs
- Avoid intubation or reduce duration as much as possible

Bundles of care specific to the ICU also usually include:

- Minimizing sedation
- Regularly assessing if the endotracheal tube may be removed; extubate patients as soon as it is safe to do so
- Selective oral decontamination (SOD) and/or selective decontamination of the digestive tract (SDD) to reduce the bacterial burden of the upper (with SOD) and lower (with SDD) digestive tract through the administration of non-absorbable antibiotics
- SOD/SDD can help reduce the incidence of VAP, yet there is concern about the risk of selecting resistant bacteria

Treatment

Clinical Considerations

Important:
- Consider stopping treatment if HAP is ruled out or an alternative diagnosis can be made
- If not severely ill, consider targeted treatment based on microbiology results

Empiric antibiotic treatment should be guided by:
- The severity of symptoms (scoring systems exist but are not addressed here), considering local prevalence of resistant pathogens and individual risk factors for resistant pathogens

In patients with VAP specifically consider:
- Need for double anti-pseudomonal coverage (risk of infection caused by isolates resistant to an antibiotic used for monotherapy)

Important:
- Simplify empiric treatment to a more narrow-spectrum antibiotic based on culture results or rapid clinical improvement if culture results unavailable
- Step down to oral treatment is based on improvement of symptoms, signs of infection and the ability to take oral antibiotics

Antibiotic Treatment Duration

7 days; reassess diagnosis and consider longer treatment if the patient is not clinically stable at day 7

HAP (non-VAP)

All dosages are for normal renal function

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV**

Consider if low-risk of multidrug-resistant infections (e.g. short hospitalization before symptom onset and no prior antibiotic exposure)

OR

WATCH Ceftriaxone 2 g q24h **IV** (1 g q24h **IM***)

**A larger volume would be painful to give as intramuscular injection*

OR

WATCH Cefotaxime 2 g q8h **IV/IM**

OR

WATCH Piperacillin+tazobactam 4 g+500 mg q6h **IV**

Piperacillin+tazobactam offers anti-pseudomonal coverage (risk of P. aeruginosa higher in patients with recent antibiotic exposure, known previous respiratory colonization and underlying lung diseases)

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Impetigo / Erysipelas / Cellulitis

Skin and Soft Tissue Infection

This guidance excludes skin infections caused by viral, fungal or parasitic pathogens; diabetic foot infections; necrotizing fasciitis; pyomyositis; severe infections with sepsis; and surgical site infections

Definition

Superficial bacterial skin infections, not affecting the deeper tissue layers

Diagnosis

Clinical Presentation

Impetigo: Acute onset of superficial skin lesions usually without systemic symptoms
- Most cases: papules progressing to vesicles and pustules that break to form crusts (**non-bullous form**)
- Minority of cases: vesicles evolve to form larger bullae (**bullous form**)

Erysipelas: Acute onset of a painful red skin lesion with well-defined indurated margins usually on face or legs
- Bullae may be present or develop in first days
- Fever (> 38.0°C) and other signs of systemic infection may be present

Cellulitis: Acute onset of a skin lesion presenting with redness, swelling and induration, warmth and pain or tenderness of the affected area
- Most commonly affected areas: legs and face
- Fever (> 38.0°C) and other signs of systemic infection may be present
- Redness alone may not indicate an infection
- **A clear clinical distinction between cellulitis and erysipelas is often difficult to make**

Microbiology Tests

Not needed in most mild cases
- Tissue swab cultures are to be avoided, especially in case of intact skin

Other Laboratory Tests

Not needed in most mild cases

Imaging

Routine imaging of mild cases not necessary
- Ultrasound may be considered if abscess or subdermal involvement suspected

Most Likely Pathogens

Bacteria (most cases):
- *Streptococcus pyogenes* (group A *Streptococcus*) - especially in case of erysipelas
- *Staphylococcus aureus* (including MRSA)

Additional bacteria (more rarely e.g immunosuppressed and/or diabetic patients, traumatic skin lesions):
- *Enterobacterales*
- *Pseudomonas* spp.
- Anaerobes

Treatment

Clinical Considerations

- **Empiric antibiotic options** need to have good activity against both *Streptococcus pyogenes* (group A *Streptococcus*) and MSSA
- **Empiric treatment against community-acquired MRSA**: Consider in selected cases based on individual risk factors, known colonization and local prevalence
- **Mild infections**: Oral treatment is adequate
- **Intravenous antibiotics**: May be required if infection rapidly spreading and not responding to oral antibiotics

Antibiotic Treatment Duration

Treat for **5 days**

Longer durations may be required in case of no clinical improvement or if an underlying medical condition is present

Topical Treatment

Localized non-bullous impetigo: Topical treatment is preferred over an oral antibiotic, whenever possible. For example, a 5 day course with mupirocin 2% ointment

Antibiotic Treatment

All dosages are for normal renal function

ACCESS Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin (or flucloxacillin) 500 mg q8h **ORAL**

World Health Organization

ADULTS

Burn Wound-Related Infections

Definition

An injury to the skin or other organic tissue primarily caused by heat or due to radiation, radioactivity, electricity, friction or contact with chemicals. Burns can be classified based on cause and depth of the burn.

Diagnosis

Clinical Presentation

Diagnosis of a wound infection relies on the clinical examination
- Burn wounds should be monitored for signs of infection such as increased pain, redness or swelling of the area surrounding the wound
- Redness alone may not indicate infection
- Signs of invasive infection (e.g. change in wound colour, signs of sepsis) should be carefully monitored

Microbiology Tests

- Routine testing (including wound cultures) is not needed in mild cases with no signs of systemic infection
- Identifying the pathogen in mild cases will not benefit the patient as it will rarely change management
- In severe cases, refer to the Sepsis infographic if this is suspected

Other Laboratory Tests

- Routine testing is not needed in mild cases with no signs of systemic infection
- Because of the inflammatory response associated with the burn, biomarkers of infection are of limited use to diagnose bacterial infections

Imaging

Routine imaging not necessary

Most Likely Pathogens

Mostly polymicrobial. Hospital-acquired multidrug-resistant organisms are a major concern in burn patients often because of prolonged hospitalization and frequent antibiotic exposure.

Early after the injury:
- *Streptococcus* spp.
- *Staphylococcus aureus* (including MRSA strains)
- *Staphylococcus* spp. other than *S. aureus*
- *Enterobacterales* (including multidrug-resistant strains)

During hospitalization:
- *Pseudomonas aeruginosa* (including multidrug-resistant strains)
- *Acinetobacter baumannii* (including multidrug-resistant strains)
- Fungi (e.g. *Candida* spp.)

This guidance excludes severe infections

Treatment

Clinical Considerations

- Meticulous observation of infection control procedures to prevent transmission of multidrug-resistant organisms
- Irrigation and debridement of necrotic tissue to prevent infection of the wound
- Appropriate daily cleaning and dressing of the wound
- Only infected wounds should be treated
- Coverage against MRSA may be considered based on local prevalence and on individual risk factors

Antibiotic Treatment Duration

- Treat for **5 days (mild cases)**
(Potentially longer if severe systemic infections)

Prophylactic Antibiotics

- Avoid the routine use of antibiotics to prevent infections (no clear evidence of a benefit and increased risk of colonization with resistant bacteria)
- Consider in selected cases (e.g. immunosuppressed individual, puncture wounds) and/or high-risk "locations" (face, hands, near joints)
- Duration: 3 days

Topical Treatment

Local antiseptics could be considered based on local protocols

Antibiotic Treatment

Only infected wounds should be treated

All dosages are for normal renal function

ACCESS Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin (or flucloxacillin) 500 mg q8h **ORAL**

World Health Organization

ADULTS

Wound and Bite-Related Infections

This guidance excludes severe infections, surgical wounds and management of bites from poisonous animals or arthropods

Definition

Any traumatic skin injury characterized by damage and exposure of deeper skin tissue

Diagnosis

Clinical Presentation

Infection may or may not be present at time of clinical evaluation

• *Superficial Infections*: Symptoms of cellulitis (redness, swelling, warmth, lymphangitis, pain around wound)

• *Invasive Wound Infection:* Change in wound colour, signs of sepsis (should be carefully monitored)

Laboratory Tests

Routine testing not needed in mild cases with no signs of systemic infection

Imaging

Routine imaging not necessary
• May be considered in selected cases based on extent and depth of lesion

Most Likely Pathogens

Infection commonly polymicrobial (mix of human skin and animal oral microbiota, and environmental organisms)

Wounds

Most cases:
• *Streptococcus* spp.
• *Staphylococcus aureus* (including MRSA strains)

More rarely:
• Anaerobes
• Enterobacterales
• *Enterococcus* spp.
• *Clostridium tetani* (soil contaminant)

Bites

Human:
• Anaerobes
• *Streptococcus* spp.
• *Staphylococcus aureus*

Cat:
• Anaerobes
• *Pasteurella multocida*
• *Staphylococcus aureus*

Dog:
• Anaerobes
• *Capnocytophaga canimorsus*
• *Pasteurella multocida*
• *Staphylococcus aureus*

Monkey:
• Anaerobes
• *Streptococcus spp.*
• *Staphylococcus aureus*

Reptile:
• Anaerobes
• Enterobacterales
• *Pseudomonas aeruginosa*

Rodent:
• *Pasteurella multocida*

Wound and Bite-Related Infections

Treatment

Clinical Considerations

• **Rapidly After Injury:** Thorough washing and flushing of the wound (~15 minutes), with soap or detergent and copious amounts of water followed by debridement and immobilization

• **Risk of Tetanus and Rabies:** Quickly evaluate need to provide adequate post-exposure prophylaxis

• **Signs/Symptoms of Infection:** Empiric treatment should include antibiotics with good activity against most likely pathogens (*Staphylococcus* spp. and *Streptococcus* spp. and anaerobes)

• **Animal/Human Bites:** Empiric treatment against both aerobic and anaerobic bacteria required; empiric treatment against community-acquired MRSA usually not required

WHO Guidance
• Rabies: https://apps.who.int/iris/handle/10665/272372
• Tetanus: https://apps.who.int/iris/handle/10665/254583

Antibiotic Treatment Duration

Treat for **5 days**

Prophylactic Antibiotics

• In the absence of systemic signs of infection avoid antibiotics to prevent infections in otherwise healthy patients

• No clear evidence that antibiotics can prevent the infection

• Consider in selected cases (e.g. immunosuppressed individual, puncture wounds) and/or high-risk "locations" (face, hands, near joints)

• Duration: 3 days

Antibiotic Treatment

All dosages are for normal renal function

ACCESS Amoxicillin+clavulanic acid 500 mg + 125 mg q8h **ORAL**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin (or flucloxacillin) 500 mg q8h **ORAL**

Not for bite-related infections because cloxacillin (or flucloxacillin) does not provide good anaerobic coverage

Lower Urinary Tract Infection

Definition

• Infection of the lower part of the urinary tract (e.g. the bladder-cystitis)

• Urinary tract infections (UTI) in individuals with mechanical anomalies of the urinary tract or who are immunosuppressed and in pregnant women are generally considered at greater risk of complicated evolution (complicated UTI)

Most Likely Pathogens

Bacteria:

- **Most common:**
  - Enterobacterales (mostly *Escherichia coli* including multidrug-resistant strains such as those producing ESBL)
- **More rarely:**
  - Coagulase-negative Staphylococci: *S. saprophyticus* (mostly in young women)
  - *Streptococcus agalactiae* (group B *Streptococcus*)
  - *Enterococcus* spp.
  - *Pseudomonas aeruginosa* or *Acinetobacter baumannii* (including multidrug-resistant strains such as those producing ESBL especially in patients with recent antibiotic exposure)

Diagnosis

Clinical Presentation

Acute (< 1 week) dysuria, increased urinary urgency and frequency, lower abdominal pain or discomfort and sometimes gross hematuria

• In women, a vaginal source of the symptoms (vaginal discharge or irritation) should be excluded first

• In elderly patients with pre-existing urinary symptoms the most reliable symptoms are acute urinary changes compared to the baseline

Other Laboratory Tests

In symptomatic patients:

• Urinalysis (dipstick or microscopy) to detect bacteriuria and/or indirect signs of infection (positive leucocyte esterase and nitrites)

• Blood tests usually not needed

Microbiology Tests

In symptomatic patients:

• Urine culture if risk of complicated UTI and/or recurrent UTI (to confirm the diagnosis and adapt empiric treatment)

Important:

• A positive urine culture in an asymptomatic patient indicates bacterial colonization and does not require treatment except in pregnant women or in patients undergoing urological procedures in which bleeding is anticipated

• The absence of urine leucocytes has a good negative predictive value but the positive predictive value of leucocyturia is suboptimal

Imaging

Usually not needed unless need to investigate possible underlying abnormalities of the urinary tract

Lower Urinary Tract Infection

Treatment

Clinical Considerations

Antibiotic treatment recommended if compatible clinical presentation AND a positive test (positive urine leucocytes/leucocyte esterase or positive urine culture)

- If tests could not be performed, treat based on clinical presentation
- Clinical improvement should be evident within 48-72h
- Antibiotics shorten duration of symptoms by 1-2 days

Antibiotic Treatment Duration

Since treatment duration varies according to the antibiotic, please refer to the corresponding antibiotic section for treatment duration

Note: in general consider longer treatments for pregnant women (usually 5 days) and men (usually 7 days)

Antibiotic Treatment

All dosages are for normal renal function

ACCESS

Nitrofurantoin **ORAL**
- 100 mg q12h (modified release formulation)
- 50 mg q6h (immediate release formulation)

Treatment duration: 5 days

Main medicine recommended for acute lower UTI and active against most ESBL-producing isolates

OR

ACCESS

Sulfamethoxazole+trimethoprim 800 mg+160 mg q12h **ORAL**
Treatment duration: 3 days

Resistance is high in many settings and NOT active against ESBL-producing isolates

OR

ACCESS

Trimethoprim 200 mg q12h **ORAL**
Treatment duration: 3 days

Resistance is high in many settings and NOT active against ESBL-producing isolates

OR

ACCESS

Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL**
Treatment duration: 3-5 days

Active against some ESBL-producing isolates

Upper Urinary Tract Infection

Focus on community-acquired pyelonephritis in patients with no catheter

Definition

Infection of the kidneys (pyelonephritis) in which microorganisms ascend the urinary tract via the urethra, bladder, ureters or reach the kidneys through the bloodstream

Classification based on complexity:
• *Uncomplicated:* Urinary tract infections (UTI) in individuals with no risk factors for complicated UTI
• *Complicated:* UTI in individuals with mechanical anomalies of the urinary tract (e.g. kidney stones, anatomical anomalies) or who are immunosuppressed and in pregnant women are generally considered complicated (or at risk of complications). UTI in patients with urinary catheters or stents are also considered complicated (not discussed here)

Most Likely Pathogens

Bacteria:

- **Most common:**
  - Enterobacterales (mostly *E. coli* including multidrug resistant strains such as those producing ESBL and carbapenemases)
- **More rarely:**
  - *Enterococcus* spp.
  - *Streptococcus agalactiae* (group B *Streptococcus*)
  - *Staphylococcus aureus* (rare in uncomplicated UTI, usually in patients with urinary catheters)
  - *Pseudomonas aeruginosa, Acinetobacter baumanni* (including multidrug-resistant strains especially in patients with recent antibiotic exposure or instrumentation of the urinary tract, rare in uncomplicated UTI)

Diagnosis

Clinical Presentation

• Flank pain, costovertebral angle tenderness, nausea and vomiting, fever and signs of systemic illness +/- symptoms of cystitis
• Severity varies from mild disease (most cases) that can be managed with oral treatment (no nausea/ vomiting, low-grade fever) to severe cases requiring intravenous treatment and hospital admission

Other Laboratory Tests

All cases:
• Urinalysis (dipstick or microscopy) to detect bacteriuria and/or indirect signs of infection (positive leucocyte esterase and nitrites)

Additionally in severe cases:
• White blood cell count, C-reactive protein and/or procalcitonin

• If sepsis is suspected consider additional laboratory tests (see sepsis infographic)

Microbiology Tests

All cases:
• Urine culture: Ideally before starting antibiotic treatment
  • The test is considered positive when bacteria are above a certain minimum cut-off that can vary between laboratories
  • A positive urine culture is not always a sign of urinary tract infection or an indication for antibiotic treatment (and urine can also become contaminated during sampling)

Additionally in severe cases:
• Blood cultures: Ideally before starting antibiotic treatment

Imaging

Routine imaging is not necessary but can be considered if urine flow is blocked or an abscess is suspected

Upper Urinary Tract Infection

Treatment

Clinical Considerations

• Patients with upper urinary tract infection are generally symptomatic

• Patients with a positive urine test but no UTI symptoms usually **do not require treatment** (exceptions exist, e.g. pregnant women or if invasive urologic procedure is scheduled)

• **Empiric antibiotic treatment should be guided by:**
  • The severity of symptoms, considering local prevalence of resistance (particularly of isolates of Enterobacterales producing ESBL) and individual risk factors for resistant pathogens

Important:

• **Simplify** empiric treatment to a more narrow-spectrum antibiotic based on culture results or rapid clinical improvement if culture results unavailable
• **Step down to oral treatment** is based on improvement of symptoms, signs of infection and the ability to take oral antibiotics
• Clinical improvement is usually evident within 48-72 hours of starting treatment; **if signs and symptoms persist**, consider and investigate a possible complication (e.g. abscess) and review the results of the urine culture to verify that the pathogen is susceptible to the antibiotic used

Antibiotic Treatment Duration

7 days

Mild Cases

All dosages are for normal renal function

WATCH Ciprofloxacin 500 mg q12h **ORAL**

Severe Cases

All dosages are for normal renal function

WATCH Ceftriaxone 1 g q24h **IV/IM**

OR

WATCH Cefotaxime 1 g q8h **IV/IM**

AND/OR

ACCESS Gentamicin 5 mg/kg q24h **IV**

AND/OR

ACCESS Amikacin 15 mg/kg q24h **IV**

Consider gentamicin or amikacin where ESBL-producing isolates are highly prevalent

In very sick patients, gentamicin (or amikacin) can be given in combination with ceftriaxone (or cefotaxime)