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AWaRe

WHO Essential Medicines List Antibiotic Book

Infographics

Version 1.2 (Nov 15, 2022)

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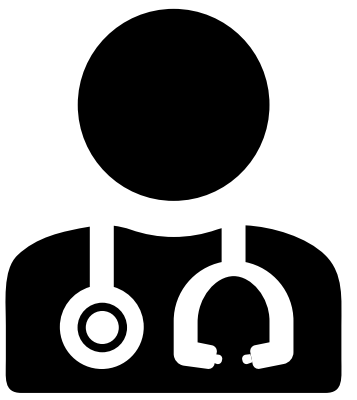

Primary Health Care

World Health Organization

ADULTS

Bronchitis

Definition

A self-limiting inflammation of the trachea and bronchi characterized by persistent cough +/- fever usually caused by a viral infection

Diagnosis

Clinical Presentation

• Acute onset (<2 weeks) of cough lasting > 5 days +/- sputum production and shortness of breath (colour of the sputum does not indicate bacterial infection) +/- fever
• Generally a mild condition; cough usually lasts 10-20 days (can last longer)

Important: Symptoms can overlap with pneumonia and this can lead to inappropriate treatment with antibiotics. This should be avoided with a careful patient assessment
• **Bronchitis:** Less severe presentation, usually self-limiting (but cough may take weeks to resolve)
• **Pneumonia (see "Community-acquired pneumonia" infographic):** More severe presentation with shortness of breath and systemic signs of infection (e.g. increased heart and respiratory rate)

Microbiology Tests

Usually not needed; consider testing for Influenza virus or SARS-CoV-2 (e.g. during influenza season or outbreaks based on local epidemiological risk/situation/ protocols)

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Most Likely Pathogens

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

Treatment

No Antibiotic Care

• Symptomatic treatment
• Bronchodilators (in case of wheezing), mucolytic or antitussive agents, can be considered based on local practices and patient preferences

Patients should be informed that:
• Great majority of cases are self-limiting and of viral origin
• Cough can persist for several weeks

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (max 4 g/day)
• **Hepatic impairment/cirrhosis:** Max 2 g/day

Antibiotic Treatment

Antibiotic treatment is **not recommended and should be avoided** as there is no evidence of a significant clinical benefit and there is a risk of side effects of antibiotics

World Health Organization

CHILDREN

Bronchitis

Definition

A self-limiting inflammation of the trachea and bronchi characterized by persistent cough +/- fever usually caused by a viral infection

Most Likely Pathogens

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

Diagnosis

Clinical Presentation

- Acute onset of cough lasting > 5 days, usually with runny nose and mild fever, with no clinical signs of pneumonia
- Generally a mild condition, cough usually lasts 1-3 weeks

Important: Symptoms can overlap with pneumonia and this can lead to inappropriate treatment with antibiotics. This should be avoided with a careful patient assessment
- **Bronchitis:** Less severe presentation, usually self-limiting (but cough may take weeks to resolve)
- **Pneumonia (see "Community-acquired pneumonia" infographic):** More severe presentation with shortness of breath and systemic signs of infection (e.g. increased heart and respiratory rate)

Microbiology Tests

Usually not needed; consider testing for Influenza virus or SARS-CoV-2 (e.g. during influenza season or outbreaks based on local epidemiological risk/situation/ protocols)

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Treatment

No Antibiotic Care

- Symptomatic treatment
- Bronchodilators (in case of wheezing), mucolytic or antitussive agents, can be considered based on local practices and patient preferences

Patients/parents should be informed that:
- Great majority of cases are self-limiting and of viral origin
- Cough can persist for several weeks

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen (do not use if <3 months of age)
- **Pain control/antipyretic:** 5-10 mg/kg q6-8h
- **Oral weight bands:**

6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen)
- **Pain control/antipyretic:** 10-15 mg/kg q6h
- **Oral weight bands:**

3-<6 kg	60 mg q6h
6-<10 kg	100 mg q6h
10-<15 kg	150 mg q6h
15-<20 kg	200 mg q6h
20-<30 kg	300 mg q6h
≥30 kg	500 mg-1 g q4-6h (Max 4 g/day or 2 g/day if hepatic impairment/cirrhosis)

Antibiotic Treatment

Antibiotic treatment is **not recommended and should be avoided** as there is no evidence of a significant clinical benefit and there is a risk of side effects of antibiotics

World Health Organization

ADULTS

Acute Otitis Media

Definition

Infection of the middle ear that occurs mostly in children under 5 years of age and is rare in adults, often as a complication of a viral upper respiratory tract infection

Prevention

Overlaps with prevention of upper respiratory tract infections; hand hygiene, vaccination against *S. pneumoniae*, and influenza viruses can be useful

Diagnosis

Clinical Presentation

Acute onset of ear pain (unilateral or bilateral), fever (≥38.0°C), +/- ear discharge

Microbiology Tests

- Not needed unless a complication is suspected
- Cultures of pus from perforated ear drums should not be used to guide treatment

Other Laboratory Tests

Not needed unless a complication is suspected

Imaging

Not needed unless a complication (e.g. mastoiditis, brain abscess) is suspected

Otoscopy

Required for definitive diagnosis if available:
Bulging, inflamed/congested tympanic membrane (may be opaque/show decreased mobility)

Most Likely Pathogens

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

Bacteria (rarely bacterial superinfections can occur):
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Streptococcus pyogenes* (group A *Streptococcus*)

Treatment

Clinical Considerations

Important: Most non-severe cases can be managed symptomatically with **no antibiotic treatment**
- Instruct patients to monitor symptoms and report back in case they worsen/persist after few days

Antibiotics should be considered if:
- Severe symptoms (e.g. systemically very unwell, ear pain despite analgesics, fever ≥39.0°C)

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (Max 4 g/day)
- **Hepatic impairment/cirrhosis:** Max 2 g/day

Antibiotic Treatment Duration

5 days

Antibiotic Treatment

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

World Health Organization

CHILDREN

Acute Otitis Media

Definition

Infection of the middle ear that occurs mostly in children under 5 years of age, often as a complication of a viral upper respiratory tract infection

Most Likely Pathogens

Respiratory viruses:

- Respiratory syncytial virus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Influenza virus (A and B)
- Other respiratory viruses

Bacteria (rarely bacterial superinfections can occur):

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Streptococcus pyogenes* (group A *Streptococcus*)

Prevention

Overlaps with prevention of upper respiratory tract infections; hand hygiene, vaccination against *S. pneumoniae*, *H. influenzae* and influenza viruses can be useful

Diagnosis

Clinical Presentation

Acute onset of ear pain (unilateral or bilateral), fever +/- ear discharge

Microbiology Tests

- Not needed unless a complication is suspected
- Cultures of pus from perforated ear drums should not be used to guide treatment

Other Laboratory Tests

Not needed unless a complication is suspected

Imaging

Not needed unless a complication (e.g. mastoiditis, brain abscess) is suspected

Otoscopy

Required for definitive diagnosis if available:

Bulging, inflamed/congested tympanic membrane (may be opaque/show decreased mobility)

Acute Otitis Media

Treatment

Clinical Considerations

Important: Most non-severe cases can be managed symptomatically with no antibiotic treatment, especially in children >2 years of age

- Instruct caregivers to monitor symptoms and report back in case they worsen/persist after few days

Antibiotics should be considered if:

- Severe symptoms (e.g. systemically very unwell, ear pain despite analgesics, fever ≥39.0°C)
- Immunocompromised children
- Bilateral acute otitis media in children <2 years

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen (do not use if <3 months of age)
- **Pain control/antipyretic:** 5-10 mg/kg q6-8h
- **Oral weight bands:**

6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen)
- **Pain control/antipyretic:** 10-15 mg/kg q6h
- **Oral weight bands:**

3-<6 kg	60 mg q6h
6-<10 kg	100 mg q6h
10-<15 kg	150 mg q6h
15-<20 kg	200 mg q6h
20-<30 kg	300 mg q6h
≥30 kg	500 mg-1 g q4-6h (Max 4 g/day or 2 g/day if hepatic impairment/cirrhosis)

Antibiotic Treatment Duration

5 days

Antibiotic Treatment

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 80-90 mg/kg/day **ORAL**
- **Oral weight bands:**

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

Second Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**
- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

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ADULTS

Pharyngitis

Definition

Inflammation of the pharynx characterized by sore throat and painful swallowing

Most Likely Pathogens

Viruses (> 80% of cases):

- Respiratory viruses (most cases)
- Epstein Barr virus (rarely)

Bacteria:

- Group A *Streptococcus* (5-10% in adults)
- Streptococci (group C and G)

Other infectious causes:

- Acute HIV-infection and other sexually transmitted diseases (syphilis, gonorrhea)
- Acute toxoplasmosis
- Diphtheria

Non infectious (rare):

- Pollution
- Allergens
- Smoking

Diagnosis

Clinical Presentation

Sore throat and painful swallowing

- **Viral:** Symptoms coincide with those of a viral upper respiratory tract infection (URTI) with cough, headache and myalgia
- **Bacterial:** More severe presentation, fever (>38.0°C), tender cervical lymph nodes and pharyngeal exudates (see "Centor Clinical Scoring System")

Microbiology Tests

Low likelihood of Group A *Streptococcus* (GAS) (Centor score 0-2):

- Tests usually not needed

Higher likelihood of GAS (Centor score 3-4):

- Rapid antigen test or throat culture could be considered, especially in countries where rheumatic fever (RF) and rheumatic heart disease are frequent
- Test should only be performed if antibiotic treatment is considered following a positive test result

Other Laboratory Tests

Blood tests usually not needed

Imaging

Usually not needed unless a complication is suspected

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ADULTS

Pharyngitis

Centor Clinical Scoring System

• This system can help indicate infection origin (bacterial or viral) and whether antibiotics are necessary

• However even with a high score of 4, the probability of GAS infection is only 50% and this score has only been validated in high-income settings

Signs & Symptoms (1 point each)

- ○ Fever > 38.0ºC
- ○ No cough
- ○ Tender anterior cervical lymphadenitis
- ○ Tonsillar exudates

Score 0-2
• GAS pharyngitis unlikely
• **Symptomatic treatment only**

Score 3-4 - In case of low risk of RF (e.g. countries with **low** prevalence of RF)
• **Antibiotic treatment can be withheld** even in cases of likely GAS pharyngitis

Score 3-4 - In case of high risk of RF (e.g. countries with **med/high** prevalence of RF)
• Antibiotic treatment recommended

Treatment

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (Max 4 g/day)
• **Hepatic impairment/cirrhosis:** Max 2 g/day

Antibiotic Treatment Duration

Depending on the local prevalence or previous history of rheumatic fever:

• Low Risk of RF: **5 days**

• High Risk of RF: **10 days**

Note: when clarithromycin or cefalexin are used treatment duration is always 5 days

Antibiotic Treatment

The only clear indication for antibiotic treatment is to reduce the probability of developing rheumatic fever in endemic settings (however, after 21 years of age the risk of RF is lower)

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Amoxicillin 500 mg q8h **ORAL**

OR

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

Second Choice

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

WATCH Clarithromycin 500 mg q12h **ORAL**

GAS remains universally susceptible to penicillin. However, resistance to macrolides is common in some communities

World Health Organization

CHILDREN

Pharyngitis

Definition

Inflammation of the pharynx characterized by sore throat and painful swallowing

Most Likely Pathogens

Viruses (> 80% of cases):
- Respiratory viruses (most cases)
- Epstein Barr virus

Bacteria:
- Group A *Streptococcus* (20-30% in children)
- Streptococci (group C and G)

Other infectious causes:
- Acute toxoplasmosis
- Diphtheria

Non infectious (rare):
- Pollution
- Allergens
- Smoking

Diagnosis

Clinical Presentation

Sore throat and painful swallowing
- **Viral:** Symptoms coincide with those of a viral upper respiratory tract infection (URTI) with cough, headache and myalgia
- **Bacterial:** More severe presentation, fever (>38.0°C), tender cervical lymph nodes and pharyngeal exudates

Microbiology Tests

Low likelihood of Group A *Streptococcus* (GAS) (Centor score 0-2):
- Tests usually not needed

Higher likelihood of GAS (Centor score 3-4):
- Rapid antigen test or throat culture could be considered, especially in countries where rheumatic fever (RF) and rheumatic heart disease are frequent
- Negative rapid antigen test could be confirmed with a throat culture if available

Other Laboratory Tests

Blood tests usually not needed

Imaging

Usually not needed unless a complication is suspected

World Health Organization

CHILDREN

Pharyngitis

Centor Clinical Scoring System

- This system can help indicate infection origin (bacterial or viral) and whether antibiotics are necessary
- However even with a high score of 4, the probability of GAS infection is only 50% and this score has only been validated in high-income settings

Signs & Symptoms (1 point each)

- ○ Fever > 38.0°C
- ○ No cough
- ○ Tender anterior cervical lymphadenitis
- ○ Tonsillar exudates

Score 0-2
- GAS pharyngitis unlikely
- **Symptomatic treatment only**

Score 3-4 - In case of low risk of RF (e.g. countries with **low** prevalence of RF)
- **Antibiotic treatment can be withheld** even in cases of likely GAS pharyngitis

Score 3-4 - In case of high risk of RF (e.g. countries with **med/high** prevalence of RF)
- Antibiotic treatment recommended

Treatment

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen (do not use if <3 months of age)
- **Pain control/antipyretic:** 5-10 mg/kg q6-8h
- **Oral weight bands:**

6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen)
- **Pain control/antipyretic:** 10-15 mg/kg q6h
- **Oral weight bands:**

3-<6 kg	60 mg q6h
6-<10 kg	100 mg q6h
10-<15 kg	150 mg q6h
15-<20 kg	200 mg q6h
20-<30 kg	300 mg q6h
≥30 kg	500 mg-1 g q4-6h (Max 4 g/day or 2 g/day if hepatic impairment/cirrhosis)

Antibiotic Treatment Duration

Depending on the local prevalence or previous history of rheumatic fever:
- Low Risk of RF: **5 days**
- High Risk of RF: **10 days**

Note: when clarithromycin or cefalexin are used treatment duration is always 5 days

Antibiotic Treatment

The only clear indication for antibiotic treatment is to reduce the probability of developing rheumatic fever in endemic settings

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Amoxicillin 80-90 mg/kg/day **ORAL**
- **Oral weight bands:**

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

OR

ACCESS

Phenoxymethylpenicillin: 10-15 mg/kg/dose (16 000-24 000 IU/kg/dose) q6-8h **ORAL**

Second Choice

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**
- **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

WATCH

Clarithromycin 7.5 mg/kg/dose q12h **ORAL**

GAS remains universally susceptible to penicillin. However, resistance to macrolides is common in some communities

World Health Organization

ADULTS

Acute Sinusitis

Definition

A symptomatic inflammation of the paranasal sinuses and nasal cavity

Most Likely Pathogens

Respiratory viruses:

- Influenza virus (A and B)
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Respiratory syncytial virus (RSV)
- Other respiratory viruses

Bacteria (rarely):

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

Diagnosis

Clinical Presentation

- Diagnosis is made clinically; symptoms of bacterial and viral sinusitis overlap considerably
- Symptoms usually last 10-14 days and are self-limiting
- Main symptoms are nasal drainage, nasal obstruction or congestion, unilateral dental or facial pain, facial fullness or pressure, and sometimes cough
- Location of pain depends on involved sinuses
- Acute bacterial sinusitis suspected when:
  - Signs/symptoms persist ≥10 days without improvement

  OR
  - Significant worsening of symptoms after initial mild phase

Microbiology Tests

Usually not needed

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed unless a complication or an alternative diagnosis is suspected

World Health Organization

ADULTS

Acute Sinusitis

Treatment

No Antibiotic Care

- Treatment is to improve symptoms, but **antibiotics have minimal impact on symptom duration in most cases**
- Symptomatic treatment includes antipyretic and analgesic medications, nasal irrigation with a saline solution and topical intranasal glucocorticoids or decongestants
- Most guidelines recommend using disease severity (duration and intensity of symptoms) to direct treatment

Mild to Moderate Presentation (<10 days duration and improving):

- Watchful waiting approach with symptom relief and **no antibiotic treatment**

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (Max 4 g/day)
- **Hepatic impairment/cirrhosis:** Max 2 g/day

Clinical Considerations

Antibiotics should be considered if:

- Severe onset of symptoms
  - **Severe onset:** Measured fever ≥39.0°C & purulent nasal discharge or facial pain for at least 3-4 consecutive days
- Patients with chronic underlying comorbid diseases (deciding on a case-by-case basis)
- Patients at increased risk of complications
- “Red flag” signs/symptoms suggestive of complicated infection such as systemic toxicity, persistent fever ≥39.0°C, periorbital redness and swelling, severe headache, or altered mental status

Antibiotic Treatment Duration

5 days

Antibiotic Treatment

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS Amoxicillin 1g q8h **ORAL**

OR

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

World Health Organization

CHILDREN

Acute Sinusitis

Definition

A symptomatic inflammation of the paranasal sinuses and nasal cavity. Much less common than in adults because sinuses are not fully developed.

Most Likely Pathogens

Respiratory viruses:

- Influenza virus (A and B)
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Respiratory syncytial virus (RSV)
- Other respiratory viruses

Bacteria (rarely):

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

Diagnosis

Clinical Presentation

- Diagnosis is made clinically; the symptoms of bacterial and viral sinusitis overlap considerably
- Symptoms usually last 10-14 days and are self-limiting
- Main symptoms are purulent nasal drainage, nasal obstruction or congestion, unilateral dental or facial pain, facial fullness or pressure, and cough
- Location of pain depends on involved sinuses
- Acute bacterial sinusitis suspected when:
  - Signs/symptoms persist ≥10 days without improvement;

    OR
  - Significant worsening of symptoms after initial mild phase

Microbiology Tests

Usually not needed

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed unless a complication or an alternative diagnosis is suspected

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CHILDREN

Acute Sinusitis

Treatment

No Antibiotic Care

- Treatment is to improve symptoms, but **antibiotics have minimal impact on symptom duration in most cases**
- Symptomatic treatment includes antipyretic and analgesic medications, nasal irrigation with a saline solution and topical intranasal glucocorticoids or decongestants
- Most guidelines recommend using disease severity (duration and intensity of symptoms) to direct treatment

Mild to Moderate Presentation (<10 days duration and improving trend of symptoms):

- Watchful waiting approach with symptom relief and **no antibiotic treatment**

Clinical Considerations

Antibiotics should be considered if:

- Severe onset of symptoms
  - **Severe onset:** Measured fever ≥39.0°C and purulent nasal discharge or facial pain for at least 3-4 consecutive days
- Patients with chronic underlying comorbid diseases (deciding on a case-by-case basis)
- Patients at increased risk of complications
- "Red flag" signs/symptoms suggestive of complicated infection such as systemic toxicity, persistent fever ≥39.0°C, periorbital redness and swelling, severe headache, or altered mental status

Antibiotic Treatment Duration

5 days

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen (do not use if <3 months of age)
- **Pain control/antipyretic:** 5-10 mg/kg q6-8h
- **Oral weight bands:**

6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen)
- **Pain control/antipyretic:** 10-15 mg/kg q6h
- **Oral weight bands:**

3-<6 kg	60 mg q6h
6-<10 kg	100 mg q6h
10-<15 kg	150 mg q6h
15-<20 kg	200 mg q6h
20-<30 kg	300 mg q6h
≥30 kg	500 mg-1 g q4-6h (Max 4 g/day or 2 g/day if hepatic impairment/cirrhosis)

Antibiotic Treatment

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin 80-90 mg/kg/day **ORAL**
- **Oral weight bands:**

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

OR

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**
- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

Oral and Dental Infections

Definitions of Conditions That May Require Antibiotic Treatment

• **Abscess:** Localized collection of pus caused by a bacterial infection in the tooth, gums or alveolar bone supporting the tooth. Abscesses can be categorized as:

  • *Apical Abscess (more common):* Infection at the apex of the dental root that originates from within the dental pulp usually resulting from untreated dental caries

  • *Periodontal abscess:* Collection of pus between the root and alveolar bone usually resulting from serious gum diseases

• **Pericoronitis:** Inflammation of the gingiva (gum) surrounding a partially erupted tooth, often a lower wisdom tooth, which may be associated with an infection

• **Necrotizing periodontal disease:** A severe gum infection characterized by necrosis and ulcerations caused by a bacterial infection. Previously known as necrotizing ulcerative gingivitis

• **Noma:** An acute necrotizing disease that destroys the soft tissues and bones of the mouth and face as it progresses from necrotizing periodontal disease (previously known as necrotizing ulcerative gingivitis), rare in adults

Dental Terminology Definitions

• **Alveolar bone:** Part of the jawbones that surrounds and supports the teeth

• **Dental pulp:** Blood vessels and nerves within the inner part of the tooth

• **Gingivae (gums):** Soft tissue covering the alveolar bone

• **Plaque:** Biofilm of microbes, mainly bacteria, which grows on surfaces within the mouth and contributes to oral diseases such as caries and periodontal disease

Only oral and dental infections where antibiotic treatment is usually required are reported

Most Likely Pathogens

Important: most dental infections are caused by conditions that favour the growth of pathogens in the mouth, including an abundance of sugars (e.g. sucrose) and reduced saliva flow (dry mouth)

Bacteria associated with caries:

• Acidogenic bacteria such as:

  • *Streptococcus* spp. (e.g. *S. mutans*)

  • *Lactobacillus* spp.

  • *Actinomyces* spp.

Bacteria associated with periodontal disease:

• Mostly anaerobes such as:

  • *Capnocytophaga* spp.

  • *Prevotella* spp.

  • *Aggregatibacter* spp.

  • *Porphyromonas* spp.

Prevention

• Minimize sugar consumption

• Prevent the accumulation of dental plaque with regular dental cleaning and good oral hygiene; fluoride is important because it strengthens the tooth enamel making it more resistant to caries

• Promote smoking cessation

Oral and Dental Infections

Diagnosis

Clinical Presentation

Dental abscess:

• Acute severe and persistent localized toothache that can radiate to the ear, jaw and neck

• Tooth tenderness (e.g. with chewing) and swelling of the cheek above the affected tooth are often present

• If left untreated, the infection can spread and present with signs of cellulitis around the eye or throat, fever (>38.0°C), tachycardia and lymphadenopathy

Pericoronitis:

• Inflamed, swollen gum tissue surrounding a partially erupted tooth

• Antibiotics are not normally required, although if infection is present, it should be carefully monitored as it can spread rapidly causing difficulty opening the mouth, swallowing or breathing

• Cellulitis of the neck (e.g. Ludwig's angina) is a medical emergency

Necrotizing periodontal disease:

• Characterized by severe pain and inflamed ulcerated gums that bleed easily, necrosis of the interdental papillae, foul breath and a bad taste in the mouth

• It may also be accompanied by systemic symptoms, such as fever >38ºC, malaise and lymphadenopathy

Noma:

• It begins as necrotizing periodontal disease, it progresses rapidly destroying the soft tissues and bones of the mouth and further progressing to perforate the hard tissues and skin of the face

• If detected early, its progression can be rapidly halted, through basic oral hygiene rules, diet supplementation with proteins and nutrients and with antibiotics

Imaging

Dental radiographs should be undertaken wherever possible as part of the diagnosis to differentiate between the various causes of dental pain

Microbiology Tests

Mild cases: Usually not needed

Severe cases requiring hospitalization: Consider doing blood and/or pus aspirates cultures

Other Laboratory Tests

Mild cases: Usually not needed

Severe cases requiring hospitalization: White blood cell count, C-reactive protein and/or procalcitonin

Point-of-Care Tests and Investigations to Assist Diagnosis

Point-of-care tests can be done to establish the source of the dental pain/infection and make appropriate treatment decisions, for example:

• **Tapping the tooth to evaluate response to percussion:**
  • Tenderness indicates that the pain originates in the supporting bone and may be due to an abscess
  • Periodontal probing can identify a periodontal abscess if pus exudes from a pocket greater than 3mm or necrotizing ulcerative disease if there is extremely tender gingival tissue and grey sloughing

• **Checking response to a cold stimulus:**
  • No response to cold may indicate a non-vital/ necrotic pulp

Oral and Dental Infections

Treatment

Clinical Considerations

Important:

• Most dental infections and dental pain can be treated without antibiotic treatment by removal of the cause and drainage of the infection using a dental procedure (e.g. extraction of the tooth)

• Antibiotics do not prevent severe complications and cannot replace local surgical treatment

• Antibiotics should not be used before a dental procedure to "decrease inflammation" or to cure toothache. Antibiotics should not be used prior to most dental procedures to prevent surgical site infections

• Regular use of mouthwashes with an antiseptic product (e.g. chlorhexidine) is not necessary for the control of dental infections; rinsing with salty water is usually adequate

• Common dental procedures are beyond the scope of this guidance

Antibiotic treatment is not needed in most cases but can be considered (always complementary to dental procedures):

• In patients with severe, spreading infections with systemic signs (e.g. facial swelling, inability to open the mouth, fever >38.0°C, tachycardia)

• In severely immunocompromised patients and patients with uncontrolled diabetes (higher risk of complications)

Antibiotic Treatment Duration

If adequate source control achieved: **3 days**

If adequate source control ***not*** achieved: **5 days**

Note: patients should be reassessed before the end of treatment to check the resolution of the infection

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen 200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen) 500 mg-1 g q4-6h (Max 4 g/day)
• **Hepatic impairment/cirrhosis**: Max 2 g/day

Antibiotic Treatment

Antibiotic treatment is not required in the great majority of cases (see "Clinical Considerations" when antibiotics may be indicated)

For the treatment of infections of dental soft tissues (e.g. pericoronitis or necrotizing periodontal disease), metronidazole is an option

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS Amoxicillin 500 mg q8h **ORAL**

OR

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

World Health Organization

CHILDREN

Oral and Dental Infections

Definitions of Conditions That May Require Antibiotic Treatment

• **Abscess:** Localized collection of pus caused by a bacterial infection in the tooth, gums or alveolar bone supporting the tooth. Abscesses can be categorized as:

  • *Apical Abscess (more common):* Infection at the apex of the dental root that originates from within the dental pulp usually resulting from untreated dental caries

  • *Periodontal abscess:* Collection of pus between the root and alveolar bone usually resulting from serious gum diseases

• **Pericoronitis:** Inflammation of the gingiva (gum) surrounding a partially erupted tooth, often a lower wisdom tooth, which may be associated with an infection

• **Necrotizing periodontal disease:** A severe gum infection characterized by necrosis and ulcerations caused by a bacterial infection. Previously known as necrotizing ulcerative gingivitis

• **Noma:** An acute necrotizing disease that destroys the soft tissues and bones of the mouth and face as it progresses from necrotizing periodontal disease (previously known as necrotizing ulcerative gingivitis), mostly in malnourished children living in extreme poverty and with weakened immune systems

Dental Terminology Definitions

• **Alveolar bone:** Part of the jawbones that surrounds and supports the teeth

• **Dental pulp:** Blood vessels and nerves within the inner part of the tooth

• **Gingivae (gums):** Soft tissue covering the alveolar bone

• **Plaque:** Biofilm of microbes, mainly bacteria, which grows on surfaces within the mouth and contributes to oral diseases such as caries and periodontal disease

Only oral and dental infections where antibiotic treatment is usually required are reported

Most Likely Pathogens

Important: most dental infections are caused by conditions that favour the growth of pathogens in the mouth, including an abundance of sugars (e.g. sucrose) and reduced saliva flow (dry mouth)

Bacteria associated with caries:

• Acidogenic bacteria such as:

  • *Streptococcus* spp. (e.g. *S. mutans*)

  • *Lactobacillus* spp.

  • *Actinomyces* spp.

Bacteria associated with periodontal disease:

• Mostly anaerobes such as:

  • *Capnocytophaga* spp.

  • *Prevotella* spp.

  • *Aggregatibacter* spp.

  • *Porphyromonas* spp.

Prevention

• Minimize sugar consumption

• Prevent the accumulation of dental plaque with regular dental cleaning and good oral hygiene; fluoride is important because it strengthens the tooth enamel making it more resistant to caries

• Promote smoking cessation

Oral and Dental Infections

Diagnosis

Clinical Presentation

Dental abscess:

• Acute severe and persistent localized toothache that can radiate to the ear, jaw and neck

• Tooth tenderness (e.g. with chewing) and swelling of the cheek above the affected tooth are often present

• If left untreated, the infection can spread and present with signs of cellulitis around the eye or throat, fever (>38.0°C), tachycardia and lymphadenopathy

Pericoronitis:

• Inflamed, swollen gum tissue surrounding a partially erupted tooth

• Antibiotics are not normally required, although if infection is present, it should be carefully monitored as it can spread rapidly causing difficulty opening the mouth, swallowing or breathing

• Cellulitis of the neck (e.g. Ludwig's angina) is a medical emergency

Necrotizing periodontal disease:

• Characterized by severe pain and inflamed ulcerated gums that bleed easily, necrosis of the interdental papillae, foul breath and a bad taste in the mouth

• It may also be accompanied by systemic symptoms, such as fever >38ºC, malaise and lymphadenopathy

Noma:

• It begins as necrotizing periodontal disease, it progresses rapidly destroying the soft tissues and bones of the mouth and further progressing to perforate the hard tissues and skin of the face

• Noma is fatal for 90% of the children affected

• If detected early, its progression can be rapidly halted, through basic oral hygiene rules, diet supplementation with proteins and nutrients and with antibiotics

Imaging

Dental radiographs should be undertaken wherever possible as part of the diagnosis to differentiate between the various causes of dental pain

Microbiology Tests

Mild cases: Usually not needed

Severe cases requiring hospitalization: Consider doing blood and/or pus aspirates cultures

Other Laboratory Tests

Mild cases: Usually not needed

Severe cases requiring hospitalization: White blood cell count, C-reactive protein and/or procalcitonin

Point-of-Care Tests and Investigations to Assist Diagnosis

Point-of-care tests can be done to establish the source of the dental pain/infection and make appropriate treatment decisions, for example:

• **Tapping the tooth to evaluate response to percussion:**
  • Tenderness indicates that the pain originates in the supporting bone and may be due to an abscess
  • Periodontal probing can identify a periodontal abscess if pus exudes from a pocket greater than 3mm or necrotizing ulcerative disease if there is extremely tender gingival tissue and grey sloughing

• **Checking response to a cold stimulus:**
  • No response to cold may indicate a non-vital/ necrotic pulp

Oral and Dental Infections

Treatment

Clinical Considerations

Important:

• Most dental infections and dental pain can be treated without antibiotic treatment by removal of the cause and drainage of the infection using a dental procedure (e.g. extraction of the tooth)

• Antibiotics do not prevent severe complications and cannot replace local surgical treatment

• Antibiotics should not be used before a dental procedure to "decrease inflammation" or to cure toothache. Antibiotics should not be used prior to most dental procedures to prevent surgical site infections

• Regular use of mouthwashes with an antiseptic product (e.g. chlorhexidine) is not necessary for the control of dental infections; rinsing with salty water is usually adequate

• Common dental procedures are beyond the scope of this guidance

Antibiotic treatment is not needed in most cases but can be considered (always complementary to dental procedures):

• In patients with severe, spreading infections with systemic signs (e.g. facial swelling, inability to open the mouth, fever >38.0°C, tachycardia)

• In severely immunocompromised patients and patients with uncontrolled diabetes (higher risk of complications)

Antibiotic Treatment Duration

If adequate source control achieved: **3 days**

If adequate source control ***not*** achieved: **5 days**

Note: patients should be reassessed before the end of treatment to check the resolution of the infection

Symptomatic Treatment

Medicines are listed in alphabetical order and should be considered equal treatment options

Ibuprofen (do not use if <3 months of age)
• **Pain control/antipyretic:** 5-10 mg/kg q6-8h
• **Oral weight bands:**

6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	200-400 mg q6-8h (Max 2.4 g/day)

OR

Paracetamol (acetaminophen)
• **Pain control/antipyretic:** 10-15 mg/kg q6h
• **Oral weight bands:**

3-<6 kg	60 mg q6h
6-<10 kg	100 mg q6h
10-<15 kg	150 mg q6h
15-<20 kg	200 mg q6h
20-<30 kg	300 mg q6h
≥30 kg	500 mg-1 g q4-6h (Max 4 g/day or 2 g/day if hepatic impairment/cirrhosis)

Antibiotic Treatment

Antibiotic treatment is not required in the great majority of cases (see "Clinical Considerations" when antibiotics may be indicated)

For the treatment of infections of dental soft tissues (e.g. pericoronitis or necrotizing periodontal disease), metronidazole is an option

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin 80-90 mg/kg/day **ORAL**
• **Oral weight bands:**

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

OR

ACCESS

Phenoxymethylpenicillin 10-15 mg/kg/dose (16 000-24 000 IU/kg/dose) q6-8h **ORAL**

World Health Organization

ADULTS

Localized Acute Bacterial Lymphadenitis

This guidance excludes management of severe or generalized infections or those caused by viral, fungal or parasitic pathogens

Definition

Lymphadenitis refers to the inflammation and acute enlargement (>1-2 cm) of one or several lymph nodes

Classification based on:

- Number of lymph node regions affected:
  - *Localized* (most cases): 1 lymph node region affected
  - *Generalized*: >1 lymph node region affected
- Location of the affected lymph node (e.g. cervical, axillary)
- Depth of the affected lymph node (superficial or deep)

Most Likely Pathogens

Viruses (most cases):

- Epstein-Barr virus, Cytomegalovirus (both viruses can cause infectious mononucleosis)
- Respiratory viruses

Bacteria (more rarely):

- *Staphylococcus aureus* (including MRSA)
- *Streptococcus pyogenes* (group A *Streptococcus*)

Consider in specific situations (based on history and physical examination):

- Sexually transmitted infections (e.g. HIV)
- Zoonoses (e.g. brucellosis, tularemia, bartonellosis - the latter mostly following cat bites or scratches)
- Mycobacterial infections (including nontuberculous)

Diagnosis

Clinical Presentation

- Acute onset of a palpable, painful red and inflamed enlarged lymph node (>1-2 cm) +/- fever (>38.0°C), and other signs/symptoms of systemic disease & cellulitis
- Bacterial cause more probable if unilateral involvement, fluctuance and skin drainage of the lymph node

Microbiology Tests

Usually not needed; consider testing for HIV and tuberculosis if these are suspected

Other Laboratory Tests

Usually not needed but may be considered in selected cases

Biopsy

Excisional biopsy or fine needle aspiration: Consider when a malignancy is suspected

Imaging

- Usually not needed
- Ultrasound can be considered to confirm lymph node involvement, to quantify the enlargement and to detect the presence of an abscess; it is not reliable to rule out malignancies (biopsy should be performed)

World Health Organization

ADULTS

Localized Acute Bacterial Lymphadenitis

Treatment

Clinical Considerations

Important:

- The great majority of cases of enlarged lymph nodes are caused by viral infections and antibiotics are **not needed**
- A watchful waiting approach with follow up is appropriate (except if malignancy is suspected)

If symptoms are consistent with a bacterial infection, empiric treatment against *S. aureus* and *Streptococcus pyogenes* (group A *Streptococcus*) is indicated

Note: history is key in order to adapt treatment if necessary

Antibiotic Treatment Duration

5 days

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL** OR 1 g+200 mg q8h **IV**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 500 mg q6h **ORAL** OR 2 g q6h **IV**

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

World Health Organization

CHILDREN

Localized Acute Bacterial Lymphadenitis

This guidance excludes management of severe or generalized infections or those caused by viral, fungal or parasitic pathogens

Definition

• Lymphadenitis refers to the inflammation and enlargement (>1-2 cm) of one or several lymph nodes

• Lymphadenopathy is another term often used

Classification based on:

• Number of lymph node regions affected:
  • *Localized* (most cases): 1 lymph node region affected
  • *Generalized*: >1 lymph node region affected

• Location of the affected lymph node (e.g. cervical, axillary)

• Depth of the affected lymph node (superficial or deep)

Most Likely Pathogens

Viruses (most cases):

• Epstein-Barr virus (can cause infectious mononucleosis)

• Cytomegalovirus (can cause infectious mononucleosis)

• Respiratory viruses

Bacteria (more rarely):

• *Staphylococcus aureus* (including MRSA)

• *Streptococcus pyogenes* (group A *Streptococcus*)

Consider in specific situations (based on history and physical examination):

• Sexually transmitted infections (e.g. HIV)

• Zoonoses (e.g. brucellosis, tularemia, bartonellosis - the latter mostly following cat bites or scratches)

• Mycobacterial infections (including nontuberculous)

Diagnosis

Clinical Presentation

• Acute onset of a palpable, painful red and inflamed enlarged lymph node (>1-2 cm) +/- fever (>38.0°C), and other signs/symptoms of systemic disease and cellulitis

• Bacterial cause more probable if unilateral involvement, fluctuance and skin drainage of the lymph node

Microbiology Tests

Usually not needed; consider testing for HIV and tuberculosis if these are suspected

Other Laboratory Tests

Usually not needed but may be considered in selected cases

Biopsy

Consider when a malignancy is suspected

Imaging

• Usually not needed

• Ultrasound can be considered to confirm lymph node involvement, to quantify the enlargement and to detect the present of an abscess; it is not reliable to rule out malignancies (biopsy should be performed)

World Health Organization

CHILDREN

Localized Acute Bacterial Lymphadenitis

Treatment

Clinical Considerations

Important:

- The great majority of cases of enlarged lymph nodes are caused by viral infections and antibiotics are **not needed**
- A watchful waiting approach with follow up is appropriate (except if malignancy is suspected)

If symptoms are consistent with a bacterial infection, empiric treatment against *S. aureus* and *Streptococcus pyogenes* (group A *Streptococcus*) is indicated

Note: history is key in order to adapt treatment if necessary

Antibiotic Treatment Duration

5 days

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**

- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin **IV**

- Neonates: 25-50 mg/kg/dose q12h
- Children: 25 mg/kg/dose q6h
- **ORAL:** 15 mg/kg/dose q6h
- **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

World Health Organization

ADULTS

Conjunctivitis

Bacterial Eye Infection

Definition

Infection of the conjunctiva (i.e. the mucosa that covers the inside part of the eyelids and the sclera, which is the white part of the eye)

Diagnosis

Clinical Presentation

- **Most cases are mild and self-limiting**
- Usually the eye is red, watery and itchy and patients have a feeling of "sand in the eye"
- Vision is normal and there is no pain (if pain is present consider corneal involvement)
- Thick purulent eye discharge can be present in bacterial infection

Hyperacute Bacterial Conjunctivitis:
- Severe infection that presents with decreased vision, purulent eye discharge, eyelid swelling, pain on palpation and preauricular adenopathy
- Consider urgent referral to an ophthalmologist due to risk for rapid progression to corneal perforation

Microbiology Tests

Usually not needed unless *Neisseria gonorrhoeae* or *Chlamydia trachomatis* are suspected

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Most Likely Pathogens

- Most cases are of viral origin
- Bacterial cases are less common than viruses
  - Consider *Chlamydia trachomatis* (serovars D to K) and *Neisseria gonorrhoeae* in the context of sexually transmitted infections (STI) see "*STI – Chlamydia urogenital infections and gonococcal infection*"
- Hyperacute bacterial conjunctivitis is mostly caused by *Neisseria gonorrhoeae*

Important: non-infectious causes (mostly allergies) should always be considered

Treatment

Clinical Considerations

- Most cases resolve without treatment in 7-10 days
- Antibiotics can be considered in case of suspected bacterial conjunctivitis or conjunctivitis in the context of a sexually transmitted infection

Antibiotic Treatment Duration

Since treatment duration varies, please refer to the corresponding treatment section

Bacterial Conjunctivitis

ACCESS
Gentamicin 0.3% **EYE DROPS**
1 drop in the affected eye q6h
Treatment duration: 5 days

OR

WATCH
Ofloxacin 0.3% **EYE DROPS**
1 drop in the affected eye q6h
Treatment duration: 5 days

OR

ACCESS
Tetracycline 1% **EYE OINTMENT**
1 cm in the affected eye q6h
Treatment duration: 5 days

Gonococcal Conjunctivitis

All dosages are for normal renal function

WATCH
Ceftriaxone 250 mg **IM**
Treatment duration: Single dose

COMBINED WITH

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

Conjunctivitis

Bacterial Eye Infection

Definition

Infection of the conjunctiva (i.e. the mucosa that covers the inside part of the eyelids and the sclera, which is the white part of the eye)

Most Likely Pathogens

- Most cases are of viral origin
- Bacterial cases can occur especially in children (although less common than viruses)
- Consider *Chlamydia trachomatis* (serovars D-K) and *Neisseria gonorrhoeae* in neonates after vaginal delivery from infected mothers

Important: non-infectious causes (mostly allergies) should always be considered

Diagnosis

Clinical Presentation

- **Most cases are mild and self-limiting**
- Usually the eye is red, watery and itchy and patients have a feeling of “sand in the eye”
- Vision is normal and there is no pain (if pain is present consider corneal involvement)
- Thick purulent eye discharge can be present in bacterial infection

Hyperacute Bacterial Conjunctivitis:

- Severe infection that presents with decreased vision, purulent eye discharge, eyelid swelling, pain on palpation and preauricular adenopathy
- Consider urgent referral to an ophthalmologist due to risk for rapid progression to corneal perforation

Microbiology Tests

Usually not needed unless *Neisseria gonorrhoeae* or *Chlamydia trachomatis* are suspected

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Conjunctivitis

Treatment

Clinical Considerations

- **Most cases resolve without treatment** in 7-10 days
- Antibiotics can be considered in case of suspected bacterial conjunctivitis

Antibiotic Treatment Duration

Since treatment duration varies, please refer to the corresponding treatment section

Bacterial Conjunctivitis

ACCESS
Gentamicin 0.3% **EYE DROPS**
• 1 drop in the affected eye q6h
Treatment duration: 5 days

OR

WATCH
Ofloxacin 0.3% **EYE DROPS**
• 1 drop in the affected eye q6h
Treatment duration: 5 days

OR

ACCESS
Tetracycline 1% **EYE OINTMENT**
• 1 cm in the affected eye q6h
Treatment duration: 5 days

Gonococcal Ophthalmia Neonatorum

All dosages are for normal renal function

WATCH
Ceftriaxone 50 mg/kg **IM**
Treatment duration: Single dose

Do not administer ceftriaxone in neonates receiving calcium-containing IV fluids and avoid in infants with hyperbilirubinaemia

Chlamydial Ophthalmia Neonatorum

Topical therapy alone is not effective

All dosages are for normal renal function

WATCH
Azithromycin 20 mg/kg q24h **ORAL**
Treatment duration: 3 days

Prevention of Both Chlamydial and Gonococcal Ophthalmia Neonatorum

WATCH
Erythromycin 0.5% **EYE OINTMENT**
• To be applied to both eyes soon after birth

OR

ACCESS
Tetracycline 1% **EYE OINTMENT**
• To be applied to both eyes soon after birth

World Health Organization

ADULTS

Endophthalmitis

Bacterial Eye Infection

Definition

• Infection of the intraocular fluids (vitreous and aqueous humor) and the retina
• Most cases occur as a result of penetrating eye trauma, after eye surgery or as a complication of keratitis
• Rare cases are due to bacteremia or fungemia from distant sites of infection (e.g. endocarditis, liver abscess)

Diagnosis

Clinical Presentation

• Usually painful red eye, blurred vision and trouble looking at bright light
• In cases where pathogens reach the eye through the bloodstream from other sites of infection, signs and symptoms of bacteremia/fungemia can be present although usually ocular symptoms occur first

Microbiology Tests

• Consider microscopy and culture of a sample of aqueous or vitreous humour aspirate
• Consider blood cultures if a distant source of infection is suspected (i.e. endogenous endophthalmitis)

Other Laboratory Tests

Consider tests to detect organ dysfunction

Imaging

Usually not needed

Most Likely Pathogens

Exogenous (Most Cases):
• **Bacteria:**
  • Mostly coagulase-negative Staphylococci, less frequently *Staphylococcus aureus*
  • *Streptococcus* spp.
  • *Klebsiella* spp. (more frequent in Asia)
  • *Bacillus cereus* (mostly in case of penetrating trauma)
• **Fungi:**
  • *Fusarium* spp.
  • *Aspergillus* spp.

Endogenous (Rare):
• **Bacteria:**
  • Mostly coagulase-negative Staphylococci, less frequently *Staphylococcus aureus*
  • *Streptococcus* spp.
  • *Klebsiella* spp. (more frequent in Asia)
  • *Bacillus cereus* (mostly in case of penetrating trauma)
• **Fungi:**
  • Mostly *Candida albicans*

Treatment

Clinical Considerations

• Endophthalmitis is an ocular emergency because it is a potentially blinding condition
• Systemic antibiotics (in combination with intravitreal antibiotics) should be considered given the severity of this condition, especially when referral to an ophthalmologist is not rapidly available

The cornerstone of treatment is intravitreal injection of antibiotics. Two common approaches to administer intravitreal antibiotics:
1. "Tap and inject": first a sample of vitreous humour is collected for culture (through vitreous aspiration), then antibiotics are injected into the vitreous
2. Vitrectomy is performed (i.e. eye surgery to remove some or all the inflamed vitreous from the eye as a form of source control) and during the procedure, the antibiotic is injected into the vitreous

Antibiotic Treatment Duration

Intravitreal: **Single dose**
• If no clinical improvement after 48 hours, the injection can be repeated

Systemic: Depends on underlying source of bacteremia

Bacterial Endophthalmitis

All dosages are for normal renal function

WATCH Vancomycin 1 mg **INTRAVITREAL INJECTION**

COMBINED WITH

WATCH Ceftazidime 2.25 mg **INTRAVITREAL INJECTION**

IF ENDOGENOUS INFECTION, ADD

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

WATCH Vancomycin 15-20 mg/kg q12h **IV**

World Health Organization

CHILDREN

Endophthalmitis

Bacterial Eye Infection

Definition

- Infection of the intraocular fluids (vitreous and aqueous humor) and the retina
- Most cases occur as a result of penetrating eye trauma, after eye surgery or as a complication of keratitis
- Rare cases are due to bacteremia or fungemia from distant sites of infection (e.g. endocarditis, liver abscess)

Diagnosis

Clinical Presentation

- Usually painful red eye, blurred vision and trouble looking at bright light
- In cases where pathogens reach the eye through the bloodstream from other sites of infection, signs and symptoms of bacteremia/fungemia can be present although usually ocular symptoms occur first

Microbiology Tests

- Consider microscopy and culture of a sample of aqueous or vitreous humour aspirate
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Other Laboratory Tests

Consider tests to detect organ dysfunction

Imaging

Usually not needed

Most Likely Pathogens

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  - *Streptococcus* spp.
  - *Klebsiella* spp. (more frequent in Asia)
  - *Bacillus cereus* (mostly in case of penetrating trauma)
- **Fungi:**
  - *Fusarium* spp.
  - *Aspergillus* spp.

Endogenous (Rare):

- **Bacteria:**
  - Mostly coagulase-negative Staphylococci, less frequently *Staphylococcus aureus*
  - *Streptococcus* spp.
  - *Klebsiella* spp. (more frequent in Asia)
  - *Bacillus cereus* (mostly in case of penetrating trauma)
- **Fungi:**
  - Mostly *Candida albicans*

Treatment

Clinical Considerations

- Endophthalmitis is an ocular emergency because it is a potentially blinding condition
- Systemic antibiotics (in combination with intravitreal antibiotics) should be considered given the severity of this condition, especially when referral to an ophthalmologist is not rapidly available

The cornerstone of treatment is intravitreal injection of antibiotics. Two common approaches to administer intravitreal antibiotics:

1. "Tap and inject": first a sample of vitreous humour is collected for culture (through vitreous aspiration), then antibiotics are injected into the vitreous
2. Vitrectomy is performed (i.e. eye surgery to remove some or all the inflamed vitreous from the eye as a form of source control) and during the procedure, the antibiotic is injected into the vitreous

Antibiotic Treatment Duration

Intravitreal: **Single dose**

- If no clinical improvement after 48 hours, the injection can be repeated

Systemic: Depends on underlying source of bacteremia

Bacterial Endophthalmitis

All dosages are for normal renal function

WATCH Vancomycin 1 mg **INTRAVITREAL INJECTION**

COMBINED WITH

WATCH Ceftazidime 2.25 mg **INTRAVITREAL INJECTION**

IF ENDOGENOUS INFECTION, ADD

WATCH Ceftriaxone 80 mg/kg/dose q24h **IV**

COMBINED WITH

WATCH Vancomycin **IV**
- Neonates: 15 mg/kg/dose q12h
- Children: 15 mg/kg/dose q8h

World Health Organization

ADULTS

Keratitis

Bacterial Eye Infection

Definition

Infection of the cornea (i.e. transparent covering of the eye)

Most Likely Pathogens

High Income Countries:
• Bacteria and viruses are the most common causes

Low and Middle Income Countries:
• Fungi predominate (especially in rural settings where eye trauma from plants is a common risk factor)

Bacteria:
• *Pseudomonas* spp. (mostly in individuals who wear contact lenses)
• *Staphylococcus epidermidis*
• *Staphylococcus aureus*
• *Streptococcus pneumoniae*

Fungi:
• Mostly *Fusarium* spp.
• *Aspergillus* spp.

Viruses:
• Reactivation of herpes simplex virus (especially in patients who are immunocompromised)

Parasites:
• Acanthamoeba (contact lenses)

Diagnosis

Clinical Presentation

Usually painful eye, decreased vision, more tears and corneal oedema with a feeling of “having something in the eye” and difficulty in keeping the eye open +/- eye discharge

Microbiology Tests

• Consider microscopy and culture of a corneal sample (e.g. corneal scrapings or corneal biopsy)
• Consider nucleic acid amplification testing for herpes simplex virus in patients who are immunocompromised

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed; specialist eye examination may be considered

Treatment

Clinical Considerations

• Infectious keratitis is an ocular emergency because it is a potentially blinding condition with poor prospects of visual restoration

• Patients with keratitis should stop wearing contact lenses until the infection is healed

• Consider giving cycloplegic eye drops (cyclopentolate 1% or atropine 1%) to reduce photophobia and to reduce the formation of pupillary adhesions to the lens

Antibiotic Treatment Duration

2 weeks
Duration is often personalized to the individual based on clinical improvement

Bacterial Keratitis

WATCH

Ofloxacin 0.3% **EYE DROPS**
• 1 drop in the affected eye q1h for 48 hours, then q4h until healed

Drops are preferred over ointments because they have a better corneal penetration

World Health Organization

CHILDREN

Keratitis

Bacterial Eye Infection

Definition

Infection of the cornea (i.e. transparent covering of the eye)

Most Likely Pathogens

High Income Countries:

• Bacteria and viruses are the most common causes

Low and Middle Income Countries:

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Bacteria:

• *Pseudomonas* spp. (mostly in individuals who wear contact lenses)
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• *Streptococcus pneumoniae*

Fungi:

• Mostly *Fusarium* spp.
• *Aspergillus* spp.

Viruses:

• Reactivation of herpes simplex virus (especially in patients who are immunocompromised)

Diagnosis

Clinical Presentation

• Usually painful eye, decreased vision, more tears and corneal oedema with a feeling of “having something in the eye” and difficulty in keeping the eye open +/- eye discharge
• Keratitis is rare in children

Microbiology Tests

• Consider microscopy and culture of a corneal sample (e.g. corneal scrapings or corneal biopsy)
• Consider nucleic acid amplification testing for herpes simplex virus in patients who are immunocompromised

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed; specialist eye examination may be considered

Treatment

Clinical Considerations

• Infectious keratitis is an ocular emergency because it is a potentially blinding condition with poor prospects of visual restoration
• Consider giving cycloplegic eye drops (cyclopentolate 1% or atropine 1%) to reduce photophobia and to reduce the formation of pupillary adhesions to the lens

Antibiotic Treatment Duration

2 weeks
Duration is often personalized to the individual based on clinical improvement

Bacterial Keratitis

WATCH

Ofloxacin 0.3% **EYE DROPS**
• 1 drop in the affected eye q1h for 48 hours, then q4h until healed

Drops are preferred over ointments because they have a better corneal penetration

World Health Organization

ADULTS

Periorbital Cellulitis

Bacterial Eye Infection

Definition

Infection of subcutaneous eyelid tissues anterior to the orbital septum (the globe and the tissues within the bony orbit are not involved)

Important: most cases result from adjacent infections (e.g. infection of the eyelid, lacrimal sac, periorbital sinuses, dental infections) or follow bites or trauma of the eyelid

Most Likely Pathogens

Bacteria:
- *Staphylococcus aureus* (including MRSA strains)
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- Anaerobes should be suspected if there is a history of animal or human bite or if necrosis is present

Viruses:
- Consider a virus (e.g. herpes simplex virus or varicella-zoster virus) if there is a vesicular skin rash

Diagnosis

Clinical Presentation

- Usually unilateral signs of inflammation around the affected eye (e.g. red, swollen, warm and tender eyelid) with no restricted or painful eye movement +/- fever
- Vision is normal

Important:
- This is usually a mild condition that is rare adults; complications are rare
- It is important to differentiate with orbital cellulitis (where there is usually restricted eye movements, protrusion of the eye and loss of vision)

Microbiology Tests

- Usually not needed
- Cultures are difficult to obtain and blood cultures when performed are usually negative

Other Laboratory Tests

Usually not needed

Imaging

Consider a CT scan of the orbits and sinuses to assess the presence of orbital involvement and possible complications (e.g. abscess)

Treatment

Clinical Considerations

Most cases can be managed in the outpatient setting with oral antibiotics especially in adults with no signs of severe infection

Antibiotic Treatment Duration

10-14 days (depending on the severity)

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS Amoxicillin+clavulanic acid 500 mg+125 mg q8h **ORAL** OR 1 g + 200 mg q8h **IV**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 500 mg q6h **ORAL** OR 2 g q6h **IV**

Cloxacillin has a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid and cefalexin with limited coverage of Gram-negative bacteria from the upper respiratory tract that may cause periorbital cellulitis. Therefore, when this infection is suspected, amoxicillin+clavulanic acid or cefalexin would be the preferred options

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

Periorbital Cellulitis

Bacterial Eye Infection

Definition

Infection of subcutaneous eyelid tissues anterior to the orbital septum (the globe and the tissues within the bony orbit are not involved)

Important: most cases result from adjacent infections (e.g. infection of the eyelid, lacrimal sac, periorbital sinuses) or follow bites or trauma of the eyelid

Most Likely Pathogens

Bacteria:

- *Staphylococcus aureus* (including MRSA strains)
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- Anaerobes should be suspected if there is a history of animal or human bite or if necrosis is present

Viruses:

- Consider a virus (e.g. herpes simplex virus or varicella-zoster virus) if there is a vesicular skin rash

Diagnosis

Clinical Presentation

- Usually unilateral signs of inflammation around the affected eye (e.g. red, swollen, warm and tender eyelid) with no restricted or painful eye movement +/- fever
- Vision is normal

Important:

- This is usually a mild condition, complications are rare
- It is important to differentiate with **orbital cellulitis** (where there is usually restricted eye movements, protrusion of the eye and loss of vision)

Microbiology Tests

- Usually not needed
- Cultures are difficult to obtain and blood cultures when performed are usually negative

Other Laboratory Tests

Usually not needed

Imaging

Consider a CT scan of the orbits and sinuses to assess the presence of orbital involvement and possible complications (e.g. abscess)

Periorbital Cellulitis

Treatment

Clinical Considerations

Most cases can be managed in the outpatient setting with oral antibiotics especially in children >1 year with no signs of severe infection

Antibiotic Treatment Duration

10-14 days (depending on the severity)

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL/IV**

- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin

Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin **IV**

- Neonates: 25-50 mg/kg/dose q12h
- Children: 25 mg/kg/dose q6h
- **ORAL:** 15 mg/kg/dose q6h
- **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

Cloxacillin has a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid and cefalexin with limited coverage of Gram-negative bacteria from the upper respiratory tract that may cause periorbital cellulitis. Therefore, when this infection is suspected, amoxicillin+clavulanic acid or cefalexin would be the preferred options

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

World Health Organization

ADULTS

Trachoma

Definition

Eye disease caused by specific serovars (A,B and C) of the bacterium *Chlamydia trachomatis* (other serovars cause urogenital diseases, see "Sexually transmitted infections – Chlamydia urogenital infections")

Pathogen

- *Chlamydia trachomatis* is a Gram-negative obligate intracellular bacterium
- Strains associated with trachoma are serovars A, B, Ba, and C

Diagnosis

Clinical Presentation

Acute:
- Usually signs and symptoms of conjunctivitis with redness of the eye, eye discomfort, mucopurulent discharge and light sensitivity
- Less common in adults

Advanced:
- Conjunctival scarring, signs of chronic conjunctival inflammation and eyelashes turned inward
- Mostly seen in adults due to repeated infections over time

WHO has a trachoma grading system used in field assessments to evaluate the extent of disease during examination (Reference: Solomon AW et al. The simplified trachoma grading system, amended. Bull World Health Organ. 2020;98(10):698-705)

Microbiology Tests

- Usually not needed
- Consider testing a conjunctival sample (culture or nucleic acid amplification tests for *Chlamydia trachomatis*) to decide whether to stop or continue antibiotic treatment at the population level

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Treatment

Clinical Considerations

- Antibiotic treatment is often given as part of mass drug administration programmes in endemic areas to reduce the reservoir of *Chlamydia trachomatis*
- If corneal damage has already occurred due to the inversion of the eyelashes, surgery is needed to correct the eyelid rotation and prevent blindness
- Repeated infections over the years can lead to permanent corneal damage and blindness

Important: Reinforce education on personal and community hygiene measures
- Infection spreads via the hands through direct contact with contaminated people or objects
- Flies can contribute by transporting contaminated eye/nose secretions to non-infected people
- Risk factors include living in overcrowded conditions and poor sanitation; most transmission occurs within families

Antibiotic Treatment Duration

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

Antibiotic Treatment

All dosages are for normal renal function

WATCH
Azithromycin 20 mg/kg (max 1 g) **ORAL**
Treatment duration: Single dose

Administered once a year for 3 years as part of mass drug administration programmes

Topical Treatment

WATCH
Azithromycin 1.5% **EYE DROPS**
- 1 drop in both eyes q12h

Treatment duration: 3 days

OR

ACCESS
Tetracycline 1% **EYE OINTMENT**
- 1 cm in both eyes q12h

Treatment duration: 6 weeks

Topical treatment is used in areas where oral azithromycin is not readily available. Topical azithromycin may be as effective as oral azithromycin

World Health Organization

CHILDREN

Trachoma

Definition

Eye disease caused by specific serovars A, B and C) of the bacterium *Chlamydia trachomatis*

Pathogen

• *Chlamydia trachomatis* is a Gram-negative obligate intracellular bacterium

• Strains associated with trachoma are serovars A, B, Ba, and C

Diagnosis

Clinical Presentation

Acute:
• Usually signs and symptoms of conjunctivitis with redness of the eye, eye discomfort, mucopurulent discharge and light sensitivity
• Most common in children living in endemic areas

Advanced:
• Conjunctival scarring, signs of chronic conjunctival inflammation and eyelashes turned inward
• Mostly seen in adults due to repeated infections over time

WHO has a trachoma grading system used in field assessments to evaluate the extent of disease during examination (Reference: Solomon AW et al. The simplified trachoma grading system, amended. Bull World Health Organ. 2020;98(10):698-705)

Microbiology Tests

• Usually not needed

• Consider testing a conjunctival sample (culture or nucleic acid amplification tests for *Chlamydia trachomatis*) to decide whether to stop or continue antibiotic treatment at the population level

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Treatment

Clinical Considerations

• Antibiotic treatment is often given as part of mass administration programmes in endemic areas to reduce the reservoir of *Chlamydia trachomatis*

• If corneal damage has already occurred due to the inversion of the eyelashes, surgery is needed to correct the eyelid rotation and prevent blindness

• Repeated infections over the years can lead to permanent corneal damage and blindness

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• Infection spreads via the hands through direct contact with contaminated people or objects
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• Risk factors include living in overcrowded conditions and poor sanitation; most transmission occurs within families

Antibiotic Treatment Duration

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

Antibiotic Treatment

All dosages are for normal renal function

WATCH
Azithromycin 20 mg/kg (max 1g) **ORAL**
Treatment duration: Single dose

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Topical Treatment

WATCH
Azithromycin 1.5% **EYE DROPS**
• 1 drop in both eyes q12h
Treatment duration: 3 days

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Tetracycline 1% **EYE OINTMENT**
• 1 cm in both eyes q12h
Treatment duration: 6 weeks

Topical treatment is used in areas where oral azithromycin is not readily available. Topical azithromycin may be as effective as oral azithromycin

World Health Organization

ADULTS

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)
- *Haemophilus influenzae* (chronic lung diseases, smoking)
- *Moraxella catarrhalis* (chronic lung diseases, smoking)
- *Staphylococcus aureus* (often associated with influenza)
- *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)
- Respiratory syncytial virus (RSV)
- Metapneumovirus
- Parainfluenza virus
- Coronavirus (including SARS-CoV-2)
- Adenovirus
- Rhinovirus
- Other respiratory viruses

Bacteria to consider in Specific Settings:

- *Burkholderia pseudomallei* (SE Asia, Australia)
- *Mycobacterium tuberculosis*
- *Pneumocystis jirovecii* (people with HIV or other immunosuppression)

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* (and the lipoarabinomannan rapid urinary antigen test in severely immunocompromised HIV patients with signs and symptoms of 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

World Health Organization

ADULTS

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

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

OR

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

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

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

World Health Organization

CHILDREN

Community-Acquired Pneumonia

Definition

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

Most Likely Pathogens

"Typical" Bacteria:

- ***Streptococcus pneumoniae*** (most common cause of CAP beyond the 1st week of life)
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus*
- *Enterobacterales*

"Atypical" Pathogens *(more frequent in children >5 years compared to younger children):*

- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*

Respiratory Viruses:

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

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), dyspnea, tachypnea, reduced oxygen saturation, crepitations, cyanosis, grunting, nasal flaring, pallor
- Pneumonia is diagnosed on: fast breathing for age and/or chest indrawing
  - Check for hypoxia with oxygen saturometer if available
- Children with runny nose and cough and no signs of severity usually do not have pneumonia and should not receive an antibiotic, only home care advice

Microbiology Tests

Mild cases: Usually not needed

Severe cases (to guide antimicrobial treatment): blood cultures

Other Laboratory Tests

No test clearly differentiates viral or bacterial CAP

Consider: full blood count and C-reactive protein

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
- Look for lobar consolidation or pleural effusion
- Radiologic appearance cannot be used to accurately predict pathogen

World Health Organization

CHILDREN

Community-Acquired Pneumonia

Severity Assessment and Considerations

Children with **pneumonia**:

• Should be treated with oral amoxicillin at home with home care advice

• Pneumonia is diagnosed on either:
1. Fast breathing (respiratory rate > 50 breaths/minute in children aged 2-11 months; resp rate > 40 breaths/min in children aged 1-5 years)
2. Chest indrawing

Children with **severe pneumonia** (or a child with pneumonia who cannot tolerate oral antibiotics):

• **Should be admitted to hospital and treated with intravenous antibiotics**

• Severe pneumonia is diagnosed on either:
1. A cough or difficulty in breathing plus one of:
   • Oxygen saturation below 90%
   • Central cyanosis
   • Severe respiratory distress (e.g. grunting or severe chest indrawing)
2. Signs of pneumonia with a general danger sign:
   • Inability to drink or breast feed
   • Persistent vomiting
   • Convulsions
   • Lethargy or unconsciousness
   • Severe respiratory distress

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

Mild to Moderate Cases

All dosages are for normal renal function

ACCESS

Amoxicillin 80-90 mg/kg/day **ORAL**
• **Oral weight bands:**

3-<6 kg	250 mg q12h
6-<10 kg	375 mg q12h
10-<15 kg	500 mg q12h
15-<20 kg	750 mg q12h
≥20 kg	500 mg q8h or 1 g q12h

Treatment

Severe Cases

Please see Severity Assessment and Considerations for diagnosis of severe cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Amoxicillin 50 mg/kg/dose **IV/IM**
• ≤1wk of life: q12h
• >1wk of life: q8h

OR

ACCESS

Ampicillin 50 mg/kg/dose **IV/IM**
• ≤1wk of life: q12h
• >1wk of life: q8h

OR

ACCESS

Benzylpenicillin 30 mg/kg (50 000 IU/kg) q8h **IV**

COMBINED WITH

ACCESS

Gentamicin **IV/IM**
• Neonates: 5 mg/kg/dose q24h
• Children: 7.5 mg/kg/dose q24h

IF HIV POSITIVE AND <1 YR OLD
To treat potential Pneumocystis jirovecii pneumonia, **ADD**

WATCH

Sulfamethoxazole+trimethoprim 40 mg/kg SMX+8 mg/kg TMP q8h **IV/ORAL** for 3 weeks

Second Choice
If NO Clinical Response to First Choice after 48-72 hours

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV/IM**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV/IM**

World Health Organization

ADULTS

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

Most Likely Pathogens

Respiratory viruses (most cases):

- Influenza virus (A and B)
- Respiratory syncytial virus
- Parainfluenza virus
- Rhinovirus
- Coronavirus (including SARS-CoV-2)
- Other respiratory viruses

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)

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

Exacerbation of Chronic Obstructive Pulmonary Disease

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

Antibiotic Treatment Duration

5 days

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

All dosages are for normal renal function

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

World Health Organization

ADULTS

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.
  - *Campylobacter* spp.
  - Diarrhoeal non-typhoidal *Salmonella*
  - 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*
  - Other protozoal parasites and very rarely *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 degrees of dehydration and can present with severe malnutrition (both a risk factor and a consequence of diarrhoea)

Important:
- Rapidly evaluate the degree 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
- Immunocompromised 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 and electrolyte replacement is the main treatment for acute infectious diarrhoea
- Low-osmolarity oral rehydration solution (ORS) is recommended
- 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:
- *Patients hospitalized with severe dehydration OR*
- *Regardless of degree of dehydration:*
  - *High purging or failure of first 4 hour course of rehydration therapy OR*
  - *Coexisting conditions (e.g. pregnancy) OR*
  - *Co-morbidities (e.g. severe acute malnutrition, HIV)*

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 acute bloody diarrhoea
  - Severely immunocompromised patients
- 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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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
In patients taking sulfamethoxazole-trimethoprim for prophylaxis, treat with a different antibiotic unless susceptibility is confirmed

OR

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

World Health Organization

CHILDREN

Acute Infectious Diarrhoea & Gastroenteritis

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
- Immunosuppression
- Severe malnutrition

Watery diarrhoea:
- Most likely cause is viral, mostly:
  - Rotavirus
  - Norovirus
  - Adenovirus
- Consider cholera in endemic settings or in the context of outbreaks

Bloody diarrhoea (dysentery):
- Most likely cause are bacteria, mostly:
  - *Shigella* spp.
  - *Campylobacter* spp.
  - Intestinal/non-invasive/diarrhoeal non-typhoidal *Salmonella*
  - 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*
  - Other protozoal parasites and very rarely *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
- Exclusive breastfeeding for the first 6 months of life
- Vaccination against rotavirus and against cholera (in endemic areas and during outbreaks)

This guidance excludes enteric fever (see separate chapter)

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 degrees of dehydration and can present with severe malnutrition (both a risk factor and a consequence of diarrhoea)

Important:
- Rapidly evaluate the degree of dehydration
- 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
- Immunocompromised patients (to exclude parasitic infections)
- Suspected cholera outbreak

Tests to consider:
- Stool culture
- Stool microscopy (for parasites)

Other Laboratory Tests

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

Imaging

Usually not needed

World Health Organization

CHILDREN

Acute Infectious Diarrhoea & Gastroenteritis

Rx Treatment

No Antibiotic Care

Important: Rehydration and electrolyte replacement is the main treatment for acute infectious diarrhoea

- Low-osmolarity oral rehydration solution (ORS) is recommended
- 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

Rx Cholera Antibiotic Treatment

Treat with antibiotics only in:

- *Patients hospitalized with severe dehydration OR*
- *Regardless of degree of dehydration:*
  - *High purging or failure of first 4 hour course of rehydration therapy OR*
  - *Co-morbidities (e.g. severe acute malnutrition, HIV)*

All dosages are for normal renal function

First Choice

WATCH

Azithromycin 20 mg/kg **ORAL**
Treatment duration: single dose

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

Second Choice

WATCH

Ciprofloxacin 15 mg/kg **ORAL**
Treatment duration: single dose

OR

ACCESS

Doxycycline **ORAL**
- <45 kg (<12 yrs): 2-4 mg/kg
- >45 kg (>12 yrs): 300 mg

Treatment duration: single dose

Clinical Considerations

- **Antibiotics usually not needed**, including in cases with fever and/or severe dehydration
- Consider antibiotic treatment ONLY if:
  - Significant bloody diarrhoea
  - Severely immunocompromised patients
- If symptoms do not resolve within 48 hours of treatment, consider giving metronidazole for treatment of *Entamoeba histolytica* and *Giardia intestinalis*

Rx Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **ORAL**
- **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

Treatment duration: 3 days

Second Choice

WATCH

Azithromycin 10 mg/kg/dose q24h **ORAL**
Treatment duration: 4 days

For children with bloody diarrhoea/dysentery ONLY azithromycin is preferred if suspected ciprofloxacin resistance

OR

WATCH

Cefixime 10 mg/kg/dose q24h **ORAL**
Treatment duration: 5 days

OR

ACCESS

Sulfamethoxazole+trimethoprim 20 mg/kg + 4 mg/kg q12h **ORAL**
- **Oral weight bands:**

3-<6 kg	100 mg+20 mg q12h
6-<10 kg	200 mg+40 mg q12h
10-<30 kg	400 mg+80 mg q12h
≥30 kg	800 mg+160 mg q12h

Treatment duration: 5 days

Use only if local data suggest susceptibility

In patients taking sulfamethoxazole-trimethoprim for prophylaxis, treat with a different antibiotic unless susceptibility is confirmed

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV/IM**
Treatment duration: 3 days

World Health Organization

ADULTS

Enteric Fever

Definition

• A severe systemic illness characterized by fever and abdominal pain caused by infection with *Salmonella enterica*
• Acquired through ingestion of contaminated food/water

Severity:
• *Mild*: Not critically ill with no signs of intestinal perforation, peritonitis, sepsis or septic shock
• *Severe*: Critically ill with confirmed/suspected intestinal perforation, peritonitis, sepsis or septic shock

Pathogen

Enteric fever is caused by *Salmonella enterica* serotypes Typhi or Paratyphi A, B or C

Diagnosis

Clinical Presentation

• **It can be difficult to distinguish enteric fever from other febrile illnesses**
• Symptoms include protracted fever (≥38.0°C for >3 days) +/- headache, loss of appetite and nausea; gastrointestinal symptoms may also be present (diarrhoea more frequent in people living with HIV)
• Consider peritonitis if there is severe pain, diffuse rebound tenderness upon sudden release of pressure on the abdomen and abdominal muscular tensing; peritonitis occurs as a result of intestinal bleeding and perforation
• Encephalopathy can also occur in severe cases

Microbiology Tests

• *Mild Cases*: Usually not needed
• *Severe Cases*: Blood cultures (ideally before starting antibiotics)
• Bone marrow culture is the reference standard test but is often not feasible
• *Note: the Widal serology is not a reliable method to diagnose acute illness (a positive result may be due to previous infection)*

Other Laboratory Tests

• *Mild Cases*: Usually not needed
• *Severe Cases*: Complete blood count, creatinine, electrolytes, glucose, C-reactive protein and / or procalcitonin

Imaging

Usually not needed

Prevention

Access to safe water and adequate sanitation, health education, appropriate hygiene among food handlers, and typhoid vaccination

Treatment

Clinical Considerations

• Antibiotic treatment should be started as soon as the diagnosis is suspected; delays are associated with higher risk of complications and severe disease
• **Empiric treatment should be chosen based on:**
  • Severity of presentation
  • Local prevalence of fluoroquinolone resistance among *Salmonella enterica* serotypes Typhi or Paratyphi
• Fever usually decreases slowly after 3-5 days of treatment
• If initially treated IV, step down from IV to oral antibiotics is suggested when the patient has clinically improved, is afebrile and is able to tolerate oral treatment

Antibiotic Treatment Duration

Mild Cases: **7 days***
Severe Cases: **10 days***
**if clinical improvement and the patient is afebrile for 48 hours*

Low Risk of Fluoroquinolone Resistance

All dosages are for normal renal function

Mild and Severe Cases

WATCH Ciprofloxacin 500 mg q12h **ORAL**

High Risk of Fluoroquinolone Resistance

All dosages are for normal renal function

Mild Cases

WATCH Azithromycin 1 g once on day 1, then 500 mg q24h **ORAL**

Severe Cases

WATCH Ceftriaxone 2 g q24h **IV**

World Health Organization

CHILDREN

Enteric Fever

Definition

• A severe systemic illness characterized by fever and abdominal pain caused by infection with *Salmonella enterica*
• Acquired through ingestion of contaminated food/water

Severity:
• *Mild*: Not critically ill with no signs of intestinal perforation, peritonitis, sepsis or septic shock
• *Severe*: Critically ill with confirmed/suspected intestinal perforation, peritonitis, sepsis or septic shock

Pathogen

Enteric fever is caused by *Salmonella enterica* serotypes Typhi or Paratyphi A, B or C

Diagnosis

Clinical Presentation

• **It can be difficult to distinguish enteric fever from other febrile illnesses**
• Symptoms include prolonged fever (≥38.0°C for >3 days) +/- headache, loss of appetite and nausea; gastrointestinal symptoms may also be present
• Diarrhoea is common
• Consider peritonitis if there is severe pain, diffuse rebound tenderness upon sudden release of pressure on the abdomen and abdominal guarding; peritonitis occurs as a result of intestinal bleeding and perforation
• Encephalopathy can also occur in severe cases

Microbiology Tests

• *Mild Cases*: Usually not needed
• *Severe Cases*: Blood cultures (ideally before starting antibiotics); Stool culture
• Note: the Widal serology is not a reliable method to diagnose acute illness (a positive result may be due to previous infection)

Other Laboratory Tests

• *Mild Cases*: Usually not needed
• *Severe Cases*: Complete blood count, creatinine, electrolytes, glucose, C-reactive protein

Imaging

Routine imaging is not needed

Prevention

Access to safe water and adequate sanitation, health education, appropriate hygiene among food handlers, and typhoid vaccination

Treatment

Clinical Considerations

• Antibiotic treatment should be started as soon as the diagnosis is suspected; delays are associated with higher risk of complications and severe disease
• **Empiric treatment should be chosen based on:**
  • Severity of presentation
  • Local prevalence of fluoroquinolone resistance among *Salmonella enterica* serotypes Typhi or Paratyphi
• Fever usually decreases slowly after 3-5 days of treatment
• If initially treated IV, step down from IV to oral antibiotics is suggested when the patient has clinically improved, is afebrile and is able to tolerate oral treatment

Antibiotic Treatment Duration

Mild Cases: **7 days***
Severe Cases: **10 days***
**if clinical improvement and the patient is afebrile for 48 hours*

Low Risk of Fluoroquinolone Resistance

All dosages are for normal renal function

Mild and Severe Cases

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **ORAL**
• **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

High Risk of Fluoroquinolone Resistance

All dosages are for normal renal function

Mild Cases

WATCH Azithromycin 20 mg/kg/dose q24h **ORAL**

Severe Cases

WATCH Ceftriaxone 80 mg/kg/dose q24h **IV**

World Health Organization

ADULTS

Impetigo / Erysipelas / Cellulitis

Skin and Soft Tissue Infection

Definition

Superficial bacterial skin infections, not affecting the deeper tissue layers

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

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
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 500 mg q6h **ORAL**

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

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

Most Likely Pathogens

Bacteria (most cases):

• *Streptococcus pyogenes* (group A *Streptococcus*) - especially in case of erysipelas

• *Staphylococcus aureus* (including MRSA)

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 area: 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 deep abscess or subdermal involvement suspected

Impetigo / Erysipelas / Cellulitis

Treatment

Clinical Considerations

- **Empiric antibiotic options** need to have good activity against both 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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**

- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin 15 mg/kg/dose q6h **ORAL**

- **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

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**

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

**Including multidrug-resistant strains*

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)

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 500 mg q6h **ORAL**

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

World Health Organization

CHILDREN

Burn Wound-Related Infections

This guidance excludes severe 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

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.)

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

Imaging

Routine imaging not necessary

Burn Wound-Related 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)

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**

- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin 15 mg/kg/dose q6h **ORAL**

- **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. From an antibiotic stewardship perspective, these would be the preferred options whenever possible

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

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. severely immunocompromised patients) and/or high-risk clinical areas (face, hands, near joints)

• Duration: 3 days

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 500 mg q6h **ORAL**

Amoxicillin+clavulanic acid is the preferred treatment option for bite wound infections because of its activity against anaerobic bacteria. Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in other cases of mild skin and soft tissue infections. Therefore, from an antibiotic stewardship perspective, these would be the preferred options whenever possible (except for bite wounds)

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

World Health Organization

CHILDREN

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. severely immunocompromised patients) and/or high-risk clinical areas (face, hands, near joints)

• Duration: 3 days

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**

• **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin

Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

• **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin 15 mg/kg/dose q6h **ORAL**

• **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

Amoxicillin+clavulanic acid is the preferred treatment option for bite wound infections because of its activity against anaerobic bacteria. Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in other cases of mild skin and soft tissue infections. Therefore, from an antibiotic stewardship perspective, these would be the preferred options whenever possible (except for bite wounds)

If cloxacillin is unavailable, dicloxacillin or flucloxacillin could be used

World Health Organization

ADULTS

Chlamydial Urogenital Infection

Sexually Transmitted Infection

In general this guidance applies to adults and young people aged over 12 years. In children, specialist advice should be sought where possible. Consideration should be given that an STI in a child may be due to child sexual abuse

For Chlamydial Ocular Infections (Trachoma) see separate infographic

Definition

A sexually transmitted infection (STI) caused by certain strains of the bacterium *Chlamydia trachomatis*

Pathogen

Chlamydia trachomatis is an intracellular Gram-negative bacterium; strains associated with urogenital infection are mostly genital tract biovars (serovars D to K) and rarely lymphogranuloma venereum biovar (serovars L1, L2, L3)

Prevention

Important elements of prevention include:
- Sexuality education
- Promoting consistent use of condoms
- Pre- and post-test counselling
- Safe sex and risk reduction counselling
- Interventions targeting high-risk groups

Important:
- Sexual partners should be informed of the disease and treated
- Reporting of this infection to health authorities is encouraged according to local regulations

Diagnosis

Clinical Presentation

- Most persons remain asymptomatic though they can still transmit the infection
- If symptoms occur they overlap with those of gonococcal infection (co-infection possible and common)

Most common symptoms:
- *In Men:* Acute urethritis with “clear” urethral discharge and dysuria
- *In Women:* Vaginal discharge, dyspareunia (painful intercourse), and dysuria
- *Additionally in both sexes:*
  - Symptoms of acute proctitis with pain, pruritus, anal discharge and bleeding
- Symptoms of lymphogranuloma venereum (men>women):
  - Ulcerative lesion or a papule usually on the genitalia or rectum and inguinal or femoral lymphadenopathy (usually unilateral)
  - Often the lesion remains unnoticed in women or when located in the rectum

Imaging

Usually not needed

Other Laboratory Tests

Usually not needed

Microbiology Tests

- See WHO guidance “Laboratory diagnosis of sexually transmitted infections” https://apps.who.int/iris/handle/10665/85343
- **Important:** all patients with suspected chlamydial urogenital infection should also be tested for gonococcal infection (as symptoms overlap) and other STIs (e.g. HIV, syphilis)

Reference standard:
- Nucleic acid amplification test (a test for both *Chlamydia* and *Neisseria gonorrhoeae* is available)
  - Samples that can be used: urine (lower sensitivity and specificity in women), urethral, vulvovaginal, endocervical or anorectal samples collected with a swab
  - Perform *Chlamydia* genovar testing for lymphogranuloma venereum in anorectal samples of men who have sex with men

Other tests to consider:
- Microscopy (Gram stain)
  - In a symptomatic patient, it can be used to exclude *Neisseria gonorrhoeae* (therefore suggesting non-gonococcal urethritis)
  - Leukocytes are usually present but not a specific finding for chlamydial infection
- Culture: if symptoms persist despite adequate treatment (but it is rarely performed)
- *Note: urines are not good specimens for microscopy and culture*

Chlamydial Urogenital Infection

Treatment

Clinical Considerations

Treatment is aligned with the WHO 2016 guidelines for chlamydial urogenital infections (https://apps.who.int/iris/handle/10665/246165) and the WHO 2021 guidelines for the management of symptomatic sexually transmitted infections (https://apps.who.int/iris/handle/10665/342523) but only options listed in the 2021 EML are reported below

Treatment is always indicated when infection is diagnosed, including in asymptomatic persons because they can transmit the infection to others

Antibiotic Treatment Duration

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

Lymphogranuloma Venereum

All dosages are for normal renal function

ACCESS
Doxycycline 100 mg q12h **ORAL**
Treatment duration: 21 days

Anorectal Infection

All dosages are for normal renal function

ACCESS
Doxycycline 100 mg q12h **ORAL**
Treatment duration: 7 days

Infection in Pregnant Women

All dosages are for normal renal function

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

Uncomplicated Urogenital Infection

All dosages are for normal renal function

ACCESS
Doxycycline 100 mg q12h **ORAL**
Treatment duration: 7 days

OR

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

Recent data suggest that doxycycline is more effective, therefore it could be given priority if adherence is not a concern (except in pregnant women where it is contraindicated)

World Health Organization

ADULTS

Gonococcal Infection

In general this guidance applies to adults and young people aged over 12 years. In children, specialist advice should be sought where possible. Consideration should be given that an STI in a child may be due to child sexual abuse

Definition

A sexually transmitted infection (STI) caused by the bacterium *Neisseria gonorrhoeae*

Pathogen

• *Neisseria gonorrhoeae* is a Gram-negative bacterium that can easily develop resistance to antibiotics leading to infections that are difficult to treat, which is an increasing public health problem worldwide

• Data on *Neisseria gonorrhoeae* resistance is available through GLASS (The WHO Global Antimicrobial Resistance Surveillance System) and GASP (The WHO Gonococcal AMR surveillance program) https://www.who.int/data/gho/data/themes/topics/who-gonococcal-amr-surveillance-programme-who-gasp

Diagnosis

Clinical Presentation

• Some persons remain asymptomatic (women>men) though they can still transmit the infection

• If symptoms occur they overlap with those of chlamydial infection (co-infection possible and common)

Most common symptoms (usually occur a few days after infection):

• *In Men:* Acute urethritis with profuse mucopurulent urethral discharge and dysuria +/- testicular discomfort

• *In Women:* Mucopurulent vaginal discharge and dysuria +/- vaginitis with vaginal pain and inflammation and lower abdominal pain, cervical discharge, cervical ectopy and friability and easy bleeding on contact may also occur

• *Additionally in both sexes:*
  • Symptoms of acute proctitis with pain, pruritus, anal discharge and bleeding
  • Pharyngitis and conjunctivitis are other possible presentations
  • Rarely infection can disseminate, typically leading to localized infection in one or more joints

• *In pregnant women:*
  • Infection can transmit to the child during vaginal delivery

• *In newborns:*
  • Acute ocular infection and pharyngitis can occur a few days after birth
  • Disseminated infection with septic arthritis (usually in multiple joints) may also occur

Microbiology Tests

• See WHO guidance “Laboratory diagnosis of sexually transmitted infections” https://apps.who.int/iris/handle/10665/85343

• **Important:** all patients with suspected gonococcal infection should also be tested for chlamydial urogenital infection (as symptoms overlap) and other STIs (e.g. HIV, syphilis)

Reference standard:
• Nucleic acid amplification test (a test for both *N. gonorrhoeae* and *Chlamydia* is available)
  • Samples that can be used: urine (lower sensitivity and specificity in women), urethral, vulvovaginal, endocervical or anorectal samples collected with a swab

Other tests to consider:
• Culture + antimicrobial susceptibility testing: If symptoms persist despite adequate treatment and for surveillance of *Neisseria gonorrhoeae* resistance
• Microscopy (Gram stain)
  • Samples that can be used: urethral, endocervical, conjunctival samples collected with a swab
• Blood cultures: If disseminated infection is suspected

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

World Health Organization

ADULTS

Gonococcal Infection

Prevention

Important elements of prevention include:
- Sexuality education
- Promoting consistent use of condoms
- Pre- and post-test counselling
- Safe sex and risk reduction counselling
- Interventions targeting high-risk groups

Important:
- Sexual partners should be informed of the disease and treated
- Reporting of this infection to health authorities is encouraged according to local regulations

Rx Treatment (Section 1 of 2)

Treatment Recommendations

- Treatment is aligned with the WHO 2016 guidelines for the treatment of gonococcal infection (https://apps.who.int/iris/handle/10665/246114) and the WHO 2021 guidelines for the management of symptomatic sexually transmitted infections (https://apps.who.int/iris/handle/10665/34252) but only options listed in the 2021 EML are reported below
- WHO is in the process of revising current treatment recommendations and dosages, please check the WHO website regularly for possible updates

Clinical Considerations

- Treatment is always indicated when infection is diagnosed, including in asymptomatic patients because they can transmit the infection to others
- Local resistance data should determine the most appropriate therapy and if data not available, dual therapy is preferred
- If symptoms do not resolve in approximately 5 days, resistant infection or alternative diagnosis should be suspected

Antibiotic Treatment Duration

Single Dose

Rx Oropharyngeal Infections

All dosages are for normal renal function

Dual Therapy

First Choice

WATCH Ceftriaxone 250 mg **IM**

COMBINED WITH

WATCH Azithromycin 1 g **ORAL**

Second Choice

WATCH Cefixime 400 mg **ORAL**

COMBINED WITH

WATCH Azithromycin 1 g **ORAL**

Single Therapy

Only use single therapy if local resistance data confirm susceptibility to the antibiotic

WATCH Ceftriaxone 250 mg **IM**

A single dose of 500 mg or 1 g ceftriaxone IM is recommended in some international guidelines

Gonococcal Infection

Treatment (Section 2 of 2)

Antibiotic Treatment Duration

Single Dose

Retreatment after Treatment Failure

Consider treatment failure if symptoms persist after 5 days of adequate treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

WATCH Cefixime 800 mg **ORAL**

OR

WATCH Ceftriaxone 500 mg **IM**

OR

ACCESS Gentamicin 240 mg **IM**

OR

ACCESS Spectinomycin 2 g **IM**

Do not use for spectinomycin for oropharyngeal infections

COMBINED WITH

WATCH Azithromycin 2 g **ORAL**

Genital and Anorectal Infections

All dosages are for normal renal function

Dual Therapy

First Choice

WATCH Ceftriaxone 250 mg **IM**

COMBINED WITH

WATCH Azithromycin 1 g **ORAL**

Second Choice

WATCH Cefixime 400 mg **ORAL**

COMBINED WITH

WATCH Azithromycin 1 g **ORAL**

Single Therapy

Only use single therapy if local resistance data confirm susceptibility to the antibiotic

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

WATCH Cefixime 400 mg **ORAL**

OR

WATCH Ceftriaxone 250 mg **IM**

A single dose of 500 mg or 1 g ceftriaxone IM is recommended in some international guidelines

OR

ACCESS Spectinomycin 2 g **IM**

World Health Organization

ADULTS

Syphilis

Sexually Transmitted Infection

In general this guidance applies to adults and young people aged over 12 years. In children, specialist advice should be sought where possible. Consideration should be given that an STI in a child may be due to child sexual abuse

Definition

- A sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum* subspecies *pallidum*
- The infection can be transmitted from the mother to her fetus because the pathogen can cross the placenta

Classification based on:

- Timing since acquisition
  - *Early:* ≤2 years (includes primary and secondary infections and the early latent phase)
  - *Late:* >2 years (includes the late latent phase and tertiary infections)
- Clinical presentation (see below)

Pathogen

Treponema pallidum subspecies *pallidum* is a bacterium of the phylum Spirochaetes

- Slow growing, difficult to culture *in vitro*, thin

Diagnosis

Clinical Presentation

Early syphilis:

- *Primary infection:* Often asymptomatic, localized non painful ulcerative lesion with indurated margins (usually on genitalia, mouth or rectum) +/- local lymphadenopathy
- *Secondary infection:*
  - Skin and mucosal manifestations over trunk and extremities including palms of hands and soles of feet
  - Rash is commonly maculopapular and non-irritant
  - Mucous membranes of mouth/perineum can show lesions
  - Fever (≥ 38.0°C), generalized lymphadenopathy and malaise usually present
  - Meningitis, hepatitis and ocular involvement can occur

Late syphilis:

- *Tertiary infection:* Can affect different organ systems
  - Cardiovascular system: usually aortitis
  - Skin/soft tissues/bones: nodular lesions (gummas)
  - Central nervous system: often progressive dementia, psychiatric symptoms, problems with coordination of movements

Other Laboratory Tests

Primary syphilis: Usually not needed

Secondary or tertiary syphilis: May be required depending on the clinical presentation

Microbiology Tests

- See WHO guidance “Laboratory diagnosis of sexually transmitted infections” https://apps.who.int/iris/handle/10665/85343
- **Important:** all patients with suspected syphilis should also be tested for other STIs (e.g. HIV, gonococcal infection)

Direct detection methods:

- Can detect the pathogen in specimens from skin or tissue lesions

Serological tests:

- All tests are negative initially in primary infection
- *Treponemal tests:* detect antibodies to treponemal antigens; they usually remain positive after infection even with successful treatment
  - Type of tests: **FTA-ABS, TPPA, TPHA**
- *Nontreponemal tests:* detect antibodies that react to lipids released in response to cellular damage caused by infection; usually become negative with successful treatment
  - Type of tests: **VDRL, RPR**
- **Both treponemal and non-treponemal tests need to be positive to confirm the diagnosis**
- To increase access and same-day treatment, a rapid treponemal test followed (if positive) by a non-treponemal test is recommended; but starting with a non-treponemal test and confirming positive results with a treponemal test is also appropriate

Imaging

Usually not needed unless a complication of late syphilis is suspected

World Health Organization

ADULTS

Syphilis

Prevention

Important elements of prevention include:
- Sexuality education
- Promoting consistent use of condoms
- Pre- and post-test counselling
- Safe sex and risk reduction counselling
- Interventions targeting high risk groups
- Access of pregnant women to early and adequate prenatal care to prevent congenital syphilis

Important:
- Sexual partners should be informed of the disease and treated
- Reporting of this infection to health authorities is encouraged according to local regulations

Treatment

Clinical Considerations

Treatment is aligned with the WHO 2016 guidelines for the treatment of *Treponema pallidum* (https://apps.who.int/iris/handle/10665/249572) and the WHO 2021 guidelines for the management of symptomatic sexually transmitted infections (https://apps.who.int/iris/handle/10665/342523) but only options listed in the 2021 EML are reported below

- Treatment is always indicated when infection is diagnosed, including in asymptomatic patients because they can transmit the infection to others
- In early syphilis (primary/secondary), partners should also be treated if exposed within 90 days
- Assess serological response by repeating non-treponemal test to detect a reduction in titer; a 4-fold reduction in titers confirms adequate response (repeat 3, 6 and 12 months after the end of treatment)

Antibiotic Treatment Duration

Since treatment duration varies according to the antibiotic used and the stage of the infection, please refer to the corresponding antibiotic section for treatment duration

Neurosyphilis

All dosages are for normal renal function

ACCESS Benzylpenicillin 2-4 million IU (1.2-2.4 g) q4h **IV**
Treatment duration: 14 days

OR

ACCESS Procaine benzylpenicillin 1.2 million IU (1.2 g) q24h **IM**
Treatment duration: 14 days

COMBINED WITH

Probenecid 500 mg q6h **ORAL**
Treatment duration: 14 days

Early Syphilis

All dosages are for normal renal function

First Choice

ACCESS Benzathine benzylpenicillin 2.4 million IU (1.8 g) **IM**
Treatment duration: single dose

Second Choice

ACCESS Procaine benzylpenicillin 1.2 million IU (1.2 g) q24h **IM**
Treatment duration: 10-14 days

Syphilis in Pregnancy

All dosages are for normal renal function

ACCESS Benzathine benzylpenicillin 2.4 million IU (1.8 g) **IM**
Treatment duration:
- Early Syphilis: Single dose
- Late or Unknown Stage Syphilis: One dose per week for 3 consecutive weeks (total of 3 administrations, the interval between doses should not exceed 14 days)

Late or Unknown Stage Syphilis

All dosages are for normal renal function

First Choice

ACCESS Benzathine benzylpenicillin 2.4 million IU (1.8 g) **IM**
Treatment duration: One dose per week for 3 consecutive weeks (total of 3 administrations, the interval between doses should not exceed 14 days)

Second Choice

ACCESS Procaine benzylpenicillin 1.2 million IU (1.2 g) q24h **IM**
Treatment duration: 20 days

World Health Organization

ADULTS

Trichomoniasis

Sexually Transmitted Infection

In general this guidance applies to adults and young people aged over 12 years. In children, specialist advice should be sought where possible. Consideration should be given that an STI in a child may be due to child sexual abuse

Definition

A sexually transmitted infection (STI) caused by *Trichomonas vaginalis*

Diagnosis

Clinical Presentation

• Most persons have mild symptoms or remain asymptomatic (especially men) though they can still transmit the infection

Symptomatic infection:
• *In women*: acute onset of vaginal inflammation and discharge (frothy and with a bad smell), dysuria and pelvic pain
• *In men*: urethral discharge, dysuria and testicular discomfort or pain; rarely epididymitis and prostatitis can be present

Microbiology Tests

• See WHO guidance "Laboratory diagnosis of sexually transmitted infections" https://apps.who.int/iris/handle/10665/85343

• **Important**: all patients with suspected trichomoniasis should also be tested for other STIs (e.g. HIV, syphilis, gonococcal infection)

Tests to consider:
• Wet mount microscopy (easy and inexpensive but should be read within 10 minutes of sample collection)
• Nucleic acid amplification tests for *T. vaginalis* (very good sensitivity; preferred if available)
• Culture (good sensitivity but requires long incubation)
• Samples that can be used: Urethral, endocervical, and vaginal swabs

Other Laboratory Tests

Usually not needed

Imaging

Usually not needed

Pathogen

Trichomonas vaginalis is an anaerobe flagellated protozoan

Prevention

Important elements of prevention include:
• Sexuality education
• Promoting consistent use of condoms
• Pre- and post-test counselling
• Safe sex and risk reduction counselling
• Interventions targeting high-risk groups

Important:
• Sexual partners should be informed of the disease and treated
• Reporting of this infection to health authorities is encouraged according to local regulations

Treatment

Clinical Considerations

Treatment is aligned with the WHO 2021 guidelines for the management of symptomatic sexually transmitted infections (https://apps.who.int/iris/handle/10665/342523)

Treatment is always indicated when infection is diagnosed, including in asymptomatic persons because they can transmit the infection to others

Antibiotic Treatment Duration

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

• Evidence supports better cure rates with 7-day course (consider if treatment adherence is not an issue)

Antibiotic Treatment

All dosages are for normal renal function

ACCESS
Metronidazole 2 g **ORAL**
Treatment duration: single dose

OR

ACCESS
Metronidazole 400 or 500 mg q12h **ORAL**
Treatment duration: 7 days

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 immunocompromised 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

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

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

Imaging

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

World Health Organization

ADULTS

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

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

Active against some ESBL-producing isolates

OR

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

Lower Urinary Tract Infection

Definition

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

• Urinary tract infections (UTI) in children with mechanical anomalies of the urinary tract (e.g. vesicoureteral reflux or other congenital anomalies) or who are immunocompromised 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:**
  - *Streptococcus agalactiae* (group B *Streptococcus*)
  - *Enterococcus* spp.
  - *Pseudomona aeruginosa* or *Acinetobacter baumannii* (including multidrug-resistant strains such those producing ESBL especially in patients with recent antibiotic exposure)

Diagnosis

Clinical Presentation

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

• Generally no systemic signs/symptoms (e.g. fever)

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

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 (always in children) 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 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/leukocyte 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 ~2 days

Amoxicillin+clavulanic acid still has activity against some ESBL-producing isolates and can be considered an acceptable option, particularly in young children

Antibiotic Treatment Duration

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

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**

- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Treatment duration: 3-5 days

Amox = amoxicillin
Active against some ESBL-producing isolates
Must refrigerate oral liquid after reconstitution

OR

ACCESS

Nitrofurantoin 2 mg/kg/dose q12h OR 1 mg/kg/dose q6h (immediate-release formulation) **ORAL**

Treatment duration: 5 days

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

OR

ACCESS

Sulfamethoxazole+trimethoprim 20 mg/kg + 4 mg/kg q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	100 mg+20 mg q12h
6-<10 kg	200 mg+40 mg q12h
10-<30 kg	400 mg+80 mg q12h
≥30 kg	800 mg+160 mg q12h

Treatment duration: 3 days

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

OR

ACCESS

Trimethoprim 4 mg/kg q12h **ORAL**

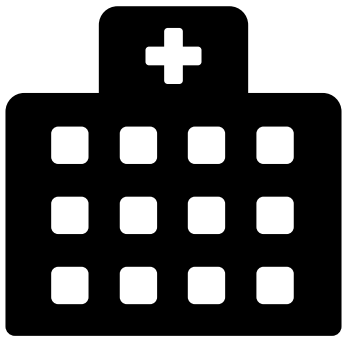
- **Oral weight bands:**

3-<6 kg	20 mg q12h
6-<10 kg	40 mg q12h
10-<30 kg	80 mg q12h
≥30 kg	200 mg q12h

Treatment duration: 3 days

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

World Health Organization



Hospital Facility

World Health Organization

ADULTS

Sepsis & Septic Shock

Definition

Sepsis (Sepsis 3):
• A life-threatening organ dysfunction caused by a dysregulated host response to infection

Septic Shock:
• A type of sepsis in which underlying circulatory and cellular and/or metabolic abnormalities substantially increase short-term mortality
• Patients have persistent hypotension and require vasopressors to maintain a mean arterial pressure ≥65 mmHg (8.7 kPa) and present with a level of serum lactate >2 mmol/L (>18 mg/dL) in the absence of hypovolemia

Important: bacteraemia is not part of the definition of sepsis, while many patients with sepsis have bacteraemia, most patients with bacteraemia do not fulfill sepsis criteria

Most Likely Pathogens

• Sepsis can originate from any type of infection in any organ system. Bacteria, viruses, fungi and protozoa can all cause sepsis (but only sepsis of bacterial origin is addressed here)
• Consider pathogens other than bacteria based on local epidemiology (e.g. malaria, viral haemorrhagic fevers, influenza, COVID-19)

Community Setting (in alphabetical order):
• Enterobacterales (*Escherichia coli, Klebsiella pneumoniae* and others)
• Invasive non-typhoidal *Salmonella* (elderly patients and patients with HIV)
• *Salmonella* Typhi and Paratyphi (causing enteric fever)
• *Staphylococcus aureus* (including MRSA)
• *S. pyogenes* (group A *Streptococcus*)
• *S. pneumoniae* (including penicillin non-susceptible strains)

Others to consider:
• *Burkholderia pseudomallei* (pathogen causing melioidosis, endemic in South-East Asia and Australia)
• *Neisseria meningitidis*

Hospital Setting (in alphabetical order):
• *Acinetobacter baumannii**
• Enterobacterales* (*Escherichia coli*, *Klebsiella pneumoniae* and others)
• *Pseudomonas aeuroginosa**
• *Staphylococcus aureus* (including MRSA)

**Including multidrug-resistant strains such as those producing ESBL and carbapenemases*

Maternal Sepsis:
• Consider *Listeria monocytogenes* and *Streptococcus agalactiae*, however UTIs represent main source of infection

Diagnosis

Clinical Presentation

• Early recognition of the source of infection and treatment is fundamental and impacts mortality
• Symptoms are highly variable and mostly non-specific
• Patients often present with fever (>38.0°C) or hypothermia (<36.0°C); tachycardia, respiratory distress, acute altered mental status and hypotension. Reduced urine output may be present

Important:
• Accurate identification of patients with sepsis is difficult and no single reference standard test exists
• Adoption and use of the internationally accepted definitions is critical to avoid overdiagnosis and overtreatment
• While it is important to rapidly treat patients with sepsis and septic shock with antibiotics it should be kept in mind that only a very small proportion of patients with an infection have sepsis

Microbiology Tests

• Guided by the suspected primary site of infection but should always include blood cultures (ideally two sets)
• Tests should ideally be performed before initiating antibiotics

Other Laboratory Tests

To Identify a Bacterial Infection:
• White blood count, CRP and/or procalcitonin
• In initial patient assessment, inflammatory markers in the normal range do not rule out sepsis if high pre-test probability

To Identify Organ Dysfunction:
• **Bilirubin, blood pH and gases**, blood urea nitrogen (required for CURB-65 score calculation if suspected pneumonia), complete blood count with **platelets**, **creatinine**, electrolytes, glucose, whole blood lactate
• *Tests in bold are required for SOFA score calculation*

Imaging

Guided by the suspected primary site of infection

Prevention

• Preventing infections includes vaccinations, adequate nutrition, and access to safe water and sanitation
• Preventing evolution of infection to sepsis relies on timely diagnosis and adequate treatment of the underlying infection

Sepsis & Septic Shock

Organ Dysfunction Assessment Scores

Sequential Organ Failure Assessment (SOFA)

	Score				
Parameter	**0**	**1**	**2**	**3**	**4**
PaO_2 mmHg (kPa) / FiO_2(%)	≥ 400 (53.3)	< 400 (53.3)	< 300 (40)	< 200 (26.7)	< 100 (13.3)
MAP mmHg (kPa) and catecholamine doses needed (µg/kg/min for ≥ 1h)	MAP ≥ 70 (9.3)	MAP < 70 (9.3)	Dopamine < 5 OR dobutamine any dose	Dopamine 5.1–15 OR epinephrine (adrenaline)/ norepinephrine ≤ 0.1	Dopamine > 15 OR epinephrine/ norepinephrine > 0.1
Platelets (x 10^3/µL, x 10^9/L)	≥ 150	< 150	< 100	< 50	< 20
Bilirubin mg/dL (µmol/L)	< 1.2 (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33-101)	6.0 - 11.9 (102 - 204)	> 12.0 (204)
Glasgow coma scale	15	13 - 14	10 - 12	6 - 9	< 6
Creatinine mg/dL (µmol/L)	< 1.2 (110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300-440)	> 5.0 (440)
Urine output (mL/day)				< 500	< 200

Definitions: FiO_2: fractional inspired oxygen; PaO_2: arterial oxygen partial pressure; MAP: mean arterial pressure

Quick SOFA (qSOFA)

Parameter	Value
Respiratory Rate	≥ 22 breaths/min
Altered Mental Status	Glasgow Coma Scale < 15
Systolic Blood Pressure	≤ 100 mmHg

Interpretation

An acute change of ≥ 2 points from the baseline score suggests organ dysfunction due to infection

Sepsis & Septic Shock

Rx Treatment (Section 1 of 2)

Clinical Considerations

- Treatment includes treatment of the underlying infection, source control, and life-saving interventions (not addressed here)
- Many infections require surgical source control; antibiotics are complementary in these cases
- Start IV antibiotics as soon as possible if sepsis is suspected; results of tests should not delay antibiotics
- To choose the best empiric treatment consider most likely infection site and pathogens, local prevalence of antibiotic resistance, comorbidities, and risk of multidrug-resistant organisms
- If pathogen and susceptibilities are known, review antibiotics and adapt treatment

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

- Varies based on underlying disease, degree of immunosuppression and clinical response
- Clinical Sepsis of Unknown Origin: **7 days**
- Meningitis: **10 days** (may differ in epidemics and with different pathogens)
- Lower Respiratory Tract Infection: **5 days**

Rx Clinical Sepsis of Unknown Origin

All dosages are for normal renal function

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

OR

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

Gentamicin and amikacin retain activity against ESBL-producing strains and can be considered as a carbapenem-sparing option

Although (for each infection) antibiotics are listed in alphabetical order they should all be considered equal treatment options

Rx Meningitis

Refer also to the bacterial meningitis infographic

All dosages are for normal renal function

Consider second choice options only when first choice options are not available

First Choice

WATCH Cefotaxime 2 g q6h **IV**

OR

WATCH Ceftriaxone 2 g q12h **IV**

Second Choice

ACCESS Amoxicillin 2 g q4h **IV**

OR

ACCESS Ampicillin 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

Rx Lower Respiratory Tract Infection

Refer also to the community-acquired pneumonia infographic

All dosages are for normal renal function

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

WATCH Clarithromycin 500 mg q12h **IV**

Sepsis & Septic Shock

Rx Treatment (Section 2 of 2)

Antibiotic Treatment Duration

- Varies based on underlying disease, degree of immunosuppression and clinical response
- Enteric Fever: **10 days**
- Intra-abdominal and Skin & Soft Tissue infections: **generally 7 days** depending on infection type, if adequate surgical source control achieved and on clinical recovery
- Urinary Tract Infection: **7 days**

Rx Enteric Fever

Refer also to the enteric fever infographic
All dosages are for normal renal function

WATCH Ceftriaxone 2 g q24h **IV**

Some countries may have problems of increasing ceftriaxone resistance

Rx Intra-abdominal Infection

Refer also to the appendicitis, cholecystitis/cholangitis, diverticulitis and liver abscess infographics
All dosages are for normal renal function

First Choice

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV**

OR

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

Piperacillin+tazobactam does not provide adequate activity against many ESBL-producing isolates; consider meropenem

Second Choice

WATCH Meropenem 2 g q8h **IV**

Although (for each infection) antibiotics are listed in alphabetical order they should all be considered equal treatment options

Rx Skin and Soft Tissues Infection

Refer also to the necrotizing fascitiis infographic
All dosages are for normal renal function

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV**

In case of suspected necrotizing fasciitis ceftriaxone and metronidazole should ONLY be used if Streptococcus pyogenes has been excluded

OR

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

COMBINED WITH

ACCESS Clindamycin 900 mg q8h **IV**

IF MRSA SUSPECTED, **ADD**

WATCH Vancomycin 15-20 mg/kg q12h **IV**

Rx Urinary Tract Infection

Refer also to the upper UTI infographic
All dosages are for normal renal function

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

Amikacin retains activity against ESBL-producing strains and can be considered as a carbapenem-sparing option

Sepsis in Children

This guideline is intended for children over the age of 1 month up to 12 years. For children 0-1 month see sepsis in neonates

Definition

"A condition characterized by the presence of acute fever (> 39.0°C) and severe illness when no other cause is found" (indicating that it is possibly caused by an infection) (WHO Integrated Management of Childhood Illnesses definition)

Alternative Definitions:

• International Pediatric Sepsis Consensus Conference: Suspected or proven infection caused by any pathogen or clinical syndrome associated with a high probability of infection AND systemic inflammatory response syndrome

• Children < 5 years of age can be classified as having "Possible Serious Bacterial Infection" (PSBI) when at least one of the following signs is present:

- Not able to feed since birth or stopped feeding well (confirmed by observation)
- Convulsions
- Fast breathing (≥ 60 breaths per minute)
- Severe chest indrawing
- Fever (≥ 38.0°C)
- Low body temperature (< 35.5°C)

Important: bacteraemia is not part of the definition of sepsis; while many patients with sepsis have bacteraemia, most patients with bacteraemia do not fulfill sepsis criteria

Prevention

Preventing infections includes:

• Vaccinations

• Adequate nutrition

• Healthy living environments (e.g. access to safe water and sanitation)

Preventing evolution of infection to sepsis relies on:

• Timely diagnosis

• Adequate treatment of the underlying infection

Diagnosis

Clinical Presentation

• Usually signs and symptoms are non-specific

• Fever (> 38.0°C), respiratory symptoms, tachycardia, acute altered mental status, hypotension, vomiting

Microbiology Tests

• Diagnostic tests will be different depending on the suspected source of infection

• Ideally perform tests before initiating antibiotics; tests should not cause a major delay to the start of antibiotic treatment

• Tests for suspected sepsis would normally include blood, urine and CSF culture

Other Laboratory Tests

To Identify a Bacterial Infection:

• White blood count

• C-reactive protein and/or procalcitonin

To Identify Organ Dysfunction:

• Complete blood count with **platelets**

• **Bilirubin**

• **Blood pH and gases**

• Blood urea nitrogen

• **Creatinine**

• Electrolytes

• Glucose

• Whole blood lactate

Tests in bold are required for pSOFA score calculation

Imaging

Guided by the suspected primary site of infection

Sepsis in Children

Paediatric Sequential Organ Failure Assessment (pSOFA) Score

Parameter	Age	Score 0	1	2	3	4
PaO_2 mmHg (kPa) / FiO_2 (%)	All ages	≥ 400 (53.3)	< 400 (53.3)	< 300 (40)	< 200 (26.7) with respiratory support	< 100 (13.3) with respiratory support
Platelets (x 10^3/μL, x 10^9/L)	All ages	≥ 150	< 150	< 100	< 50	< 20
Bilirubin mg/dL (μmol/L)	All ages	< 1.2 (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	> 12.0 (204)
Glasgow coma scale	All ages	15	13 - 14	10 - 12	6 - 9	< 6
MAP mmHg (kPa) and catecholamine doses needed (μg/kg/min for ≥ 1h)	<1 mo	≥ 46 (6.1)	< 46 (6.1)	Dopamine < 5 OR dobutamine any dose	Dopamine 5.1–15 OR epinephrine (adrenaline)/ norepinephrine ≤ 0.1	Dopamine > 15 OR epinephrine/ norepinephrine > 0.1
	1-11 mo	≥ 55 (7.3)	< 55 (7.3)			
	1-2 yrs	≥ 60 (8.0)	< 60 (8.0)			
	2-5 yrs	≥ 62 (8.2)	< 62 (8.2)			
	6-11 yrs	≥ 65 (8.6)	< 65 (8.6)			
	12-18 yrs	≥ 67 (8.9)	< 67 (8.9)			
Creatinine mg/dL (μmol/L)	<1 mo	< 0.8 (71)	0.8 - 0.9 (71 - 80)	1.0 - 1.1 (88 - 97)	1.2 - 1.5 (110 - 133)	≥ 1.6 (141)
	1-11 mo	< 0.3 (26)	0.3 - 0.4 (26 - 35)	0.5 - 0.7 (44 - 62)	0.8 - 1.1 (71 - 97)	≥ 1.2 (110)
	1-2 yrs	< 0.4 (35)	0.4 - 0.5 (35 - 44)	0.6 - 1.0 (53 - 88)	1.1 - 1.4 (97 - 124)	≥ 1.5 (133)
	2-5 yrs	< 0.6 (53)	0.6 - 0.8 (53 - 71)	0.9 - 1.5 (79 - 133)	1.6 - 2.2 (141 - 195)	≥ 2.3 (203)
	6-11 yrs	< 0.7 (62)	0.7 - 1.0 (62 - 88)	1.1 - 1.7 (97 - 150)	1.8 - 2.5 (159 - 221)	≥ 2.6 (230)
	12-18 yrs	< 1.0 (88)	1.0 - 1.6 (88 - 141)	1.7 - 2.8 (150 - 247)	2.9 - 4.1 (256 - 362)	≥ 4.2 (371)

Definitions: FIO_2: fractional inspired oxygen; PaO_2: arterial oxygen partial pressure; MAP: mean arterial pressure

Bacteria Most Frequently Identified in Blood Cultures in Children with Sepsis

- Sepsis can originate from any type of infection in any organ system; it is most commonly caused by bacteria
- Hospital-acquired infections have a higher risk of being caused by multidrug-resistant organisms
- Sepsis related with malaria and viral haemorrhagic fevers should always be considered in endemic settings
- Consider sepsis related with respiratory viruses

	Low and Middle Income Setting	High Income Setting
Community Acquired	• Gram-negative bacilli (mostly *E. coli*, *Klebsiella* spp.)* • *Salmonella* Typhi and Paratyphi • Invasive non-typhoidal *Salmonella*** • *Streptococcus pneumoniae* • *Streptococcus pyogenes* • *Staphylococcus aureus* • *Neisseria meningitidis* • *Haemophilus influenzae* type b	• *Streptococcus pneumoniae* • *Streptococcus pyogenes* • *Staphylococcus aureus* • *Neisseria meningitidis* • Gram-negative bacilli (mostly *E. coli, Klebsiella* spp.)*
Hospital Acquired	• *Klebsiella* spp.* • *Escherichia coli** • *Staphylococcus aureus* (including MRSA) • Other Gram-negative bacteria • *Enterococcus* spp.	• *Klebsiella* spp.* • *Escherichia coli** • *Staphylococcus aureus* (including MRSA) • Other Gram-negative bacteria • *Enterococcus* spp.

**Including multi-drug resistant strains such as those producing ESBL and carbapenemases*

***Mostly sub-Saharan Africa, < 5 years with recent malaria, anaemia, malnutrition or HIV*

Sepsis in Children

Treatment

Clinical Considerations

• Start IV antibiotics as soon as possible if sepsis is suspected; results of tests should not delay antibiotics

• Choose treatment based on most likely infection site and infecting pathogens, local prevalence of antibiotic resistance, comorbidities, and risk of infection with multidrug-resistant organisms; if susceptibilities & pathogen are known, review and adapt antibiotics

Antibiotic Treatment Duration

• **7 days**
• **14 days** in case of meningitis

Duration may vary according to underlying condition responsible for sepsis

Referral to Hospital Not Possible

All dosages are for normal renal function

ACCESS Amoxicillin 50 mg/kg/dose q12h **ORAL**

COMBINED WITH

ACCESS Gentamicin 7.5 mg/kg/dose q24h **IM**

Referral to Hospital Possible

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Ampicillin 50 mg/kg/dose q8h **IV**

OR

ACCESS Benzylpenicillin 30 mg/kg/dose (50 000 IU/kg/dose) q8h **IV**

COMBINED WITH

ACCESS Gentamicin 7.5 mg/kg/dose q24h **IV**

Second Choice

WATCH Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH Ceftriaxone 80 mg/kg/dose q24h **IV**

OR

ACCESS Cloxacillin 25 mg/kg/dose q6h **IV**

Cloxacillin is a useful second-choice option when an infection caused by S. aureus is suspected (in community settings with high MRSA prevalence, consider vancomycin instead). If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used

COMBINED WITH

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

Amikacin would mostly be used as a treatment for infections caused by Gram-negative bacteria and when antibiotic-resistant bacteria are suspected

In settings with high prevalence of resistance, particularly for suspected health care-associated infections, a broad-spectrum antibiotic with activity against Gram-negative bacteria should also be considered (e.g. piperacillin+tazobactam)

World Health Organization

CHILDREN

Sepsis in Neonates

This guideline is intended for infants under the age of 1 month

Definition

A serious systemic condition of infectious origin (usually bacterial) associated with a combination of clinical and laboratory signs that occurs in the first month of life

Commonly Used Classifications:

- By timing of clinical onset:
  - *Early onset sepsis*: Occurring ≤ 3 days after birth, often acquired vertically or in peripartum period
  - *Late onset sepsis*: Occurring > 3 days after birth, often hospital acquired
- By setting of acquisition:
  - *Community-acquired*
  - *Hospital-acquired*

Alternative Definition:

- A young infant is classified as having "Possible Serious Bacterial Infection" (PSBI) when at least one of the following signs is present:
  - Not able to feed since birth or stopped feeding well (confirmed by observation)
  - Convulsions
  - Fast breathing (≥ 60 breaths per minute)
  - Severe chest indrawing
  - Fever (≥ 38.0°C)
  - Low body temperature (< 35.5°C)

Important: bacteraemia is not part of the definition of sepsis; while many patients with sepsis have bacteraemia, most patients with bacteraemia do not fulfill sepsis criteria

Prevention

Preventing infections includes:

- Vaccinations
- Adequate nutrition
- Healthy living environments (e.g. access to safe water and sanitation)

Preventing evolution of infection to sepsis relies on:

- Timely diagnosis
- Adequate treatment of the underlying infection

Diagnosis

Clinical Presentation

- Usually signs and symptoms are non-specific
- Hypothermia (< 35.5°C) or fever (> 38.0°C), severe chest indrawing, tachycardia, poor feeding, reduced spontaneous movements, hypotension, vomiting
- More rarely irritability, diarrhea, abdominal distention, convulsions

Microbiology Tests

- Diagnostic tests will be different depending on the suspected source of infection
- Ideally perform tests before initiating antibiotics; tests should not cause a major delay to the start of antibiotic treatment
- Tests for suspected sepsis in young infants would normally include blood, urine and culture of the cerebrospinal fluid (CSF)

Other Laboratory Tests

To Identify a Bacterial Infection:

- White blood count
- C-reactive protein and/or procalcitonin

To Identify Organ Dysfunction:

- Complete blood count with platelets
- Bilirubin
- Blood pH and gases
- Blood urea nitrogen
- Creatinine
- Electrolytes
- Glucose
- Whole blood lactate

Imaging

Guided by the suspected primary site of infection

Sepsis in Neonates

Pathogens Most Frequently Identified in Blood Cultures in Neonates with Sepsis

- Sepsis can originate from any type of infection in any organ system; it is most commonly caused by bacteria
- Hospital-acquired infections have a higher risk of being caused by multidrug-resistant organisms
- Sepsis related with malaria and viral haemorrhagic fevers should always be considered in endemic settings
- Consider sepsis related with respiratory viruses

	Low and Middle Income Setting	High Income Setting
Community Acquired	• *Escherichia coli** • *Staphylococcus aureus* (including MRSA) • *Klebsiella* spp.* • *Acinetobacter* spp.* • *Streptococcus agalactiae* • *Streptococcus pyogenes* • *Streptococcus pneumoniae*	• *Escherichia coli** • *Staphylococcus aureus* (including MRSA) • *Streptococcus agalactiae*
Hospital Acquired	• *Klebsiella* spp.* • *Escherichia coli** • *Acinetobacter* spp.* • *Staphylococcus aureus* (including MRSA) • Other Gram-negative bacteria* • *Enterococcus* spp.	• *Escherichia coli** • *Klebsiella* spp.* • *Staphylococcus aureus* (including MRSA) • Other Gram-negative bacteria* • *Enterococcus* spp.

**Including multidrug-resistant strains such as those producing ESBL and carbapenemases*

World Health Organization

CHILDREN

Sepsis in Neonates

Rx Treatment

Clinical Considerations

• Start IV antibiotics as soon as possible if sepsis is suspected; results of tests should not delay antibiotics
• Choose treatment based on most likely infection site and infecting pathogens, local prevalence of antibiotic resistance, comorbidities, and risk of infection with multidrug-resistant organisms; if susceptibilities & pathogen are known, review and adapt antibiotics

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**
• **14 days** in case of meningitis

Duration may vary according to underlying condition responsible for sepsis

Prophylactic Antibiotics

• Consider giving ampicillin AND gentamicin for 2 days if significant risk factors for infection as follows:
  • Membranes ruptured > 18 hours before delivery
  • Mother had fever > 38°C before delivery or during labour
  • Amniotic fluid was foul smelling or purulent

Rx Referral to Hospital Not Possible

All dosages are for normal renal function

ACCESS Amoxicillin 50 mg/kg/dose q12h **ORAL**

COMBINED WITH

ACCESS Gentamicin 5 mg/kg/dose q24h **IM**

Rx Referral to Hospital Possible

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Ampicillin 50 mg/kg/dose **IV**
• ≤1wk of life: q12h
• >1wk of life: q8h

OR

ACCESS Benzylpenicillin 30 mg/kg/dose (50 000 IU/kg/dose) q8h **IV**

COMBINED WITH

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

Second Choice

WATCH Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH Ceftriaxone 80 mg/kg/dose q24h **IV**

OR

ACCESS Cloxacillin 25-50 mg/kg/dose q12h **IV**

Cloxacillin is a useful second-choice option when an infection caused by S. aureus is suspected (in community settings with high MRSA prevalence, consider vancomycin instead). If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used

COMBINED WITH

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

Amikacin would mostly be used as a treatment for infections caused by Gram-negative bacteria and when antibiotic-resistant bacteria are suspected

In settings with high prevalence of resistance, particularly for suspected health care-associated infections, a broad-spectrum antibiotic with activity against Gram-negative bacteria should also be considered (e.g. piperacillin+tazobactam)

World Health Organization

ADULTS

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-immunocompromised patients:

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*

Immunocompromised 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 patients living with HIV)
- Cryptococcal meningitis and cerebral toxoplasmosis in severely immunocompromised 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)

World Health Organization

ADULTS

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

Unknown pathogen: **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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

Consider second choice options only when first choice options are not available

First Choice

WATCH Cefotaxime 2 g q6h **IV**

OR

WATCH Ceftriaxone 2 g q12h **IV**

Add Ampicillin (or IV amoxicillin) to ceftriaxone/ cefotaxime if risk factors for Listeria monocytogenes are present (e.g. patients ≥50 years, pregnancy)

Second Choice

ACCESS Amoxicillin 2 g q4h **IV**

OR

ACCESS Ampicillin 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

World Health Organization

CHILDREN

Bacterial Meningitis

Definition

• Acute inflammation of the meninges, the membranes lining the brain and spinal cord

• It can be infectious or non-infectious in origin (e.g. associated with autoimmunity)

Most Likely Pathogens

Neonates (0-2 months):

• *Streptococcus agalactiae* (Group B *Streptococcus*)

• *Escherichia coli*

• *Listeria monocytogenes*

• *Streptococcus pneumoniae*

Children/adolescents:

• *Streptococcus pneumoniae*

• *Neisseria meningitidis*

• *Haemophilus influenzae* type b

• Invasive non-typhoidal *Salmonella* (HIV/sickle cell disease)

• *Salmonella* Typhi (rare)

Consider in specific situations:

• Viral infections (especially Enteroviruses, Herpesviridae and Arboviruses) and non-infectious causes

• *Mycobacterium tuberculosis* (mostly in endemic settings and/or in patients living with HIV)

• Cryptococcal meningitis and cerebral toxoplasmosis in severely immunocompromised patients

• Cerebral malaria (in patients living or travelling to endemic settings)

• *Staphylococcus aureus* or Gram-negative bacteria, including multidrug-resistant strains after neurosurgical interventions

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

Neonates:

• Symptoms are usually non-specific; often a combination of fever, poor feeding, lethargy, drowsiness, vomiting, irritability, seizures or a full fontanelle

• Neck stiffness is very uncommon

Older children:

• Acute onset (<48 h) of:
  • Fever (>38.0°C) and /or
  • Headache and/or confusion and/or
  • Neck stiffness

• 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: testing should not delay giving antibiotics*

Other Laboratory Tests

• Cerebrospinal fluid (CSF) examination (leukocyte count and differential leukocyte count, protein and glucose

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)

• 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)

World Health Organization

CHILDREN

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

- **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

Neonates (< 2 Months)

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Ampicillin **IV**
- 1st week of life: 50 mg/kg/dose q12h
- >1st week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS Gentamicin **IV**
- 1st week of life: 5 mg/kg q24h
- >1st week of life: 7.5 mg/kg q24h

OR

WATCH Cefotaxime **IV**
- 1st week of life: 50 mg/kg/dose q12h
- >1st week of life: 50 mg/kg/dose q6h

OR

WATCH Ceftriaxone 100 mg/kg q24h **IV**

COMBINED WITH

ACCESS Gentamicin **IV**
- 1st week of life: 5 mg/kg q24h
- >1st week of life: 7.5 mg/kg q24h

Second Choice

WATCH Meropenem 40 mg/kg/dose q8h **IV**

Consider only if resistant Gram-negative organisms are suspected

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
- Steroids are not recommended in neonatal meningitis

Antibiotic Treatment Duration

Unknown pathogen: **10 days** in older children & **3 weeks** in neonates

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

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

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

Children

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH Ceftriaxone 100 mg/kg q24h **IV**

Second Choice

ACCESS Amoxicillin 40-50 mg/kg/dose q12h **IV**

OR

ACCESS Ampicillin 50 mg/kg/dose q8h **IV**

OR

ACCESS Benzylpenicillin 60 mg (100 000 IU)/kg/dose q6h **IV**

OR

ACCESS Chloramphenicol 25 mg/kg/dose q6h **IV**

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

Community-Acquired Pneumonia (Severe)

For community-acquired pneumonia in the hospital setting, please refer to the management of severe cases presented in the infographic on page 39 in the Primary Health Care section

World Health Organization

ADULTS

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:

• Gram-negative bacteria including *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (including multidrug-resistant strains)
• *Streptococcus pneumoniae*
• *Haemophilus influenzae*
• *Staphylococcus aureus* (including MRSA)
• 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

World Health Organization

ADULTS

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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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 Cefotaxime 2 g q8h **IV/IM**

OR

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

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

OR

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

Piperacillin+tazobactam offers anti-pseudomonal coverage, which the other options do not (risk of P. aeruginosa higher in patients with recent antibiotic exposure, known previous respiratory colonization and underlying lung diseases)

World Health Organization

CHILDREN

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:

• Gram-negative bacteria including *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (including multidrug-resistant strains)
• *Streptococcus pneumoniae*
• *Haemophilus influenzae*
• *Staphylococcus aureus* (including MRSA)
• 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)

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)

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

Important: a positive 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

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
• The radiographic pattern cannot be used to accurately predict the microbial cause

World Health Organization

CHILDREN

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

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

HAP: **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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**
- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Consider if low-risk of multidrug-resistant infections (e.g. short hospitalization before symptom onset and no prior antibiotic exposure)
Oral liquid must be refrigerated after reconstitution

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV/IM**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV/IM**

OR

WATCH

Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

Piperacillin+tazobactam offers anti-pseudomonal coverage, which the other options do not (risk of P. aeruginosa is higher in patients with recent antibiotic exposure, known previous respiratory colonization and underlying lung diseases)

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*

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

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

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)

Imaging

• Abdominal ultrasound to confirm the diagnosis

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

World Health Organization

ADULTS

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 Cholangitis:

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

Mild Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h IV OR 875 mg+125 mg q8h **ORAL**

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

Second Choice

WATCH Ciprofloxacin 500 mg q12h **ORAL**

COMBINED WITH

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

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

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

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

OR

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

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

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*

Diagnosis

Clinical Presentation

Acute Cholecystitis:

• Acute abdominal pain especially in the right upper quadrant +/- fever, nausea and vomiting

Acute Cholangitis:

• Abdominal pain with fever and jaundice +/- nausea and vomiting

Important:

• Both conditions are **rare in children**

• 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

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

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)

Imaging

• Abdominal ultrasound to confirm the diagnosis

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

Acute Cholecystitis & Cholangitis

℞ Treatment (Section 1 of 2)

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

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 Cholangitis:

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

℞ Mild Cases

See the following page for treatment recommendations

℞ Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS
Ampicillin **IV**
• First week of life: 50 mg/kg/dose q12h
• Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS
Gentamicin **IV**
• Neonates: 5 mg/kg q24h
• Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS
Metronidazole **IV/ORAL**
• Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
• Children: 7.5 mg/kg/dose q8h
• **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH
Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

Second Choice

WATCH
Meropenem 20 mg/kg/dose q8h **IV**

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

Acute Cholecystitis & Cholangitis

℞ Treatment (Section 2 of 2)

℞ Mild Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Ampicillin **IV**

- First week of life: 50 mg/kg/dose q12h
- Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS

Gentamicin **IV**

- Neonates: 5 mg/kg q24h
- Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV**

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

Second Choice

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

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

World Health Organization

ADULTS

Pyogenic Liver Abscess

Intra-abdominal Infection

Definition

A collection of pus within the liver

Classification based on severity:
• *Mild:* Not critically ill with no signs of sepsis or septic shock
• *Severe:* Critically ill with signs of sepsis or septic shock

Diagnosis

Clinical Presentation

Fever (>38.0°C) and abdominal pain (mostly localized in the right upper abdominal quadrant) +/- vomiting, nausea, anorexia, malaise and jaundice

Microbiology Tests

• Blood cultures (ideally before starting antibiotics)

• Microscopy and culture of abscess fluid material (if this can be drained) to adjust empiric antibiotic treatment

• Tests for *Entamoeba histolytica:*
  • Antigen or nucleic acid amplification tests of abscess aspirate material
  • Serology (however in endemic settings, serology can remain positive for months/years after resolution of infection)

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)

Imaging

• Abdominal ultrasound to confirm the diagnosis

• Consider a CT scan of the abdomen especially if complications are suspected or diagnosis is uncertain

Most Likely Pathogens

Infections are often polymicrobial

Bacteria:
• Enterobacterales (mostly *Escherichia coli, K. pneumoniae, Enterobacter* spp.) including multidrug-resistant strains
• *Burkholderia pseudomallei* (mostly Southeast Asia and northern Australia)
• *Staphylococcus* spp.
• *Streptococcus* spp. (e.g. of the *S. anginosus* group)
• *Enterococcus* spp.
• Anaerobes (mostly *Bacteroides* spp.)

Fungi:
• Mostly *Candida albicans* (not a cause of "pyogenic" abscess but consider in immunocompromised patients or recent course of antibiotics)

Parasites (consider in endemic settings):
• *Entamoeba histolytica* (not a cause of “pyogenic” abscess but consider in the differential diagnosis)

Rx Treatment (Section 1 of 2)

Clinical Considerations

• **Drainage of the abscess remains the main approach to eliminate the source of infection** (especially for large abscesses >5 cm with higher risk of rupture)

• Drainage is also important to identify the causative pathogen and its resistance profile

• **Mild:** Targeted antibiotic treatment preferred (risk of infection due to Enterobacterales producing ESBL or carbapenemases)

• **Severe:** Empiric treatment considering local prevalence of resistance (particularly of isolates of Enterobacterales producing ESBL or carbapenemases) 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
• **If signs and symptoms persist**, abdominal imaging is suggested, or an alternative extra-abdominal source of infection should be considered

Pyogenic Liver Abscess

Treatment (Section 2 of 2)

Antibiotic Treatment Duration

- Usually long (at least 4 weeks) depending on adequate source control with drainage procedures
- Longer treatment in case of *B. pseudomallei* infection (months)
- Follow up imaging can help defining antibiotic treatment duration

Mild Cases

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV**
OR 875 mg+125 mg q8h **ORAL**

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

Second Choice

WATCH Ciprofloxacin 500 mg q12h **ORAL**

COMBINED WITH

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

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

Severe Cases

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

OR

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

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

Amoebic Abscess

All dosages are for normal renal function

ACCESS Metronidazole 750 mg q8h **ORAL**

FOLLOWED BY

Paromomycin 25-35 mg/kg divided in 3 doses **ORAL**

World Health Organization

CHILDREN

Pyogenic Liver Abscess

Definition

A collection of pus within the liver

Classification based on severity:
• *Mild:* Not critically ill with no signs of sepsis or septic shock
• *Severe:* Critically ill with signs of sepsis or septic shock

Diagnosis

Clinical Presentation

Fever (>38.0°C) and abdominal pain (mostly localized in the right upper abdominal quadrant) +/- vomiting, nausea, anorexia, malaise and jaundice

Microbiology Tests

• Blood cultures (ideally before starting antibiotics)

• Microscopy and culture of abscess fluid material (if this can be drained) to adjust empiric antibiotic treatment

• Tests for *Entamoeba histolytica:*
  • Antigen or nucleic acid amplification tests of abscess aspirate material
  • Serology (however in endemic settings, serology can remain positive for months/years after resolution of infection)

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)

Imaging

• Abdominal ultrasound to confirm the diagnosis

• Consider a CT scan of the abdomen especially if complications are suspected or diagnosis is uncertain

Most Likely Pathogens

Infections are often polymicrobial

Bacteria:
• Enterobacterales (mostly *Escherichia coli, K. pneumoniae, Enterobacter* spp.) including multidrug-resistant strains
• *Burkholderia pseudomallei* (mostly Southeast Asia and northern Australia)
• *Staphylococcus* spp.
• *Streptococcus* spp. (e.g. of the *S. anginosus* group)
• *Enterococcus* spp.
• Anaerobes (mostly *Bacteroides* spp.)

Fungi:
• Mostly *Candida albicans* (not a cause of "pyogenic" abscess but consider in immunocompromised patients or recent course of antibiotics)

Parasites (consider in endemic settings):
• *Entamoeba histolytica* (not a cause of “pyogenic” abscess but consider in the differential diagnosis)

Rx Treatment (Section 1 of 2)

Clinical Considerations

• **Drainage of the abscess remains the main approach to eliminate the source of infection** (especially for large abscesses >5 cm with higher risk of rupture)

• Drainage is also important to identify the causative pathogen and its resistance profile

• **Mild:** Targeted antibiotic treatment preferred (risk of infection due to Enterobacterales producing ESBL or carbapenemases)

• **Severe:** Empiric treatment considering local prevalence of resistance (particularly of isolates of Enterobacterales producing ESBL or carbapenemases) 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
• **If signs and symptoms persist**, abdominal imaging is suggested, or an alternative extra-abdominal source of infection should be considered

Pyogenic Liver Abscess

Treatment (Section 2 of 3)

Antibiotic Treatment Duration

- Usually long (at least 4 weeks) depending on adequate source control with drainage procedures
- Longer treatment in case of *B. pseudomallei* infection (months)
- Follow up imaging can help defining antibiotic treatment duration

Amoebic Abscess

All dosages are for normal renal function

ACCESS Metronidazole 10-15 mg/kg/dose q8h **ORAL**

Mild Cases

See the following page for treatment recommendations

Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Ampicillin **IV**
- First week of life: 50 mg/kg/dose q12h
- Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS Gentamicin **IV**
- Neonates: 5 mg/kg q24h
- Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS Metronidazole **IV/ORAL**
- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

Second Choice

WATCH Meropenem 20 mg/kg/dose q8h **IV**

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

Pyogenic Liver Abscess

℞ Treatment (Section 3 of 3)

℞ Mild Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Ampicillin **IV**

- First week of life: 50 mg/kg/dose q12h
- Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS

Gentamicin **IV**

- Neonates: 5 mg/kg q24h
- Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV**

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

Second Choice

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

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

World Health Organization

ADULTS

Acute Appendicitis

Intra-abdominal Infection

Definition

Acute inflammation of the appendix sometimes followed by ischemia and perforation

Classification based on complexity:
- *Uncomplicated* (>70% of cases): No involvement of the peritoneal cavity and no abscess
- *Complicated*: Involvement of the peritoneal cavity and/or presence of an 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

Bacteria:
- Enterobacterales (mostly *E. coli* 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):
- *Enterobius vermicularis* (pinworm) can contribute by causing obstruction of the appendix

Diagnosis

Clinical Presentation

Acute abdominal pain (usually located in the right lower quadrant or migrating from the periumbilical area to the right lower quadrant), with nausea and vomiting; fever (>38.0°C) may be absent

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

Microbiology Tests

Mild Uncomplicated Cases:
- Not usually needed

Severe Cases:
- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of abscess fluid material (taken at the time of surgery) is not routinely recommended, but may be considered in specific cases to adjust empiric antibiotic 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

Identify an alternative cause of abdominal pain:
- Urinalysis (dipstick or microscopy) to exclude an infection of the urinary tract
- Pregnancy test in women: to exclude an ectopic pregnancy

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

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

Acute Appendicitis

Treatment

Antibiotic Treatment Duration

Antibiotic Treatment Complementary to Surgery
• ***Uncomplicated Cases*:** Antibiotics can be stopped once appendix is removed
• ***Complicated Cases*:** Antibiotics can be continued for a total of **5 days** provided that symptoms resolved and the source of infection was eliminated with surgery

Treatment with Antibiotics Alone: 7 days
• Consider in selected cases if close clinical monitoring is feasible and considering patient preference (avoiding risks associated with surgery versus higher risk of recurrences and later need for surgery - about 30-40% over 5 years)

Mild Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h IV
OR 875 mg+125 mg q8h **ORAL**

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

Second Choice

WATCH Ciprofloxacin 500 mg q12h **ORAL**

COMBINED WITH

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

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

Clinical Considerations

• **Appendectomy remains the main approach to eliminate the source of infection**

• **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
• **If signs and symptoms persist**, abdominal imaging is suggested, or an alternative extra-abdominal source of infection should be considered

Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

OR

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

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

World Health Organization

CHILDREN

Acute Appendicitis

Intra-abdominal Infection

Definition

Acute inflammation of the appendix sometimes followed by ischemia and perforation

Complexity:
• *Uncomplicated* (>70% of cases): 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

Bacteria:
• Enterobacterales (mostly *E. coli* 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):
• *Enterobius vermicularis* (pinworm) can contribute by causing obstruction of the appendix

Diagnosis

Clinical Presentation

Acute abdominal pain (usually located in the right lower quadrant or migrating from the periumbilical area to the right lower quadrant), with nausea and vomiting; fever (>38.0°C) may be absent

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

Microbiology Tests

Mild Uncomplicated Cases:
• Not usually needed

Severe Cases:
• Blood cultures (ideally before starting antibiotics)
• Microscopy and culture of abscess fluid material (taken at the time of surgery) is not routinely recommended, but may be considered in specific cases to adjust empiric antibiotic treatment

Imaging

• Abdominal ultrasound if available is helpful to confirm the diagnosis

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

Other Laboratory Tests

Identify an alternative cause of abdominal pain:
• Urinalysis (dipstick or microscopy) to exclude an infection of the urinary tract
• Consider pregnancy test where appropriate to exclude an ectopic pregnancy

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

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

World Health Organization

CHILDREN

Acute Appendicitis

℞ Treatment (Section 1 of 2)

Clinical Considerations

• **Appendectomy remains the main approach to eliminate the source of infection**

• Treatment with antibiotics alone is not recommended in children by WHO

• **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
• **If signs and symptoms persist**, abdominal imaging is suggested, or an alternative extra-abdominal source of infection should be considered

Antibiotic Treatment Duration

• ***Uncomplicated Cases:*** Antibiotics can be stopped once surgery has been performed and child is well

• ***Complicated Cases:*** Antibiotics can be continued for a total of **5 days** provided that symptoms resolved and the source of infection was eliminated with surgery

℞ Mild Cases

See the following page for treatment recommendations

℞ Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Ampicillin **IV**
• First week of life: 50 mg/kg/dose q12h
• Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS Gentamicin **IV**
• Neonates: 5 mg/kg q24h
• Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS Metronidazole **IV/ORAL**
• Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
• Children: 7.5 mg/kg/dose q8h
• **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

Second Choice

WATCH Meropenem 20 mg/kg/dose q8h **IV**

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

Acute Appendicitis

℞ Treatment (Section 2 of 2)

℞ Mild Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Ampicillin **IV**

- First week of life: 50 mg/kg/dose q12h
- Beyond first week of life: 50 mg/kg/dose q8h

COMBINED WITH

ACCESS

Gentamicin **IV**

- Neonates: 5 mg/kg q24h
- Children: 7.5 mg/kg q24h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV**

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

Second Choice

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **IV/ORAL**

- **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

COMBINED WITH

ACCESS

Metronidazole **IV/ORAL**

- Neonates: 7.5 mg/kg/dose q12h (for IV loading dose: 15 mg/kg)
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

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

World Health Organization

ADULTS

Acute Diverticulitis

Intra-abdominal Infection

Definition

Acute inflammation of diverticula (sac-like protrusions of the wall of the colon) that can cause severe abdominal pain

Classification based on complexity:
- *Uncomplicated:* No involvement of 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

Diagnosis

Clinical Presentation

- Acute pain in the left or right lower abdominal quadrants with chills, nausea and vomiting; fever (>38.0°C) may be absent
- Left diverticulitis is more common in Europe and North America, right diverticulitis in Asia

Important:
- Consider peritonitis if 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

Microbiology Tests

Mild Cases: Not usually needed
Severe Cases:
- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of abscess fluid material (if this can be drained) to adjust empiric antibiotic treatment

Other Laboratory Tests

- **Determine disease severity and help identify a bacterial infection:** White blood cell count, C-reactive protein and/or procalcitonin
- If sepsis is suspected consider additional laboratory tests (see sepsis infographic)

Imaging

Abdominal ultrasound or CT of the abdomen (depending on availability) to confirm the diagnosis

Most Likely Pathogens

Bacteria
- Enterobacterales (mostly *E. coli* 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):
- *Enterobius vermicularis* (pinworm)

Rx Treatment (Section 1 of 2)

Clinical Considerations

- **Uncomplicated cases in immunocompetent patients:** antibiotics **not** needed if there are no systemic signs of infection; if these cases do not resolve spontaneously after 2-3 days, consider antibiotics
- **Uncomplicated cases in severely immunocompromised patients:** treat with antibiotics alone (if close follow up possible)
- **Complicated cases:** treat with antibiotics and surgical source control (e.g. drainage of large abscesses >5 cm or colonic resection)

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
- **If signs and symptoms persist**, abdominal imaging is suggested, or an alternative extra-abdominal source of infection should be considered

Acute Diverticulitis

Treatment (Section 2 of 2)

Antibiotic Treatment Duration

- **Most mild cases do not need antibiotic treatment**
- **Treatment with antibiotics alone: 4 days** (if good clinical recovery and symptoms resolved)
- **Treatment with antibiotics & surgical source control:** Stop **4 days** after adequate source control (surgery) is achieved otherwise, continue until clinically stable and afebrile

Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

OR

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

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

Mild Cases

Most mild cases do not need antibiotic treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

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

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

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

Second Choice

WATCH Ciprofloxacin 500 mg q12h **ORAL**

COMBINED WITH

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

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

World Health Organization

ADULTS

Clostridioides difficile Infection

Intra-abdominal Infection

Definition

Infection of the colon caused by the bacterium *C. difficile* that occurs mostly in patients with current/recent antibiotic use and with regular exposure to healthcare settings

Diagnosis

Clinical Presentation

Usually diarrhea (≥3 unformed/liquid stools in 24 hrs or more than normal for individual) with no other plausible cause +/- abdominal pain, cramping and fever

Severe cases (e.g. pseudomembranous colitis):
- Severe abdominal pain, high fever, organ dysfunction
- Toxic megacolon presents with signs of acute surgical abdomen and/or sepsis (diarrhea is often absent)

Microbiology Tests

- Consider testing symptomatic patients with no other plausible reason for diarrhea especially if recent or current exposure to antibiotics
- Currently no single test to diagnose CDI is completely reliable and the best approach remains controversial

Two commonly used approaches:

1. Start with highly sensitive test to detect *C. difficile*, if positive follow with a test to confirm toxin production
   - If toxin test negative: Consider *C. difficile* colonization
2. Perform two tests simultaneously, one to detect the presence of *C. difficile* and one to detect toxin production
   - Concordant results can reliably confirm (both tests positive) or exclude (both tests negative) infection
   - If results conflict and patient is symptomatic, treatment should be based on the pre-test probability of *C. difficile* infection

Important: in case of confirmed CDI, do not repeat testing during the same episode and do not test to confirm the resolution of the infection at the end of treatment

Other Laboratory Tests

Mild Cases: Not usually needed

Severe Cases:
- White blood cell count
- Creatinine and electrolytes

Imaging

Usually not needed unless a complication is suspected; in these cases, consider abdominal CT

Pathogen

C. difficile
- Gram-positive spore-forming bacterium widely present in the environment that can be acquired through ingestion of spores
- Infection can be caused by strains producing toxins when the intestinal mucosa of the colon is inflamed and disrupted

NAP1/027
- *C. difficile* toxigenic strain with a particular virulence that caused outbreaks in recent years especially in North America

Treatment

Clinical Considerations

- **Discontinue any other antibiotics except those treating *C. difficile* infection as soon as possible and adopt infection control measures to prevent transmission**
- Always recommend rehydration in patients with diarrhea; anti-diarrheal drugs not routinely necessary
- Diarrhea may resolve slowly over days, but clinical deterioration of a patient on appropriate treatment should precipitate escalation of treatment and a surgical referral

Antibiotic Treatment Duration

10 days

Antibiotic Treatment

Refers to a first episode, not recurrences (within 8 weeks of previous episode)

All dosages are for normal renal function

First Choice

ACCESS — Metronidazole 500 mg q8h **ORAL**

Second Choice

WATCH — Vancomycin 125 mg q6h **ORAL**

***In severe cases**: Oral vancomycin is preferred; vancomycin dose can be increased to 500 mg q6h and can be given in combination with IV metronidazole*

World Health Organization

CHILDREN

Clostridioides difficile Infection

Definition

Infection of the colon caused by the bacterium *C. difficile* that occurs mostly in patients with current/recent antibiotic use and with regular exposure to healthcare settings

Pathogen

C. difficile
• Gram-positive spore-forming bacterium widely present in the environment that can be acquired through ingestion of spores
• Infection can be caused by toxigenic strains when the intestinal mucosa of the colon is inflamed and disrupted

NAP1/027
• *C. difficile* toxigenic strain with a particular virulence that caused outbreaks in recent years especially in North America

Diagnosis

Clinical Presentation

Usually diarrhea (≥3 unformed/liquid stools in 24 hrs or more than normal for individual) with no other plausible cause +/- abdominal pain, cramping and fever

Severe cases (e.g. pseudomembranous colitis):
• Severe abdominal pain, high fever, organ dysfunction
• Toxic megacolon presents with signs of acute surgical abdomen and/or sepsis (diarrhea is often absent)

Clinical disease is rare in young children (esp. <2 years); they are often asymptomatic carriers

Other Laboratory Tests

Mild Cases:
• Not usually needed

Severe Cases:
• White blood cell count
• Creatinine and electrolytes

Imaging

Usually not needed unless a complication is suspected; in these cases, consider abdominal CT

Microbiology Tests

• Consider testing symptomatic patients with no other plausible reason for diarrhea especially if recent or current exposure to antibiotics

• **Testing <1 year of age is not recommended due to high prevalence of colonization in this age group**

• Currently no single test to diagnose CDI is completely reliable and the best approach remains controversial

Two commonly used approaches:

1. Start with highly sensitive test to detect *C. difficile*, if positive follow with a test to confirm toxin production
   • If toxin test negative: Consider *C. difficile* colonization
2. Perform two tests simultaneously, one to detect the presence of *C. difficile* and one to detect toxin production
   • Concordant results can reliably confirm (both tests positive) or exclude (both tests negative) infection
   • If results conflict and patient is symptomatic, treatment should be based on the pre-test probability of *C. difficile* infection

Important: in case of confirmed CDI, do not repeat testing during the same episode and do not test to confirm the resolution of the infection at the end of treatment

Clostridioides difficile Infection

Treatment

Clinical Considerations

• **Discontinue any other antibiotics except those treating *C. difficile* infection as soon as possible and adopt infection control measures to prevent transmission**

• Always recommend rehydration in patients with diarrhea; anti-diarrheal drugs not routinely necessary

• Diarrhea may resolve slowly over days, but clinical deterioration of a patient on appropriate treatment should precipitate escalation of treatment and a surgical referral

Antibiotic Treatment Duration

10 days

Antibiotic Treatment

First episode, not recurrences (within 8 weeks of previous episode)

All dosages are for normal renal function

First Choice

ACCESS

Metronidazole **ORAL**
- Neonates: 7.5 mg/kg/dose q12h
- Children: 7.5 mg/kg/dose q8h
- **Oral weight bands:**

3-<6 kg	30 mg q8h
6-<10 kg	50 mg q8h
10-<15 kg	100 mg q8h
15-<20 kg	150 mg q8h
20-<30 kg	200 mg q8h
≥30 kg	500 mg q8h

Second Choice

WATCH

Vancomycin 5-10 mg/kg/dose q6h **ORAL**

***In severe cases**: Oral vancomycin is preferable to metronidazole*

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, can be associated with bacteremia)
  - *Pseudomonas aeruginosa, Acinetobacter baumannii* (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 (if upper UTI is suspected clinically):

- 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 (if upper UTI is suspected clinically):

- 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

World Health Organization

ADULTS

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, for whom pre-emptive antibiotic therapy may be indicated)
- **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

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

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

OR

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

AND/OR

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

AND/OR

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

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

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

Upper Urinary Tract Infection

Urinary Tract Infection

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 children with no risk factors for complicated UTI
- *Complicated:* More common in girls, infants and children with structural malformations of the urinary tract (e.g. vesicoureteral reflux or other congenital anomalies)

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.
  - Other Gram-negative bacilli (e.g. *Klebsiella* spp.)
  - *Staphylococcus aureus* (rare in uncomplicated UTIs, usually in patients with urinary catheters)
  - Group B *Streptococcus* (*Streptococcus agalactiae*)

Diagnosis

Clinical Presentation

- Fever is most common symptom, with irritability, vomiting and diarrhoea
- In older children (e.g. over 2 years of age) abdominal pain, urgency, frequency and dysuria are more common, along with flank pain/tenderness and increased wetting
- 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 (if upper UTI is suspected clinically):

- 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 (if upper UTI is suspected clinically):

- 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

Ultrasound is helpful if available

Upper Urinary Tract Infection

Treatment

Clinical Considerations

• **In young children with mild cases** it is often difficult to clearly distinguish between lower and upper UTI, therefore oral options recommended for lower UTI can be used initially (if no need for IV treatment) or as step down treatment (see Lower Urinary Tract for antibiotic options)

• **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

Severe Cases

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

WATCH Cefotaxime 50 mg/kg/dose q8h **IV/IM**

OR

WATCH Ceftriaxone 80 mg/kg/dose q24h **IV/IM**

AND/OR

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

AND/OR

ACCESS Gentamicin **IV**
• Neonates: 5 mg/kg/dose q24h
• Children: 7.5 mg/kg/dose q24h

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

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

Mild Cases

All dosages are for normal renal function

WATCH Ciprofloxacin 15 mg/kg/dose q12h **ORAL**
• **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

Acute Bacterial Osteomyelitis

Bone and Joint Infection

This guidance does not cover prosthetic-joint infections in detail

Definition

An infection of the bone characterized by inflammation and bone destruction

Classification based on:
- *Mechanism of dissemination in the body*: Through the bloodstream (less common in adults), local spread or direct inoculation
- *Duration of symptoms*: Acute (days to weeks), chronic (months to years with presence of dead bone fragments)

Consequences of classification for management:
- Differences in the causative pathogens:
  - Local spread: more variability in possible causative pathogens
  - Spread through the bloodstream: more common with certain pathogens (e.g. *S. aureus*)
- Necessity for surgery (e.g. dead bone, usually present in chronic infections, needs removal for antibiotic treatment to be successful)

Most Likely Pathogens

Bacteria (most cases):
- *Staphylococcus aureus* (including MRSA)
- *Staphylococcus* spp. other than *S. aureus*
- *Streptococcus* spp. (mostly in patients with splenic dysfunction)

Additionally in immunocompromised patients:
- *Candida* spp.
- *Cryptococcus* spp.
- *Histoplasma* spp.
- *Mycobacterium tuberculosis*
- *Pseudomonas aeruginosa*

Consider in specific situations:
- *Acinetobacter baumannii* (open fractures)
- *Bartonella* spp. (history of cat bite wounds)
- *Brucella* spp. (exposure to infected animals or ingestion of contaminated food, mostly dairy products)
- Enterobacterales and anaerobes (pressure ulcers, diabetic foot infections, open fractures)
- Invasive non-typhoidal *Salmonella* (sickle cell disease)

Diagnosis

Clinical Presentation

- Gradual onset of localized pain with redness, swelling, and warmth of the affected area +/- fever and other signs of systemic infection
- If vertebral spine, hip and pelvis involved, pain is usually the main symptom
- Suspect in case of defective healing of a fractured bone
- Osteomyelitis can occur with/without septic arthritis
- Tuberculous osteomyelitis: consider when illness is chronic (less ill, less marked local signs), pus drains from the infected bone to the surface of the skin or patient has other signs of tuberculosis

Other Laboratory Tests

To differentiate between bacterial and reactive viral infections:
- White blood cell count

To detect inflammation:
- C-reactive protein (CRP) and/or procalcitonin
- Erythrocyte sedimentation rate (ESR could complement CRP especially during follow up)

To help exclude other bone diseases:
- Calcium, phosphate and alkaline phosphatase tests
  - These tests are usually normal in osteomyelitis but abnormal in other bone diseases

Microbiology Tests

All microbiology tests ideally before starting antibiotics
- Blood cultures
- Microscopy and culture of bone biopsy material
- Microscopy and culture of deep samples of tissue / bone collected during debridement to adjust empiric antibiotic treatment

It is **important** to determine the causative pathogen to adequately target antibiotic treatment because the number of potential pathogens is large and antibiotic resistant pathogens (e.g. MRSA) are not infrequent
- Samples should also be tested for special pathogens (e.g. mycobacteria, fungi, *Brucella* spp.) based on clinical/epidemiological features

Imaging

- X-ray of the affected bone
  - Normal X-ray on admission does not rule out acute osteomyelitis but can help exclude alternative diagnosis
- CT or MRI could also be considered if available
  - MRI has a high sensitivity/specificity to detect bone changes (especially in early phase)

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ADULTS

Acute Bacterial Osteomyelitis

Treatment

Clinical Considerations

- **Surgical treatment not required in most cases**
- Surgical debridement of the bone can be considered in some selected cases to reduce the risk of complications
- Prosthetic-joint infections: Surgical approach depends on the location of the prosthesis, characteristics of the patient and local practices

Antibiotic Treatment:

- The intravenous route is preferred at least in the first week of treatment
- **Targeted antibiotic treatment** based on microbiology results always preferred (many potential causative pathogens and high levels of resistance)
- **If empiric treatment** is required consider most likely pathogens including local prevalence and individual risk factors for MRSA
- Adjust therapy once microbiology results available

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

4 to 6 weeks

Based on:
- Presence/absence of dead bone or foreign bodies
- Causative organism and its resistance profile
- Ability of the antibiotic to penetrate into bone tissues
- Imaging studies are usually not useful to determine duration

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Cloxacillin 2 g q6h **IV**

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. A higher dose (e.g. 12 g/day) could be considered given the concerns with bone penetration

Second Choice

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

OR

WATCH Cefazolin 2 g q8h **IV**

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

Ceftriaxone or cefotaxime are the preferred options if invasive non-typhoidal Salmonella or Enterobacterales infection is suspected

OR

ACCESS Clindamycin 600 mg q8h **IV/ORAL**

Acceptable option for CA-MRSA if MRSA is susceptible or in settings where MRSA maintains high levels of susceptibility to clindamycin, otherwise consider vancomycin

World Health Organization

CHILDREN

Acute Bacterial Osteomyelitis

Definition

An infection of the bone characterized by inflammation and bone destruction

Classification based on:
• *Mechanism of dissemination in the body*: Through the bloodstream (more common when <5 years of age), local spread or direct inoculation
• *Duration of symptoms*: Acute (days to weeks), chronic (months to years with presence of dead bone fragments)

Consequences of classification for management:
• Differences in the causative pathogens:
  • Local spread: more variability in possible causative pathogens
  • Spread through the bloodstream: more common with certain pathogens (e.g. *S. aureus*)
• Necessity for surgery (e.g. dead bone, usually present in chronic infections, needs removal for antibiotic treatment to be successful)

Most Likely Pathogens

Bacteria (most cases):
• *Staphylococcus aureus* (including MRSA)
• *Streptococcus* spp. (mostly Group A *Streptococcus*)
• *Kingella kingae* (young children, usually with milder clinical disease)
• *Haemophilus influenzae* type b (young children not vaccinated against Hib)
• Invasive non-typhoidal *Salmonella* (in children with sickle cell disease)
• *Acinetobacter baumannii* (open fractures)

Additional bacteria in immunocompromised children:
• Enterobacterales (open fractures)
• *Pseudomonas aeruginosa*

Diagnosis

Clinical Presentation

• Gradual onset of localized pain with redness, swelling, and warmth of the affected area +/- fever and other signs of systemic infection
• Often the femur and tibia are affected and the infection presents with difficulty/inability to walk or reluctance to move the limb
• Suspect in case of defective healing of a fractured bone
• If vertebral spine, hip and pelvis involved, pain is usually the main symptom
• Osteomyelitis can occur with/without septic arthritis
• Tuberculous osteomyelitis: consider when illness is chronic (less ill, less marked local signs), pus drains from the infected bone to the surface of the skin or patient has other signs of tuberculosis

Microbiology Tests

All microbiology tests ideally before starting antibiotics
• Blood cultures
• Microscopy and culture of bone biopsy material
• Microscopy and culture of deep samples of tissue / bone collected during debridement to adjust empiric antibiotic treatment

It is **important** to determine the causative pathogen to adequately target antibiotic treatment because the number of potential pathogens is large and antibiotic resistant pathogens (e.g. MRSA) are not infrequent
• Samples should also be tested for special pathogens (e.g. mycobacteria, fungi, *Brucella* spp.) based on clinical/epidemiological features

Other Laboratory Tests

To differentiate between bacterial and reactive viral infections:
• White blood cell count

To detect inflammation:
• C-reactive protein (CRP)
• Erythrocyte sedimentation rate (could complement CRP especially during follow up)

Imaging

• X-ray of the affected bone
  • Normal X-ray on admission does not rule out acute osteomyelitis but can help exclude alternative diagnosis
• CT or MRI could also be considered if available
  • MRI has a high sensitivity/specificity to detect bone changes (especially in early phase)

World Health Organization

CHILDREN

Acute Bacterial Osteomyelitis

Treatment

Clinical Considerations

Surgical treatment not required in most cases

Antibiotic Treatment

- The intravenous route is preferred at least in the first few days of treatment
- **In children empiric treatment is common practice** and *S. aureus* remains the most common pathogen
- In **neonates**, *S. aureus* is also the most common pathogen but empiric treatment should also cover Enterobacterales (very rare in older children)
  - For Enterobacterales use:
    - Cefotaxime or
    - Ceftriaxone (not in infants with hyperbilirubinemia)

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

Around **3 weeks** in children with uncomplicated infections

Based on:
- Clinical recovery
- Causative organism and its resistance profile

Imaging studies are usually not useful to determine duration

Antibiotic Treatment

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Cloxacillin **IV**
- Neonates: 25-50 mg/kg/dose q12h
- Children: 25 mg/kg/dose q6h
- **ORAL:** 15 mg/kg/dose q6h
- **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

Second Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**
- **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

WATCH

Cefazolin 25 mg/kg/dose q12h **IV**

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV**

Ceftriaxone or cefotaxime are the preferred options if invasive non-typhoidal Salmonella or Enterobacterales infection is suspected

OR

ACCESS

Clindamycin **IV**
- Neonates: 5 mg/kg/dose q8h
- Children: 10 mg/kg/dose q8h

Acceptable option for CA-MRSA if MRSA is susceptible or in settings where MRSA maintains high levels of susceptibility to clindamycin, otherwise consider vancomycin

World Health Organization

ADULTS

Septic Arthritis

Bone and Joint Infection

This guidance does not cover prosthetic-joint infections in detail

Definition

An infection of one or several joints, usually of bacterial origin

Gonococcal arthritis:

• Rare complication of gonococcal infection (predominantly affects women)

• Characterized by dissemination of the infection via the bloodstream

Classification based on:

• *Causative pathogen*: Gonococcal or non-gonococcal

• *Type of affected joint*: Large or small joint

• *Mechanism of dissemination in the body*:
  • Spread through the bloodstream (more common)
  • Local spread or direct inoculation

Most Likely Pathogens

Bacteria (most cases):

• *Staphylococcus aureus* (including MRSA)
• *Staphylococcus* spp. other than *S. aureus*
• *Streptococcus* spp.

Additionally in immunocompromised patients:

• *Candida* spp.
• *Cryptococcus* spp.
• *Histoplasma* spp.
• *Mycobacterium tuberculosis*
• *Pseudomonas aeruginosa*

Consider in specific situations:

• *Acinetobacter baumannii* (open skin wounds with exposed joint)
• Anaerobes (penetrating injuries)
• *Bartonella* spp. (history of cat bite wounds)
• *Brucella* spp. (exposure to infected animals or ingestion of contaminated food, mostly dairy products)
• Enterobacterales (pressure ulcers, diabetic foot infections, and open skin wounds with exposed joint)
• *Neisseria gonorrhoeae* (if gonococcal infection)

Diagnosis

Clinical Presentation

• Acute onset (usually a few days, but up to 2 weeks) of joint pain and reduced range of motion with redness, swelling, warmth of the joint (may be less evident in "deep" joints)
• Usually, a single joint is affected (often knee)
• Polyarticular infection is more common in patients with underlying rheumatoid arthritis
• Other signs of systemic infection are usually present
• Septic arthritis can occur with/without osteomyelitis

Gonococcal arthritis:

• Typical signs and symptoms of septic arthritis (usually affecting knees and ankles) + skin manifestations (rash, small papules)
• Often no signs/symptoms of cervicitis/urethritis

Important: if left untreated, septic arthritis can rapidly lead to destruction of the cartilage; it therefore needs to be rapidly diagnosed and treated

Other Laboratory Tests

To differentiate between bacterial and reactive viral infections:

• White blood cell count (WBC)

To detect inflammation:

• C-reactive protein (CRP)
• Erythrocyte sedimentation rate (ESR could complement CRP especially during follow up)

Synovial fluid examination:

• WBC and microscopy for crystals
• WBC usually >20 000 cells/µL (> 20 x 10^9/L) with >90% neutrophils

Microbiology Tests

All microbiology tests ideally before starting antibiotics

• Blood cultures
• Microscopy and culture of synovial fluid
  • Culture is usually negative in gonococcal arthritis
• Microscopy and culture of deep samples of tissue collected during debridement in prosthetic joint implant to adjust empiric antibiotic treatment
• Nucleic acid amplification test of urogenital specimens and urine for *Neisseria gonorrhoeae* infection

It is **important** to determine the causative pathogen to adequately target antibiotic treatment because the number of potential pathogens is large and antibiotic resistant pathogens (e.g. MRSA) are not infrequent
• Samples should also be tested for special pathogens (e.g. mycobacteria, fungi, *Brucella* spp., *Neisseria gonorrhoeae*) based on clinical/epidemiological features

Imaging

• Ultrasound of the affected joint to detect joint effusion and synovial swelling (due to increased intra-articular fluid)
• Consider MRI if available, especially if concomitant osteomyelitis is suspected (more sensitive/specific to detect bone changes)

Septic Arthritis

Treatment

Clinical Considerations

• **Prompt surgical drainage of purulent material and lavage of the joint is a key part of the management of septic arthritis** (antibiotic treatment alone is usually not sufficient) and can reduce risk of complications

• Immobilization of the joint is not necessary except for pain control

• Prosthetic-joint infections: Surgical approach depends on the location of the prosthesis, characteristics of the patient and local practices

Antibiotic Treatment:

• The intravenous route is preferred at least in the first week of treatment

• **Targeted antibiotic treatment** based on microbiology results always preferred (many potential causative pathogens and high levels of resistance)

• **If empiric treatment** is required consider most likely pathogens including local prevalence and individual risk factors for MRSA or *N. gonorrhoeae* based on individual risk factors

• Adjust therapy once microbiology results available

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

• **4 to 6 weeks**

• **2 weeks** in case of gonococcal infection

Based on:

• Presence/absence/removal of foreign bodies

• Causative organism and its resistance profile

• Presence/absence of osteomyelitis

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS Cloxacillin 2 g q6h **IV**

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. A higher dose (e.g. 12 g/day) could be considered given the concerns with bone penetration

Second Choice

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

OR

WATCH Cefazolin 2 g q8h **IV**

OR

WATCH Cefotaxime 2 g q8h **IV**

OR

WATCH Ceftriaxone 2 g q24h **IV**

Ceftriaxone or cefotaxime are the preferred options if invasive non-typhoidal Salmonella or Enterobacterales infection is suspected

OR

ACCESS Clindamycin 600 mg q8h **IV/ORAL**

Acceptable option for CA-MRSA if MRSA is susceptible or in settings where MRSA maintains high levels of susceptibility to clindamycin, otherwise consider vancomycin

World Health Organization

CHILDREN

Septic Arthritis

Bone and Joint Infection

Definition

An infection of one or several joints, usually of bacterial origin

Classification based on:
- *Type of affected joint*: Large or small joint
- *Mechanism of dissemination in the body*:
  - Spread through the bloodstream (more common)
  - Local spread or direct inoculation

Most Likely Pathogens

Bacteria (most cases):
- *Staphylococcus aureus* (including MRSA)
- *Streptococcus* spp. (mostly Group A *Streptococcus*)
- *Kingella kingae* (young children, usually with milder clinical disease)
- *Haemophilus influenzae* type b (young children not vaccinated against Hib
- Invasive non-typhoidal *Salmonella* (in children with sickle cell disease)

Diagnosis

Clinical Presentation

- Acute onset (usually a few days, but up to 2 weeks) of joint pain and reduced range of motion with redness, swelling, warmth of the joint (may be less evident in "deep" joints)
- Usually, a single joint is affected (often knee)
- Other signs of systemic infection are usually present
- Septic arthritis can occur alone or with osteomyelitis

Important: if left untreated, septic arthritis can rapidly lead to destruction of the cartilage (especially in young children); it therefore needs to be rapidly diagnosed and treated

Other Laboratory Tests

To differentiate between bacterial and reactive viral infections:
- White blood cell count (WBC)

To detect inflammation:
- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR could complement CRP especially during follow up)

Synovial fluid examination:
- WBC and microscopy for crystals
- WBC usually >20 000 cells/µL (> 20 x 10^9/L) with >90% neutrophils

Microbiology Tests

All microbiology tests ideally before starting antibiotics
- Blood cultures
- Microscopy and culture of synovial fluid
- Microscopy and culture of deep samples of tissue collected during debridement in case of prosthetic joint implant to adjust empiric antibiotic treatment

It is **important** to determine the causative pathogen to adequately target antibiotic treatment because the number of potential pathogens is large and antibiotic resistant pathogens (e.g. MRSA) are not infrequent
- Samples should also be tested for special pathogens (e.g. mycobacteria, fungi, *Brucella* spp.) based on clinical/epidemiological features

Imaging

- Ultrasound of the affected joint to detect joint effusion and synovial swelling (due to increased intra-articular fluid)
- Consider MRI if available, especially if concomitant osteomyelitis is suspected (more sensitive/specific to detect bone changes)

World Health Organization

CHILDREN

Septic Arthritis

℞ Treatment

Clinical Considerations

• Prompt surgical drainage of purulent material and lavage of the joint can reduce risk of complications

• Immobilization of the joint is not necessary except for pain control

• Prosthetic-joint infections: Surgical approach depends on the location of the prosthesis, characteristics of the patient and local practices

Antibiotic Treatment:

• The intravenous route is preferred at least in the first few days of treatment

• **In children empiric treatment is common practice**

• **In neonates**, empiric treatment should also cover Enterobacterales (very rare in older children)

  • For Enterobacterales use:

    ▫ Cefotaxime or

    ▫ Ceftriaxone (not in infants with hyperbilirubinemia)

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

• Early oral step down in the first week may be used in uncomplicated patients

Antibiotic Treatment Duration

About **3 weeks**

Based on:
• Presence/absence/removal of foreign bodies
• Causative organism and its resistance profile
• Presence/absence of osteomyelitis

℞ Antibiotic Treatment

All dosages are for normal renal function
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

First Choice

ACCESS

Cloxacillin **IV**
• Neonates: 25-50 mg/kg/dose q12h
• Children: 25 mg/kg/dose q6h
• **ORAL:** 15 mg/kg/dose q6h
• **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

Second Choice

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin **IV/ORAL**
• **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

WATCH

Cefazolin 25 mg/kg/dose q12h **IV**

OR

WATCH

Cefotaxime 50 mg/kg/dose q8h **IV**

OR

WATCH

Ceftriaxone 80 mg/kg/dose q24h **IV**

Ceftriaxone or cefotaxime are the preferred options if invasive non-typhoidal Salmonella or Enterobacterales infection is suspected

OR

ACCESS

Clindamycin **IV/ORAL**
• Neonates: 5 mg/kg/dose q8h
• Children: 10 mg/kg/dose q8h

Acceptable option for CA-MRSA if MRSA is susceptible or in settings where MRSA maintains high levels of susceptibility to clindamycin, otherwise consider vancomycin

Necrotizing Fasciitis

Skin and Soft Tissue Infection

Definition

Life-threatening necrotizing infection of the deep soft tissues affecting the muscular fascia; caused mostly by bacteria and characterized by acute/fulminant necrosis with tissue destruction and systemic signs of toxicity

Classification based on:

- *Causative pathogen*:
  - Type 1/polymicrobial
  - Type 2/monomicrobial
- *Presence or absence of gas in tissues*
  - For example, presence of gas is common in polymicrobial infections
- *Involved site*:
  - Leg
  - Head and neck
  - Perineum (Fournier's gangrene)
- *Risk of poor outcome*:
  - High versus moderate risk

Most Likely Pathogens

Monomicrobial / Type 2:

- **Most cases:**
  - *Streptococcus pyogenes* (group A *Streptococcus*)
  - *Streptococcus agalactiae*
  - *Streptococcus dysgalactiae* (mostly in elderly and chronically ill patients)
- **Less frequently:**
  - *Staphylococcus aureus* (including MRSA)
- **Specific environmental exposures:**
  - *Aeromonas hydrophila* (freshwater)
  - *Vibrio vulnificus* (seawater)

Polymicrobial / Type 1:

- Anaerobes (e.g. *Bacteroides* spp., *Clostridium perfringens*, *Peptostreptococcus* spp. or mouth anaerobes when head/neck involved)
- Enterobacterales
- *Pseudomonas* spp.
- *Streptococcus* spp.
- *Staphylococcus aureus* (including MRSA)

Diagnosis

Clinical Presentation

- Acute onset of localized pain out of proportion to physical findings accompanied by rapid onset of systemic signs
- Signs and symptoms of skin and soft tissue infections (redness, warmth, swelling) usually present when portal of entry is the skin but severe pain is the main symptom; rapid progression of redness, ecchymosis and bullae is also suggestive
- Definitive diagnosis requires direct visualization of necrotic tissue in the muscular fascia through surgical exploration

Fournier's gangrene:

- Severe pain accompanied by signs of necrosis in the perineal area; rapid progression of the infection to the abdominal wall and gluteal muscles is possible

Microbiology Tests

- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of deep samples of tissue collected at debridement to adjust empiric antibiotic treatment

Other Laboratory Tests

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

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

Initial evaluation for suspected necrotizing fasciitis:

- Complete blood count
- Creatinine
- Electrolytes
- Glucose

Imaging

- Ultrasound may be helpful to evaluate the extent of the affected tissue and gas and fluid along the muscular fascia
- Consider CT scan of the affected area

Imaging should not delay surgical exploration/inspection since surgery is the best way to diagnose/treat this infection

World Health Organization

ADULTS

Necrotizing Fasciitis

Treatment

Clinical Considerations

- Clinical progression to severe disease is rapid, carefully monitor signs of sepsis/septic shock
- **Early surgical removal of necrotic tissue through drainage/debridement is key; delays associated with increased mortality**
- Antibiotic treatment is a complementary measure to surgical source control
- IVIG sometimes used when shock complicates necrotizing fasciitis (and toxic shock syndrome suspected) however very expensive and unclear effect on mortality

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

Usually **2-3 weeks**

Based on:

- Clinical response
- Surgical source control, and
- Evolution of laboratory markers of infection

Antibiotic Treatment

All dosages apply to normal renal function

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

COMBINED WITH

ACCESS Clindamycin 900 mg q8h **IV**

OR

Use this treatment option only if Streptococcus pyogenes infection has been excluded first

WATCH Ceftriaxone 2 g q24h **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg q8h **IV**

IF MRSA SUSPECTED, CONSIDER ADDING

WATCH Vancomycin 15-20 mg/kg q12h **IV**

Necrotizing Fasciitis

Skin and Soft Tissue Infection

Definition

Life-threatening necrotizing infection of the deep soft tissues, specifically affecting the muscular fascia; caused mostly by bacteria and characterized by acute/fulminant necrosis with tissue destruction and systemic signs of toxicity

Classification based on:

- *Causative pathogen*:
  - Type 1/polymicrobial
  - Type 2/monomicrobial
- *Presence or absence of gas in tissues*
  - For example, presence of gas is common in polymicrobial infections
- *Involved site*:
  - Leg
  - Head and neck
  - Perineum (Fournier's gangrene)
- *Risk of poor outcome*:
  - High versus moderate risk

Most Likely Pathogens

Monomicrobial / Type 2:

- **Most cases:**
  - *Streptococcus pyogenes* (group A *Streptococcus*)
  - *Streptococcus agalactiae*
  - *Streptococcus dysgalactiae* (mostly in chronically ill patients)
- **Less frequently:**
  - *Staphylococcus aureus* (including MRSA)
- **Specific environmental exposures:**
  - *Aeromonas hydrophila* (freshwater)
  - *Vibrio vulnificus* (seawater)

Polymicrobial / Type 1:

- Anaerobes (e.g. *Bacteroides* spp., *Clostridium perfringens*, *Peptostreptococcus* spp. or mouth anaerobes when head/neck involved)
- Enterobacterales
- *Pseudomonas* spp.
- *Streptococcus* spp.
- *Staphylococcus aureus* (including MRSA)

Diagnosis

Clinical Presentation

- **Very rare**, may occur as a complication of varicella/chicken pox (or associated with a compromised immune system)
- Most elements described for adults also apply to children, but certain specificities exist:
  - Areas affected: torso (neonates and infants); extremities and face (older children)
  - Early signs and symptoms: fever >38.0°C, redness/skin discolouration, localized swelling, marked tenderness and pain of the affected area

Microbiology Tests

- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of deep samples of tissue collected at debridement to adjust empiric antibiotic treatment

Other Laboratory Tests

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

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

Initial evaluation for suspected necrotizing fasciitis:

- Complete blood count
- Creatinine
- Electrolytes
- Glucose

Imaging

Imaging should not delay surgical exploration/inspection since surgery is the best way to diagnose/treat this infection

- Ultrasound may be helpful to evaluate the extent of the affected tissue and gas and fluid along the muscular fascia
- Consider CT scan of the affected area

World Health Organization

CHILDREN

Necrotizing Fasciitis

Treatment

Clinical Considerations

- Clinical progression to severe disease is rapid, carefully monitor signs of sepsis/septic shock
- **Early surgical removal of necrotic tissue through drainage/debridement is key; delays associated with increased mortality**
- Antibiotic treatment is a complementary measure to surgical source control
- IVIG sometimes used when shock complicates necrotizing fasciitis (and toxic shock syndrome suspected) however very expensive and unclear effect on mortality

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

Usually **2-3 weeks**

Based on:

- Clinical response
- Surgical source control, and
- Evolution of laboratory markers of infection

Antibiotic Treatment

All dosages apply to normal renal function

WATCH — Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

COMBINED WITH

ACCESS — Clindamycin **IV**
- Neonates: 5 mg/kg/dose q8h
- Children: 10 mg/kg/dose q8h

OR

Use this treatment option only if Streptococcus pyogenes infection has been excluded first

WATCH — Ceftriaxone 80 mg/kg/dose q24h **IV**

COMBINED WITH

ACCESS — Metronidazole **IV**
- Neonates: 7.5 mg/kg/dose q12h
- Children: 7.5 mg/kg/dose q8h

IF MRSA SUSPECTED, CONSIDER ADDING

WATCH — Vancomycin **IV**
- Neonates: 15 mg/kg/dose q12h
- Children: 15 mg/kg/dose q8h

World Health Organization

ADULTS

Pyomyositis

Skin and Soft Tissue Infection

Definition

An infection of a skeletal muscle caused by bacteria usually accompanied by abscess formation

Diagnosis

Clinical Presentation

- Acute onset of localized muscle pain with cramping usually in the lower limbs/gluteal muscles with fever >38.0°C +/- swelling and induration of the affected area
- Other signs of systemic infection are usually present (e.g. tachycardia, leukocytosis)
- Abscess can form within days / weeks
- Signs of severe clinical progression (e.g. signs of sepsis/septic shock) should always be carefully monitored
- Complications due to bacteremia can occur (e.g. septic emboli, septic arthritis, endocarditis)

Microbiology Tests

- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of abscess fluid material (if this can be drained) to adjust empiric antibiotic treatment

Other Laboratory Tests

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

Imaging

Initial X-ray is important to localize the site and extent of the infection and/or to exclude alternative diagnosis
- Ultrasound is helpful to detect the presence of abscess (and to guide its drainage)
- If available, also consider MRI or CT-scan because of their higher sensitivity to identify muscle swelling (i.e. inflammation) and the presence of purulent material

Most Likely Pathogens

- *Staphylococcus aureus* (>90%, including MRSA*)
  - *Some strains can produce the Panton-Valentine leukocidin, a toxin that can cause a more severe disease. Consider especially in case of recurrent skin infections (decolonization measures can be considered to prevent recurrence and transmission)
- *Streptococcus* spp. (mostly *Streptococcus pyogenes*)
- *Escherichia coli* (sometimes, especially in oncologic patients)

Treatment

Clinical Considerations

- **Drainage of the abscess remains the main approach to eliminate the source of infection**
- Drainage is also important to obtain material for culture and identify the causative pathogen and its resistance profile
- **Mild:** Targeted antibiotic treatment preferred after having obtained culture results
- **Severe or impossible to obtain a clinical sample for microbiological examination:** Empiric treatment considering most likely pathogens including local prevalence and individual risk factors for MRSA

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

Treat for 2-3 weeks:
- 2 weeks in otherwise healthy patients and adequate source control
- 3 weeks if source control is not optimal or underlying diseases

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV** OR 875 mg+125 mg q8h **ORAL**

OR

ACCESS Cefalexin 500 mg q8h **ORAL**

OR

ACCESS Cloxacillin 2 g q6h **IV** OR 500 mg q6h **ORAL**

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

Pyomyositis

Skin and Soft Tissue Infection

Definition

An infection of a skeletal muscle caused by bacteria usually accompanied by abscess formation

Most Likely Pathogens

- *Staphylococcus aureus* (> 90%, including MRSA*)
  - *Some strains can produce the Panton-Valentine leukocidin, a toxin that can cause a more severe disease. Consider especially in case of recurrent skin infections (decolonization measures can be considered to prevent recurrence and transmission)
- *Streptococcus* spp. (mostly *Streptococcus pyogenes*)
- *Escherichia coli* (sometimes, especially in oncologic patients)

Diagnosis

Clinical Presentation

- Acute onset of localized muscle pain with cramping usually in the lower limbs/gluteal muscles with fever >38.0°C +/- swelling and induration of the affected area
- Other signs of systemic infection are usually present (e.g. tachycardia, leukocytosis)
- Abscess can form within days / weeks
- Signs of severe clinical progression (e.g. signs of sepsis/septic shock) should always be carefully monitored
- Complications due to bacteremia can occur (e.g. septic emboli, septic arthritis, endocarditis)

Microbiology Tests

- Blood cultures (ideally before starting antibiotics)
- Microscopy and culture of abscess fluid material (if this can be drained) to adjust empiric antibiotic treatment

Other Laboratory Tests

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

Imaging

Initial X-ray is important to localize the site and extent of the infection and/or to exclude alternative diagnosis

- Ultrasound is helpful to detect the presence of abscess (and to guide its drainage)
- If available, also consider MRI or CT-scan because of their higher sensitivity to identify muscle swelling (i.e. inflammation) and the presence of purulent material

Pyomyositis

Treatment

Clinical Considerations

• **Drainage of the abscess remains the main approach to eliminate the source of infection**

• Drainage is also important to obtain material for culture and identify the causative pathogen and its resistance profile

• **Mild:** Targeted antibiotic treatment preferred after having obtained culture results

• **Severe or impossible to obtain a clinical sample for microbiological examination:** Empiric treatment considering most likely pathogens including local prevalence and individual risk factors for MRSA

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

Treat for 2-3 weeks:

• 2 weeks in otherwise healthy patients and adequate source control

• 3 weeks if source control is not optimal or underlying diseases

Antibiotic Treatment

All dosages are for normal renal function

Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **IV/ORAL**

• **Oral weight bands**:

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

OR

ACCESS

Cefalexin 25 mg/kg/dose q12h **ORAL**

• **Oral weight bands:**

3-<6 kg	125 mg q12h
6-<10 kg	250 mg q12h
10-<15 kg	375 mg q12h
15-<20 kg	500 mg q12h
20-<30 kg	625 mg q12h
≥30 kg	500 mg q8h

OR

ACCESS

Cloxacillin **IV**

• Neonates: 25-50 mg/kg/dose q12h
• Children: 25 mg/kg/dose q6h
• **ORAL:** 15 mg/kg/dose q6h
• **Oral weight bands:**

3-<6 kg	62.5 mg q6h
6-<10 kg	125 mg q6h
10-<15 kg	250 mg q6h
15-<20 kg	375 mg q6h
≥20 kg	500 mg q6h

If cloxacillin is unavailable, any other IV antistaphylococcal penicillin could be used. For oral administration, dicloxacillin and flucloxacillin are preferred options within the class as they have better oral bioavailability

Febrile Neutropenia

This guidance covers suspected bacterial infections in neutropenic patients (including neutropenic sepsis) but not antiviral or antifungal treatment nor antibiotic prophylaxis for patients with afebrile neutropenia or prophylaxis with granulocyte colony-stimulating factors

Definition

• A severe syndrome that can occur in patients with neoplastic diseases receiving cytotoxic myelosuppressive chemotherapy

• Two elements need to be considered:
  • *Fever:* Body temperature ≥38.0°C
  • *Neutropenia:* Temporary reduction of the absolute neutrophil count (ANC) <1000 cells/µL (<1.0 x 10^9/L)

Severity:
• *Severe Neutropenia:* ANC <500 cells/µL (<0.5 x 10^9/L)
• *Profound Neutropenia:* ANC <100 cells/µL (<0.1 x 10^9/L)

Categorized by risk of developing severe infections (requiring or prolonging hospitalization):
• *Low Risk:* ≤7 days of severe neutropenia and no ongoing comorbidities (beside cancer) or renal or hepatic disfunction
• *High Risk:* >7 days of severe neutropenia and ongoing comorbidities (beside cancer) or renal or hepatic disfunction

Note: these are ways to classify neutropenia and narrow down the differential diagnosis

Characterized according to identification of causative pathogen and source of infection:
1. Microbiologically proven infection (causative pathogen identified)
2. Clinical source of infection diagnosed but no pathogen identified (e.g. pharyngitis)
3. Unexplained fever (no pathogen identified and no clear source of infection) (most common scenario)
4. Non-infectious fever (e.g. drug-induced)

Most Likely Pathogens

Mostly bacteria that colonize patient's own skin and bowel including multidrug-resistant organisms

Gram-positive bacteria:
• *Staphylococcus* spp. (including MRSA)
• *Streptococcus* spp.
• *Enterococcus* spp. (including vancomycin-resistant Enterococci)

Gram-negative bacteria:
• Enterobacterales and *Pseudomonas aeruginosa* (including ESBL and carbapenemase-producing strains)

Other pathogens:
• Anaerobes
• Consider fungi (mostly *Candida albicans* and *Aspergillus* spp.) and viruses (e.g. cytomegalovirus, human herpesvirus 6) if longer duration of neutropenia

Diagnosis

Clinical Presentation

• Presentation is highly variable depending on the underlying infection
• Fever is usually present but because patients with neutropenia fail to produce effective inflammatory responses, they can sometimes present with few clinical findings and no fever despite infection
• Clinical progression to severe disease or death can be very rapid (over a few hours); signs of sepsis/septic shock should always be carefully monitored

Microbiology Tests

Important: microbiology tests to consider in the initial assessment depend on the most likely source of infection and should ideally be taken before starting antibiotic treatment

Always obtain:
• Blood cultures
• Urine culture

In selected cases, consider:
• Sputum microscopy and culture
• Nasopharyngeal swab for nucleic acid test for influenza and other respiratory viruses (including SARS-CoV-2)
• Cerebrospinal fluid (CSF) microscopy and bacterial culture
• Stool culture
• *C. difficile* testing
• Tests to diagnose invasive fungal infections and other viral etiologies (especially in high-risk patients)

Other Laboratory Tests

Important: tests to consider in the initial assessment depend on the most likely source of infection

• Complete blood count, bilirubin, creatinine, electrolytes, blood pH and gases, whole blood lactate, C-reactive protein and/or procalcitonin

Imaging

• Consider imaging in initial assessment to identify the source of infection (depending on clinical presentation)
• Consider additional imaging to expand diagnostic work-up or to exclude a complicated infection if no clinical improvement after a few days of treatment

Febrile Neutropenia

Treatment

Clinical Considerations

- Antibiotic treatment should consider the most likely site of infection, local prevalence of resistance and individual risk factors for resistant pathogens (especially ESBL, carbapenemase-producing isolates and MRSA)
- In addition to antibiotic treatment, it is important that source control is achieved; consider removal of an infected Central Venous Catheter
- If fever persists and there is no clinical improvement after 48-72 hours, consider further tests to identify source or assess whether a local complication has developed (consider a resistant organism or non-bacterial infection)

Patients with severe neutropenia (<500 cells/µL or <0.5 x 10^9/L) who develop fever:

- Should promptly receive antibiotic treatment even when a clear site of infection is not identified

Low-risk patients:

- Outpatient setting with monitoring and follow-up, if oral treatment tolerated

High-risk patients (or close follow-up unfeasible):

- Hospitalization and initial IV treatment
- Step down from IV to oral antibiotics is suggested when the patient has clinically improved, is afebrile and is able to tolerate oral treatment

Antibiotic Treatment Duration

Low Risk Patients: **7 days**

High Risk Patients: Until clinical signs of infection resolved AND no fever for at least 48 hours

- Mostly depends on clinical response and (if identified) infectious site and causative pathogen
- Current evidence suggests discontinuation based on clinical approach and not neutrophil count

Important: If using combination therapy, reassess the need to continue combination over time based on microbiology test results and clinical response

Low Risk

Important: treatment escalation in case of persistent fever is beyond the scope of this guidance

All dosages are for normal renal function

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

CONSIDER ADDING

WATCH Ciprofloxacin 500 mg q12h **ORAL**

High Risk

Important: treatment escalation in case of persistent fever is beyond the scope of this guidance

All dosages are for normal renal function

First Choice

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

Second Choice

WATCH Meropenem 1 g q8h **IV**

Consider meropenem only in settings with high prevalence of ESBL-producing Enterobacterales or in patients with known prior colonization or infection with resistant pathogens

CONSIDER ADDING TO EITHER REGIMEN

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

If resistant Gram-negative bacteria suspected

AND/OR

WATCH Vancomycin 15-20 mg/kg q12h **IV**

If MRSA suspected

World Health Organization

CHILDREN

Febrile Neutropenia

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Other pathogens:
• Anaerobes
• Consider fungi (mostly *Candida albicans* and *Aspergillus* spp.) and viruses (e.g. cytomegalovirus, human herpesvirus 6) if longer duration of neutropenia

Diagnosis

Clinical Presentation

• Presentation is highly variable depending on the underlying infection
• Fever is usually present but symptoms and signs are masked and a child can present with no fever and few signs despite infection
• Clinical progression to severe disease or death can be very rapid (over a few hours); signs of sepsis/septic shock should always be carefully monitored

Microbiology Tests

Important: microbiology tests to consider in the initial assessment depend on the most likely source of infection and should ideally be taken before starting antibiotic treatment

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• Stool culture
• *C. difficile* testing
• Tests to diagnose invasive fungal infections and other viral etiologies (especially in high-risk patients)

Other Laboratory Tests

Important: tests to consider in the initial assessment depend on the most likely source of infection

• Complete blood count, bilirubin, creatinine, electrolytes, blood pH and gases, whole blood lactate, C-reactive protein and/or procalcitonin

Imaging

• Consider imaging in initial assessment to identify the source of infection (depending on clinical presentation)
• Consider additional imaging - CT chest and abdominal ultrasound to expand diagnostic work-up or to exclude a complicated infection if no clinical improvement after a few days of treatment

World Health Organization

CHILDREN

Febrile Neutropenia

Treatment

Clinical Considerations

- Antibiotic treatment should consider the most likely site of infection, local prevalence of resistance and individual risk factors for resistant pathogens (especially ESBL, carbapenemase-producing isolates and MRSA)
- In addition to antibiotic treatment, it is important that source control is achieved; consider removal of an infected Central Venous Catheter
- If fever persists and there is no clinical improvement after 48-72 hours, consider further tests to identify source or assess whether a local complication has developed (consider a resistant organism or non-bacterial infection)

Patients with severe neutropenia (<500 cells/µL or <0.5 x 10^9/L) who develop fever:

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Low-risk patients:

- Outpatient setting with monitoring and follow-up, if oral treatment tolerated

High-risk patients (or close follow-up unfeasible):

- Hospitalization and initial IV treatment
- Step down from IV to oral antibiotics is suggested when the patient has clinically improved, is afebrile and is able to tolerate oral treatment

Low Risk

All dosages are for normal renal function

ACCESS

Amoxicillin+clavulanic acid 80-90 mg/kg/day of amoxicillin component **ORAL**

- **Oral weight bands:**

3-<6 kg	250 mg of amox/dose q12h
6-<10 kg	375 mg of amox/dose q12h
10-<15 kg	500 mg of amox/dose q12h
15-<20 kg	750 mg of amox/dose q12h
≥20 kg	500 mg of amox/dose q8h or 1 g of amox/dose q12h

Amox = amoxicillin
Oral liquid must be refrigerated after reconstitution

CONSIDER ADDING

WATCH

Ciprofloxacin 15 mg/kg/dose q12h **ORAL**

- **Oral weight bands:**

3-<6 kg	50 mg q12h
6-<10 kg	100 mg q12h
10-<15 kg	150 mg q12h
15-<20 kg	200 mg q12h
20-<30 kg	300 mg q12h
≥30 kg	500 mg q12h

Antibiotic Treatment Duration

Low Risk Patients: **7 days**

High Risk Patients: Until clinical signs of infection resolved AND no fever for at least 48 hours

- Mostly depends on clinical response and (if identified) infectious site and causative pathogen
- Current evidence suggests discontinuation based on clinical approach and not neutrophil count

Important: If using combination therapy, reassess the need to continue combination over time based on microbiology test results and clinical response

High Risk

All dosages are for normal renal function

First Choice

WATCH

Piperacillin+tazobactam 100 mg/kg/dose of piperacillin component q8h **IV**

Second Choice

WATCH

Meropenem 20 mg/kg/dose q8h **IV**

Consider meropenem only in settings with high prevalence of ESBL-producing Enterobacterales or in patients with known prior colonization or infection with resistant pathogens

CONSIDER ADDING TO EITHER REGIMEN

ACCESS

Amikacin 15 mg/kg q24h **IV**

If resistant Gram-negative bacteria suspected

AND/OR

WATCH

Vancomycin **IV**

- Neonates: 15 mg/kg/dose q12h
- Children: 15 mg/kg/dose q8h

If MRSA suspected

World Health Organization

ADULTS

Surgical Prophylaxis

Antibiotic prophylaxis prior to dental surgeries is not addressed

Definition

Prevention of infectious complications by administering an effective antibiotic before exposure to contamination during surgery

Types of surgical procedures:

• **Clean:** Respiratory, alimentary, genital or urinary tracts are not entered during surgery

• **Clean-contaminated:** Respiratory, alimentary, genital or urinary tracts are entered under controlled conditions and without unusual contamination

• **Contaminated:** Significant interruptions in sterile technique or gross spillage from the gastrointestinal tract

WHO guidelines for the prevention of surgical site infections: https://apps.who.int/iris/handle/10665/277399

Most Likely Pathogens

Depends on the anatomical site of the procedure; often bacteria belonging to the human microbiota

Antibiotic Prophylaxis Before Surgical Procedures (Section 1 of 2)

Clinical Considerations

• Choice of antibiotic prophylaxis depends on the type and anatomical site of surgical procedure

• Patients colonized with multidrug-resistant Gram-negative bacteria: Lack of high-quality evidence to support expanding the spectrum of antibiotic prophylaxis; decisions usually made on a case-by-case basis

• Patients colonized with MRSA who will have a skin incision: Consider adding vancomycin to the routine recommended surgical regimen

Timing of Antibiotic Prophylaxis

120 minutes or less before starting surgery

Single dose before surgery. Do not continue the antibiotic after the surgical procedure to prevent infection. Consider an additional dose only for prolonged procedures or if major blood loss.

Bowel Surgery

Includes appendectomy, small intestine and colorectal surgical procedures

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 2 g single dose **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg single dose **IV**

Second Choice

ACCESS Amoxicillin+clavulanic acid 2 g+200 mg single dose **IV**

World Health Organization

ADULTS

Surgical Prophylaxis

℞ Antibiotic Prophylaxis Before Surgical Procedures (Section 2 of 2)

℞ Clean or Clean-Contaminated Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 2 g single dose **IV**

Second Choice

WATCH Cefuroxime 1.5 g single dose **IV**

℞ Urologic Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 2 g single dose **IV**

Second Choice

ACCESS Gentamicin 5 mg/kg single dose **IV**

℞ Contaminated Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 2 g single dose **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg single dose **IV**

Second Choice

ACCESS Amoxicillin+clavulanic acid 2 g+200 mg single dose **IV**

OR

ACCESS Gentamicin 5 mg/kg single dose **IV**

COMBINED WITH

ACCESS Metronidazole 500 mg single dose **IV**

Gentamicin should be given in combination with metronidazole because, if given alone, it provides insufficient coverage of anaerobic bacteria

World Health Organization

CHILDREN

Surgical Prophylaxis

Antibiotic prophylaxis prior to dental surgeries is not addressed

Definition

Prevention of infectious complications by administering an effective antibiotic before exposure to contamination during surgery

Types of surgical procedures:

• **Clean:** Respiratory, alimentary, genital or urinary tracts are not entered

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WHO guidelines for the prevention of surgical site infections: https://apps.who.int/iris/handle/10665/277399

Most Likely Pathogens

Depends on the anatomical site of the procedure; often bacteria belonging to the human microbiota

Rx Antibiotic Prophylaxis Before Surgical Procedures (Section 1 of 2)

Clinical Considerations

• Choice of antibiotic prophylaxis depends on the type and anatomical site of surgical procedure

• Patients colonized with multidrug-resistant Gram-negative bacteria: Lack of high-quality evidence to support expanding the spectrum of antibiotic prophylaxis; decisions usually made on a case-by-case basis

• Patients colonized with MRSA who will have a skin incision: Consider adding vancomycin to the routine recommended surgical regimen

Timing of Antibiotic Prophylaxis

120 minutes or less before starting surgery

Single dose before surgery. Do not continue the antibiotic after the surgical procedure to prevent infection. Consider an additional dose only for prolonged procedures or if major blood loss.

Rx Bowel Surgery

Includes appendectomy, small intestine and colorectal surgical procedures

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 50 mg/kg single dose **IV**

COMBINED WITH

ACCESS Metronidazole 7.5 mg/kg single dose **IV**

Second Choice

ACCESS Amoxicillin+clavulanic acid 40-50 mg/kg of amoxicillin component single dose **IV**

World Health Organization

CHILDREN

Surgical Prophylaxis

℞ Antibiotic Prophylaxis Before Surgical Procedures (Section 2 of 2)

℞ Clean or Clean-Contaminated Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 50 mg/kg single dose **IV**

Second Choice

WATCH Cefuroxime 50 mg/kg single dose **IV**

℞ Urologic Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 50 mg/kg single dose **IV**

Second Choice

ACCESS Gentamicin single dose **IV**
- Neonates: 5 mg/kg
- Children: 7.5 mg/kg

℞ Contaminated Procedure

All dosages are for normal renal function

First Choice

ACCESS Cefazolin 50 mg/kg single dose **IV**

COMBINED WITH

ACCESS Metronidazole 7.5 mg/kg single dose **IV**

Second Choice

ACCESS Amoxicillin+clavulanic acid 40-50 mg/kg of amoxicillin component single dose **IV**

OR

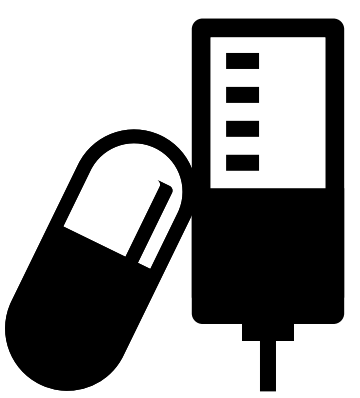
ACCESS Gentamicin single dose **IV**
- Neonates: 5 mg/kg
- Children: 7.5 mg/kg

COMBINED WITH

ACCESS Metronidazole 7.5 mg/kg single dose **IV**

Gentamicin should be given in combination with metronidazole because, if given alone, it provides insufficient coverage of anaerobic bacteria

World Health Organization



Reserve Antibiotics

World Health Organization

RESERVE

Cefiderocol

Pharmacology

- Siderophore cephalosporin
- **Mechanism of Action:** Inhibition of bacterial enzymes responsible for cell-wall synthesis

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed carbapenem-resistant Enterobacterales and/or *P. aeruginosa* (particularly infections caused by MBL-producing pathogens)
  - Caution needed with *A. baumannii* infections because of higher mortality than best available alternative therapy described in a clinical trial (https://pubmed.ncbi.nlm.nih.gov/33058795/)

Empiric Use

- Only in very selected cases of seriously ill patients (e.g. sepsis/septic shock):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded first and there is strong suspicion that the infection is caused by a carbapenem-resistant pathogen (especially in settings with a high prevalence of MBL-producing pathogens)
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to cefiderocol
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to cefiderocol

Important Considerations

- Efficacy demonstrated in clinical trials for empiric use for complicated UTI, VAP/HAP, BSI and sepsis in adults
- Very limited evidence for other infections and use in children

Formulations

- Powder for intravenous infusion: 1 g/vial

Spectrum of Activity

- **Active against:**
  - Aerobic Gram-negative bacteria including many carbapenem-resistant Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*
    - Carbapenemases: KPC, OXA-48 and metallo-β-lactamases (MBL)
    - ESBL and AmpC β-lactamases
- **Not active against:**
  - Gram-positive bacteria and anaerobes
- **New resistance to Cefiderocol in Enterobacterales, *A. baumanii* and *P. aeruginosa*:**
  - The proportion of isolates resistant to cefiderocol is low but data is very limited

Toxicity

Well tolerated with side effects similar to other beta-lactams (mostly gastrointestinal)

Dose

Antibiotic Treatment Duration

- Treatment duration varies according to indication and should be as short as possible
- Usually between **7-14 days**

Adults

Dosage is for normal renal function; dose adjustment required in case of renal impairment

RESERVE Cefiderocol 2 g q8h **IV**

Children or Neonates

No data for children or neonates

World Health Organization

RESERVE

Ceftazidime+Avibactam

Pharmacology

- Combination of a third-generation cephalosporin (ceftazidime) and a novel non-β-lactam β-lactamase inhibitor (avibactam)
- **Mechanism of Action:**
  - Ceftazidime inhibits bacterial enzymes responsible for cell-wall synthesis
  - Avibactam inactivates certain serine β-lactamases, protecting ceftazidime from degradation

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed carbapenem-resistant Enterobacterales or *P. aeruginosa* (not *A. baumannii*) susceptible to ceftazidime+avibactam (CAZ-AVI)

Empiric Use

- Only in very select cases of seriously ill patients (e.g. patients with sepsis/septic shock):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded first and there is strong suspicion that the infection is caused by a carbapenem-resistant pathogen
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to CAZ-AVI
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to CAZ-AVI

Important Considerations

- When used to treat complicated intra-abdominal infections CAZ-AVI should be given with metronidazole due to its unpredictable activity against anaerobes
- Since it is not active against metallo-β-lactamases, it is important to know the local epidemiology of the most prevalent genotypes for aerobic Gram-negative bacteria

Formulations

- Powder for intravenous infusion: 2 g + 500 mg in vial

Toxicity

- Side effects are similar to those previously reported for ceftazidime alone
- The most frequent are diarrhoea, nausea and vomiting

Spectrum of Activity

- **Active against:**
  - Aerobic Gram-negative bacteria including ceftazidime-resistant and many carbapenem-resistant isolates Enterobacterales and *Pseudomonas aeruginosa*
    - Carbapenemases: KPC and OXA-48
    - ESBL and AmpC β-lactamases
- **Variable activity against:**
  - *Streptococcus* spp.
  - *Staphylococcus* spp.
  - Anaerobes
- **Not active against:**
  - Metallo-β-lactamase-producing Gram-negative bacteria (inactive against NDM, VIM, IMP carbapenemases unless co-prescribed with aztreonam)
  - *Enterococcus* spp.
  - *Acinetobacter* spp.
- **New resistance to CAZ-AVI in Enterobacterales and *Pseudomonas aeruginosa*:**
  - The proportion of isolates resistant to CAZ-AVI is low (higher for *P. aeruginosa*) with geographical variability

Dose

Antibiotic Treatment Duration

- Treatment duration varies according to indication and should be as short as possible
- Usually between **7-14 days**

Adults

Dosage is for normal renal function; dose adjustment required in case of renal impairment

RESERVE Ceftazidime+avibactam 2.5 g (2 g ceftazidime + 500 mg avibactam) q8h **IV**

Children

Dosage is for normal renal function; dose adjustment required in case of renal impairment

RESERVE Ceftazidime+avibactam 62.5 mg/kg (50 mg/kg ceftazidime + 12.5 mg/kg avibactam; Max 2 g ceftazidime + 500 mg avibactam) q8h **IV**

World Health Organization

RESERVE

Fosfomycin

This infographic only addresses the IV formulation of fosfomycin. Oral formulations are not currently included in the EML/EMLc

Pharmacology

- Antibiotic belonging to the class of phosphonic acid antibiotics
- **Mechanism of Action:** Inhibition of bacterial enzymes responsible for cell-wall synthesis

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed carbapenem-resistant Enterobacterales or *Pseudomonas aeruginosa* susceptible to fosfomycin
- Salvage therapy for otherwise untreatable infections caused by MRSA and vancomycin-resistant *Enterococcus* (VRE) susceptible to fosfomycin

Empiric Use

- Only in very select cases of seriously ill patients (e.g. sepsis/septic shock):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded and there is strong suspicion that the infection is caused by a carbapenem-resistant pathogen
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to fosfomycin
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to fosfomycin

Important Considerations

- Usually given in combination with other antibiotics due to concerns about the rapid emergence of resistance when used alone
- Very limited data from clinical trials about efficacy and safety (children and adults)

Formulations

- Powder for intravenous infusion: 2 g/vial or 4 g/vial (as sodium)

Spectrum of Activity

- **Active against:**
  - ESBL and AmpC β-lactamases-producing Enterobacterales
  - Gram-positive bacteria including MRSA, VRE and *S. epidermidis*
- **Variable activity against:**
  - *Pseudomonas aeruginosa*
  - Aerobic Gram-negative bacteria including many carbapenem-resistant Enterobacterales
    - Carbapenemases: KPC, OXA-48 and metallo-β-lactamases (MBL)
- **Not active against:**
  - *Acinetobacter baumannii*
- **New resistance to fosfomycin in Enterobacterales:**
  - Rare in clinical practice even though it can rapidly develop *in vitro*

Toxicity

- Generally well tolerated
- Consider risk of:
  - Sodium overload in patients with heart failure (related to the sodium salt formulation)
  - Hypokalaemia (need to monitor potassium levels regularly)

Dose

Antibiotic Treatment Duration

- Treatment duration varies according to indication and should be as short as possible
- Usually between **7-14 days**

Adults

Dosage is for normal renal function; dose adjustment required in case of renal impairment

RESERVE

Fosfomycin 6 g q8h **IV**
- Total daily dose may vary: range 12-24 g depending on indication and renal function

Children

Dosage is for normal renal function

RESERVE

Fosfomycin 200-400 mg/kg/day divided q6-8h **IV**

World Health Organization

RESERVE

Linezolid

Pharmacology

- Synthetic antibiotic of the oxazolidinone class
- **Mechanism of Action:** Inhibition of bacterial protein synthesis

Spectrum of Activity

- **Active against:**
  - Gram-positive bacteria including MRSA, VRE and penicillin non-susceptible pneumococci
  - *Mycobacterium tuberculosis* including extensively drug-resistant strains
- **Not active against:**
  - Gram-negative bacteria
  - Anaerobes
- **New resistance to Linezolid in MRSA, VRSA, VRE:**
  - Reported but remains low

Indications for Use

Targeted Treatment

- MRSA infections in selected situations:
  - Severe renal impairment
  - Hypersensitivity to vancomycin
  - Need to use oral treatment and other cheaper oral options are unavailable or not indicated
- VRSA or VRE infections
- Mycobacterial infections, including extensively drug-resistant *M. tuberculosis* (second-line option)

Empiric Use

Only in very selected cases of seriously ill patients with invasive infections who are known to be colonized with VRE or VRSA

Important Considerations

The high oral bioavailability of linezolid allows initiation with oral treatment as an alternative to intravenous treatment

Formulations

- Solution for intravenous infusion: 2 mg/mL in 300 mL bag
- Oral formulations:
  - Tablet: 400 mg; 600 mg
  - Tablet (dispersible): 150 mg
  - Powder for oral liquid: 100 mg/5 mL

Toxicity

- Generally well tolerated, risks increase with prolonged use (>4 weeks)
- Consider risk of:
  - Myelosuppression (mostly thrombocytopenia)
    - Monitor complete blood cell count every week
  - Severe optic neuropathy and peripheral neuropathy (both rare)

Dose

Antibiotic Treatment Duration

Treatment duration varies according to indication and should be as short as possible (increased risk of side effects if used for >4 weeks)

Adults

Dosage is for normal renal function; no need to adjust the dose in case of renal impairment

RESERVE Linezolid 600 mg q12h **IV/ORAL**

Children

Dosage is for normal renal function; no need to adjust the dose in case of renal impairment

RESERVE Linezolid 10 mg/kg q8h **IV/ORAL**

Neonates

Dosage is for normal renal function; no need to adjust the dose in case of renal impairment

RESERVE Linezolid **IV/ORAL**
- 1st week of life: 10 mg/kg q12h
- >1st week of life: 10 mg/kg q8h

World Health Organization

RESERVE

Meropenem+Vaborbactam

Pharmacology

- Combination of a carbapenem (meropenem) and a new β-lactamase inhibitor (vaborbactam)
- **Mechanism of Action:**
  - Meropenem inhibits bacterial enzymes responsible for cell wall synthesis
  - Vaborbactam inactivates certain serine β-lactamases, thus protecting meropenem from degradation

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed KPC-producing Enterobacterales, including bacteria resistant to ceftazidime+avibactam but susceptible to meropenem+vaborbactam

Empiric Use

- Only in very selected cases of seriously ill patients (e.g. sepsis/septic shock):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded and there is strong suspicion that the infection is caused by a carbapenem-resistant pathogen
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to meropenem+vaborbactam
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to meropenem+vaborbactam

Important Considerations

- Since it is not active against metallo-β-lactamases (Ambler class B) or class D carbapenemases (such as OXA-48), it is important to know the local epidemiology of the most prevalent genotypic variants for aerobic Gram-negative bacteria

Formulations

- Powder for intravenous infusion: 1 g + 1 g in vial

Spectrum of Activity

- **Active against:**
  - Aerobic Gram-negative bacteria including many carbapenem-resistant Enterobacterales
    - KPC Carbapenemases
    - ESBL and AmpC β-lactamases
  - Aerobic Gram-positive bacteria
  - Anaerobes
- **Variable activity against:**
  - *Acinetobacter baumannii*
  - *Pseudomonas aeruginosa*
- **Not active against:**
  - Gram-negative bacteria producing metallo-β-lactamases (NDM, VIM, IMP) or Ambler class D carbapenemases (such as OXA-48)
- **New resistance to meropenem+vaborbactam in Enterobacterales:**
  - Very rare in clinical practice

Toxicity

- Generally well tolerated
- Side effects similar to meropenem alone

Dose

Antibiotic Treatment Duration

- Treatment duration varies according to indication and should be as short as possible
- Usually between **7-14 days**

Adults

Dosage is for normal renal function; dose adjustment required in case of renal impairment

RESERVE Meropenem+vaborbactam 4 g (2 g meropenem + 2 g vaborbactam) q8h **IV**

Children or Neonates

Currently not licensed for use in children or neonates

World Health Organization

RESERVE

Plazomicin

Pharmacology

- New semisynthetic aminoglycoside
- **Mechanism of Action:** Inhibition of bacterial protein synthesis

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed carbapenem-resistant Enterobacterales susceptible to plazomicin (not *P. aeruginosa* or *A. baumannii*)
- Infections caused by Gram-negative bacteria resistant to other aminoglycosides

Empiric Use

- Only in very selected cases of seriously ill patients (e.g. sepsis/septic shock caused by urinary tract infections if used as monotherapy - for other infections aminoglycosides are usually used in combination with other antibiotics):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded first and there is strong suspicion that the infection is caused by a carbapenem-resistant pathogen
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to plazomicin
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to plazomicin

Important Considerations

- Efficacy demonstrated in clinical trials only for complicated urinary tract infections in adults
- Very limited evidence for other infections and use in children

Formulations

- Intravenous injection: 500 mg/10 mL

Spectrum of Activity

- **Active against:**
  - Aerobic Gram-negative bacteria including many carbapenem-resistant Enterobacterales
    - Carbapenemases: KPC and OXA-48
    - ESBL and AmpC β-lactamases
  - Bacteria producing aminoglycoside-modifying enzymes
- **Variable activity against:**
  - Strains producing metallo-β-lactamases
- **Not active against:**
  - *Acinetobacter baumannii*
  - *Pseudomonas aeruginosa*
- **New resistance to Plazomicin in Enterobacterales:**
  - Very limited data

Toxicity

- Side effects similar to other aminoglycosides
- The most frequent are:
  - Kidney damage (monitor creatinine levels regularly)
  - Hearing loss and vestibular toxicity

Dose

Antibiotic Treatment Duration

- Treatment duration varies according to indication and should be as short as possible
- Usually between **7-14 days**

Adults

Weight-based once-daily dosing is used; dosage is for normal renal function

RESERVE Plazomicin 15 mg/kg q24h **IV**

Children or Neonates

No data for children or neonates

World Health Organization

RESERVE

Polymyxin B and Colistin (Polymyxin E)

Pharmacology

- Polymyxin B and colistin are polypeptides belonging to the polymyxin class of antibiotics
- Polymyxin B and colistin have very similar chemical structures, however:
  - Polymyxin B is administered directly as the active antibiotic
  - Colistin is administered as inactive prodrug (colistimethate sodium)
- **Mechanism of Action:** Polymyxin B and colistin act by disrupting the bacterial cell membrane, leading to cell lysis

Spectrum of Activity

- Polymyxin B and colistin have the same antibacterial spectrum
  - **Active against:**
    - Aerobic Gram-negative bacteria (including many multi-drug resistant isolates)
  - **Not active against:**
    - Anaerobes
    - Gram-positive bacteria
    - Gram-negative cocci (e.g. *Neisseria* spp.)
- **New resistance to Polymyxins in Enterobacterales, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*:**
  - Resistance can be due to chromosomal mutations leading to changes in the bacterial membrane that impair the ability of polymyxin B and colistin to bind to their target
  - Transmissible resistance due to mobilized colistin resistance (mcr) genes is also being increasingly described

Toxicity

- Polymyxin B and colistin can cause kidney damage (colistin > polymyxin B) and, more rarely, neurotoxicity (e.g. paresthesia)
- Side effects are reversible in most cases and are associated with the cumulative dose and duration of therapy

Indications for Use

Targeted Treatment

- Severe infections caused by laboratory-confirmed carbapenem-resistant Gram-negative bacteria susceptible to polymyxins (including infections caused by carbapenemase-producing strains susceptible to polymyxins)

Empiric Use

- Only in very selected cases of seriously ill patients (e.g. patients with sepsis/septic shock):
  - who have not responded to carbapenems if other causes of treatment failure have been excluded first and there is a strong suspicion that the infection is caused by a carbapenem-resistant pathogen
  - who have previously been treated for infections caused by carbapenem-resistant pathogens susceptible to polymyxins
  - who are known to be colonized with carbapenem-resistant pathogens susceptible to polymyxins

Important Considerations

- If both are available, polymyxin B is usually preferred to colistin (**important:** except for urinary tract infections) because it has better pharmacokinetic characteristics and less potential to cause kidney damage
- Usually given as part of combination therapy depending on the type of infection even though currently there is no evidence from randomized clinical trials that combination therapy was superior to colistin monotherapy for short-term clinical success – at least for infections caused by extensively drug-resistant *Acinetobacter* spp.

World Health Organization

RESERVE

Polymyxin B and Colistin (Polymyxin E)

Formulations

Polymyxin B:
• Powder for intravenous infusion: 50 mg (500 000 IU) in vial
Colistin:
• Powder for intravenous infusion: 1 million IU (as colistimethate sodium) in vial (equivalent to 34 mg colistin base activity)

Clinical Considerations

• Great care must be taken to avoid dosing errors with polymyxin B and colistin; errors can arise because doses can be given in different units on labels

• **Polymyxin B doses** can be expressed in:
  • mg
  • International Units (IU)
• 1 mg of polymyxin B corresponds to 10 000 IU

• **Colistin (polymyxin E) doses** can be expressed in:
  • International Units (IU) of colistimethate sodium (CMS)
  • mg of colistimethate sodium
  • mg of colistin base activity (CBA)
• 34 mg of colistin base activity corresponds to:
  • 1 million IU of colistimethate sodium
  • 80 mg of colistimethate sodium

• When using polymyxins, it is crucial to start therapy with a loading dose (to achieve more rapidly effective plasma concentrations) followed by maintenance dose after 12-24 hours

• For colistin (but not for polymyxin B), dose adjustments are necessary in cases of renal impairment

Adults

All dosages are for normal renal function

Polymyxin B

RESERVE
Polymyxin B **IV**
• Loading dose: 2.5 mg/kg (25 000 IU/kg)
• Maintenance dose: 1.5 mg/kg (15 000 IU/kg) q12h

Colistin

RESERVE
Colistin **IV**
• Loading dose: 300 mg CBA (9 Million IU of CMS)
• Maintenance dose: 150 mg CBA q12h (4.5 Million IU CMS q12h)

Dose

Antibiotic Treatment Duration

• Treatment duration varies according to indication and should be as short as possible

• Usually between **7-14 days**

Children

All dosages are for normal renal function

Few data are available for dosing in children; doses approved by regulatory agencies may be suboptimal for many children due to interpatient variability

Polymyxin B

RESERVE
Polymyxin B **IV**
• Loading dose: 2.5 mg/kg (25 000 IU/kg)
• Maintenance dose:
  • *Children <2 years*: 0.75-2.25 mg/kg (7 500–22 500 IU/kg) q12h
  • *Children ≥2 years*: 1.5 mg/kg (15 000 IU/kg) q12h

Colistin

RESERVE
Colistin **IV**
• 0.625-1.25 mg/kg CBA (18 750-37 500 IU/kg CMS) q6h
• 1.25-2.5 mg/kg CBA (37 500-75 000 IU/kg CMS) q12h

Neonates

All dosages are for normal renal function

Polymyxin B

RESERVE
Polymyxin B **IV**
• Loading dose: 2.5 mg/kg (25 000 IU/kg)
• Maintenance dose: 0.75-2.25 mg/kg (7 500-22 500 IU/kg) q12h

Colistin

RESERVE
Colistin **IV**
• 0.625-1.25 mg/kg CBA (18 750-37 500 IU/kg CMS) q6h
• 1.25-2.5 mg/kg CBA (37 500-75 000 IU/kg CMS) q12h