­­CHAPTER 9

SYSTEMIC AND HEALTHCARE-ASSOCIATED INFECTIONS

## ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship refers to a systematic approach to optimising the appropriate use of an antibiotic to improve patient outcome(s) and limit emergence of resistant pathogens, whilst ensuring patient safety. It is one arm of the national and international response to the increasing public health crisis of antibiotic resistance. A critical component is adequate infection control. Antibiotics should only be used for the treatment and prevention of bacterial infections. The following checklist will help optimize prescribing:

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| **Checklist for optimal antibiotic prescribing** |
| 1. **Medicine** – which is the narrowest-spectrum antibiotic that I can use to treat this bacterial infection?
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| 1. **Dose** – many antibiotics require weight-based dosing and their dosing depends on renal and/or hepatic function
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| 1. **Dose frequency** – dependent on the half-life of the drug and whether the action of the antibiotic depends on the time above the MIC, the peak concentration relative to MIC, or the area under the concentration/time curve. Guidance for dosing frequency may require therapeutic drug monitoring, e.g. vancomycin and aminoglycosides.
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| 1. **Duration** – should be dictated by evidence from randomised controlled trials whenever possible. Expert opinion from national and international guidelines should be consulted where evidence is weak.
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| 1. **Route** – most antibiotics have good oral bioavailability, but some infections will require intravenous therapy either for the whole or part of the course. Patients who are critically ill, or who would be expected to have impaired gastrointestinal absorption of medicines (e.g. excessive vomiting) may also require intravenous antibiotics initially.
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| 1. **De-escalation** – applies to the spectrum of antibiotic use and route of administration. All attempts to convert early from parenteral to oral use should be made.
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| MIC = minimum inhibitory concentration. |

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# 9.1 HEALTHCARE-ASSOCIATED AND HOSPITAL AcQUIRED INFECTIONS

### Definition and principles

Patients with healthcare associated and hospital acquired infections are at increased risk of being infected with drug resistant organisms. A hospital acquired infection is a new infection that develops after at least 48 hours of hospitalisation without evidence that the infection was present or incubating at the time of admission. Healthcare-associated infections should also be considered in persons with extensive healthcare contact such as: residence in a nursing home or other long-term care facility, hospitalisation in an acute care hospital for >2 days during the prior 90 days, or attendance at a hospital or haemodialysis clinic during the prior 30 days.

**It is essential to obtain specimens for culture and sensitivity testing in all cases before starting antibiotics.**

Empiric therapy suggestions below are only rough guidelines due to heterogenity of resistance patterns between facilities and over time. Close liaison with regional microbiologists and regular review of hospital antibiotic policy based on local resistance patterns are essential.

## 9.1.1 Intravascular catheter infections

L53.9/t80.2 + (B95.8/Y84.8/B37.8)

### Peripheral line Infection:

Common organisms:

1. coagulase negative staphylococci, particularly *S. epidermis*
2. *S. aureus*

**The intravascular line should always be removed.**

Small, localised area of erythema at the catheter insertion site will usually resolve without antibiotic therapy.

In patients with larger areas of erythema and tenderness extending beyond the insertion site who are systemically well:

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| *LoE:IIIb[[1]](#endnote-2)* |

* Clindamycin, oral, 450 mg 8 hourly for 5 days.

If patients are systemically unwell they should be treated as for a central venous catheter related systemic blood infection.

### SHORT-TERM CENTRAL VENOUS CATHETER INFECTION

Microbiologic specimens: peripheral blood culture, blood culture from central catheter prior to removal, and culture of the catheter tip.

If peripheral blood culture negative but central catheter culture positive, monitor closely for signs of infection, and repeat peripheral blood cultures accordingly. If central line has grown *S. aureus*, 5-7 days of treatment is recommended (assuming peripheral blood cultures remain negative).

If peripheral blood culture is positive, remove catheter, and treat with systemic antibiotics, guided by the culture results.

Duration of antibiotic therapy should generally be for 48–72 hours after resolution of fever **except** for:

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| *LoE:IIIb[[2]](#endnote-3)* |

1. confirmed *S. aureus* infection, and
2. candidaemia,

where treatment should be continued for 2 weeks after the 1st negative

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| *LoE:IIIb[[3]](#endnote-4)* |

 blood culture.

**Note:** For candidaemia and *S. aureus* infection, perform blood cultures every 2-3 days after therapy has been initiated until 2 consecutive cultures are negative, and 2 weeks after the 1st negative blood culture.

**Empiric antibiotic therapy *(prior to obtaining susceptibility results):***

***S. aureus* infection** (B95.8/Y84.8)

* Vancomycin, IV, 25–30 mg/kg, empirically as a loading dose.
* Follow with 15­–20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and therapeutic drug monitoring).

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| *LoE:IIIa[[4]](#endnote-5)* |

* Tailor therapy to drug-susceptibility results.

**Candidaemia** (B37.8/Y84.8)

**Note:** Candida isolated from blood culture should **always** be treated, even if the fever has settled after line removal because of a high risk of late complications.

Candidaemia with species other than *Candida albicans* is becoming increasingly common – these species are often resistant to azoles.

Treatment duration should be 2 weeks after 1st negative blood culture:

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| *LoE:IIa[[5]](#endnote-6)* |

* Amphotericin B, IV, 0.7 mg/kg daily.
* Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and

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| *LoE:Ia[[6]](#endnote-7)* |

 management of toxicity).

Follow up susceptibility:

Once improved, if sensitive complete course with:

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| *LoE:IIa[[7]](#endnote-8)* |

* Fluconazole, oral, 800 mg daily.

Invasive candidiasis (resistant to fluconazole/amphotericin B or renal impairment is present and amphotericin B cannot be used):

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| *LoE:IIIb[[8]](#endnote-9)* |

* Echinocandins. (Specialist motivation).

**REFERRAL/CONSULTATION**

*S. aureus* endocarditis.

## 9.1.2 Surgical wound infections

t81.4 + (Y83.6/Y83.8-9/B95.6/U82.1)

### description

Common organisms: Gram positive bacteria, especially *S. aureus*, are the commonest cause. Gram negative and anaerobic bacteria are important causes following gynaecological and intestinal surgery.

Microbiologic specimen (in patients with a larger area of erythema or systemic evidence of infection): deep wound swab (NOT a superficial swab), aspirate of pus, or tissue biopsy, and blood culture.

Suture removal plus incision and drainage is essential. Antibiotics are not usually necessary except if there is marked surrounding cellulitis or features of systemic infection.

### medicine treatment

**Empiric antibiotic therapy:** Total duration of therapy should not exceed 7 days.

**If surrounding cellulitis or systemic sepsis not involving the gastro-intestinal (GI) or female genital tract:**

* Cefazolin, IV, 1 g 8 hourly.

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| *LoE:IIa[[9]](#endnote-10)* |

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8oC for 24 hours:

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| *LoE:IVb[[10]](#endnote-11)* |

* Flucloxacillin, oral, 500 mg 6 hourly.

Check Gram stain of exudate. If Gram negative organism:

**ADD**

* Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

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| *LoE:IVb* |

**Severe penicillin allergy:** (Z88.0)

* Clindamycin, IV, 600 mg 8 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8oC for 24 hours, based on culture results:

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| *LoE:IIIb[[11]](#endnote-12)* |

* Clindamycin, oral, 450 mg 8 hourly, and

Check Gram stain of exudate. If Gram negative organism:

**ADD**

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| *LoE:Ia[[12]](#endnote-13)* |

* Ertapenem, IV, 1g daily.

**Methicillin (cloxacillin) reistant *S. aureus* (MRSA)**

T81.4+(B95.6+U82.1+Y83.9)

* Vancomycin, IV, 25–30 mg/kg as a loading dose. Follow with 15–20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and monitoring).

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| *LoE:IIIb[[13]](#endnote-14)* |

* Drain wound and obtain cultures to verify MRSA.

**If female uro-genital tract surgery or open GIT surgery:**

T81.4 +(Y83.6/Y83.8)

* Ceftriaxone, IV, 2 g daily.

**AND**

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| *LoE:IIIb[[14]](#endnote-15)* |

* Metronidazole, IV, 500 mg 8 hourly.

## 9.1.3 Hospital-acquired pneumonia (HAP) and VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

J12.0-3/J12.8-9/J13/J14/J15.0-9/J16.0/J16.8/J18.0-2/J18.8-9 + (Y95)

**Note:** If patient is neutropaenic - See section 2.2: Febrile neutropenia.

### description

HAP is defined as a new lung infiltrate (not present on admission) plus clinical evidence that the infiltrate is an infection (e.g. new onset of fever, purulent sputum, leukocytosis) occurring >48 hours after admission to hospital. HAP has a high morbidity and mortality and early appropriate antibiotic therapy is essential.

Infection may be due to multi-drug resistant organisms, particularly in

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| *LoE:IIa[[15]](#endnote-16)* |

patients with prior intravenous antibiotic use within 90 days.

Ventilator-associated pneumonia (VAP) occurs >48 hours after intubation. VAP is more often due to multi-drug resistant organisms than HAP.

Microbiologic specimens: blood culture and sputum/tracheal aspirate bacterial culture. Therapy should be adjusted according to culture result. A good quality Gram stain may be useful in guiding the choice of initial therapy.

### MEDICINE treatment

**Empiric antibiotic therapy**

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| *LoE:IIa[[16]](#endnote-17)* |

Duration: 7 days.

Antibiotic choice will depend on local susceptibility patterns: NICD AMR surveillance dashboard

* Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

**and**

* Amikacin, IV, 15 mg/kg daily. (See Appendix II, for individual dosing and monitoring for response and toxicity).

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| *LoE:IIIb[[17]](#endnote-18)* |

**OR ALTERNATIVE**

* Cefepime, IV, 2 g 12 hourly. (See Appendix II for guidance on dosing in renal impairment).

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| *LoE:IIIb[[18]](#endnote-19)* |

**IF HIGH LOCAL RESISTANCE RATES TO THE ABOVE REGIMENS, THEN CONSIDER CARBAPENEM**

Instead of piperacillin/tazobactam + amikacin **OR** cefepime:

Carbapenem with activity against Pseudomonas:

* Imipenem/cilastin, IV, 1000/1000 mg 8 hourly.

**Note:** Do not use imipenem/cilastin in patients with central nervous system disorders or history of seizures. for patients with known epilepsy – use

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| *LoE:IVb[[19]](#endnote-20)* |

meropenem.

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| *LoE:IIIb[[20]](#endnote-21)* |

**OR**

Instead of piperacillin/tazobactam + amikacin **OR** cefepime **OR** imipenem:

* Meropenem, IV, 2 g 8 hourly (known epileptics).

**Note:**

1. De-escalate as soon as the culture is available.
2. For severe pencillin allergy, consult an infectious diseases specialist or microbiologist.

## 9.1.4 Urinary tract infections, catheter associated

T83.5 + (Y84.6+N39.0)

### description

Common organisms: resistant aerobic Gram-negative bacteria.

Microbiologic specimen: blood culture and MSU/CSU for microscopy and bacterial culture.

In most patients with long-term catheters bacteria cultured on CSU represent colonisation rather than infection – only treat with antibiotics if there are features of sepsis or pyelonephritis.

**GENERAL MEASURES**

Remove catheter.

### medicine treatment

**Empiric antibiotic therapy** (Duration of therapy 7–14 days):

* Amikacin, IV, 15 mg/kg daily.

**OR**

If local resistance patterns show low level resistance to ciprofloxacin or culture shows sensitivity:

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| *LoE:IIIb[[21]](#endnote-22)* |

* Ciprofloxacin, oral, 500 mg 12 hourly.

# 9.2 ADULT VACCINATION

**Note:** As COVID vaccination recommendations are being updated regularly as new evidence emerges, please consult the latest National Department of Health vaccine policy recommendations.

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| **Vaccine** | **Indications** | **Comments** |
| * Influenza vaccine

Z25.1 | 1. Pregnant women
2. Elderly patients >65 years.
3. HIV-infected patients.
4. Patients with chronic pulmonary, cardiac, and renal conditions.
5. Healthcare workers with direct patient contact.\*\*
 | * Contraindication: severe egg allergy, <6 months of age.
* Dose: IM, 0.5 mL.
* Repeat annually.
 |
| * Pneumococcal vaccine (23 valent polysaccharide)

Z23.8 | 1. Asplenic patients.
2. Chronic cerebrospinal fluid (CSF) leak.
 | * Contraindication: pregnancy.
* Dose: IM, 0.5 mL.

Booster: after 5 years and at 65 years of age.

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| *LoE:IIIb[[22]](#endnote-23)* |

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| * Hepatitis B vaccine\*

Z24.6 | 1. High risk groups, e.g. hospital personnel or sexual contacts of infected patients.
2. Sexual assault.
 | * Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after 1stdose.
* Administer deep IM in deltoid muscle.
 |
| * Tetanus toxoid vaccine

Z23.5 | Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus. | * Dose: IM, 40 iu (0.5 mL).
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\* Not to be given to patients who have already been immunised.

\*\*Healthcare workers are not routinely offered immunisation during the annual campaign. Although it is recommended that healthcare workers are vaccinated against influenza, they will not be provided with publicly funded vaccines unless they fall within any of the designated high-risk groups.

**NOTE: Prioritisation strategies may vary in a pandemic.**

## 9.2.1 Rabies vaccination

Z24.2

\*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 21.3.1.1: Animal bites.

# 9.3 BRUCELLOSIS

A23.0-3/A23.8-9

\*Notifiable medical condition.

### Description

Zoonotic infection, usually due to *B. abortu*s in South Africa. Infection is usually acquired from unpasteurised milk products or handling raw meat.

### Medicine treatment

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| Exclude TB before starting therapy. |

* Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

**AND**

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| *LoE:IVb[[23]](#endnote-24)* |

* Gentamicin, IV, 6 mg/kg daily for 3 weeks (see Appendix II for guidance on prescribing).

 - Preferred regimen for osteo-articular or cardiac involvement.

**OR**

* Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

**AND**

* Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.

# 9.4 EMERGING respiratory Pathogens, e.g. COVID-19: CORONAVIRUS DISEASE-19; Middle East ResPiratory Syndrome CoronaVirus infection: Mers CoV

B34.2/U07.1

\*Notifiable medical condition.

**Note:** Consult most recent guidelines from National Department of Health/ NICD.

**DESCRIPTION**

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Individuals with MERS-CoV present with a wide spectrum of clinical presentation ranging from asymptomatic infection to acute upper respiratory illness, and rapidly progressing lower respiratory illness; respiratory failure, septic shock and multi-organ failure resulting in death.

A typical presentationof MERS includes:

1. fever (>38°C), chills or rigors, cough, shortness of breath

Presentation may include:

1. hemoptysis, sore throat, myalgias, diarrhoea, vomiting, abdominal pain

Complications:

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| 1. severe pneumonia
 | 1. acute renal failure
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| 1. ARDS
 | 1. refractory hypoxaemia
 |

**GENERAL MEASURES**

All suspected, probable cases and contacts must be discussed and managed in consultation with the regional virologist or infectious diseases specialist at the referral centre.

In addition cases should be discussed with the Centre for Respiratory Diseases of the National Institute for Communicable Diseases (NICD).

**Tel: 011 386 6392/ 011 3866390 , Outbreak hotline: 082 883 9920**

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| **COVID-19 HOTLINE NUMBERS****Clinicians: 080011131****Public: 080002999****http://www.nicd.ac.za/** **;**  **https://sacoronavirus.co.za/** |

Transfer of patients will only occur once all relevant arrangements have been made to limit further exposure to a potential contagious and life threatening agent.

Droplet precautions should be added to the standard precautions. Airborne precautions should be applied when performing aerosol-generating procedures.

**ISOLATE SUSPECTED SYMPTOMATIC CASES AT ALL TIMES.**

If MERS coronavirus is suspected, isolate patient to limit further exposure.

**MANAGEMENT**

**Treatment**

Treatment is supportive.

No antiviral agents or vaccines are currently available.

Management of contact: consult with NICD and isolate contact.

Record and follow-up all patient contacts.

**Prevention**

Handwashing and the careful disposal of materials infected with nasal secretions. Antiseptic/disinfectant solutions:choroxylenol, benzalkonium chloride, and cetrimide. Chlorhexidine has been shown to be ineffective.

**REFERRAL**

All cases after consultation with infectious diseases and NICD.

# 9.5 HAEMORRHAGIC FEVER SYNDROME

A98.0-4/A98.8/A99

\* Notifiable medical condition.

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| Severe bacterial infections can mimic the features of haemorrhagic fever syndrome, and broad-spectrum antibiotics, e.g. ceftriaxone, IV, 2 g daily, are indicated in every case until the diagnosis is confirmed. |

### description

High fever, together with disseminated intravascular coagulation (DIC) and bleeding tendency. Other symptoms and organ involvement vary according to the causative virus.

Some important causes other than viral haemorrhagic fevers (VHF) are:

1. severe bacterial infections, particularly *N. meningitidis,*
2. severe tick bite fever,
3. severe falciparum malaria,
4. fulminant hepatitis,
5. leptospirosis, and
6. other causes for DIC or bleeding tendency.

Endemic causes of VHF in South Africa are Crimean-Congo fever and Rift Valley Fever, both of which may be transmitted between humans by means of blood and body fluids.

### Referral

All suspected VHF cases need to be discussed and managed in consultation with the Regional Virologist or Infectious Diseases Consultant at the referral centre.

Cases may also be discussed with the Special Pathogens Unit of the National Institute for Communicable Diseases (NICD):

**Tel: 011 386 6000, Outbreak hotline: 082 883 9920**

Transfer of patients will only occur once all relevant arrangements have been made to limit further exposure to a potentially contagious and life threatening virus.

### Management

A detailed travel and clinical history is crucial. If VHF is still considered, isolate patient in a single room and take proper precautions to limit further exposure. These include:

1. long sleeved disposable gown,
2. vinyl or rubber apron if the patient is bleeding,
3. two pairs of latex gloves, one below the gown and one over the gown,
4. disposable face mask preferably with a visor,
5. goggles if a mask without the visor is used, and
6. waterproof boots or 2 pairs of overshoes, one over the other.

Exclude alternate diseases by means of appropriate laboratory testing.

Support patients with packed red cells and fresh frozen plasma, as required.

Testing for VHF may be required, both to confirm or exclude the possibility of VHF - this must be arranged with the NICD (see above), before sending the specimens, as specific precautions apply.

Record and follow up all patient contacts.

# 9.6 HYDATID DISEASE

B67.0-9

### Description

Cysts of *E. granulosus*, acquired from ingestion of helminth ova passed out in dog faeces, particularly in sheep-farming areas. Cysts may occur in any organ, but are most commonly found in the liver and lungs.

**Note:** Definitive treatment with surgery or PAIR (**p**ercutaneous **a**spiration **i**njection of helminthicidal agent and **r**e-aspiration) is preferred for all accessible lesions.

With medical therapy as below, cure is achieved in about half, improvement in about a quarter and no response in about a quarter of cases.

**MEDICINE TREATMENT**

* Albendazole, oral, 15 mg/kg/day up to maximum of 400 mg 12 hourly

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| *LoE:IIIb[[24]](#endnote-25)* |

with a fatty meal (e.g. a glass of full cream milk).

* Duration is 3–6 months according to response on imaging for inoperable cysts **or** 14–28 days before and 28 days after

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| *LoE:Ia[[25]](#endnote-26)* |

PAIR or surgery.

* Monitor liver function tests and FBCs monthly.

**ReferraL**

All cases to a centre with experience in surgery and PAIR.

# 9.7 malaria

See the Primary Health Care STGs and EML - Section 10.7: Malaria.

## 9.7.1 Malaria, UNCOMPLICATED

B54/B51.9/B52.9/B53.0

\*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.1: Malaria, non-severe/uncomplicated.

## 9.7.2 malaria, Severe

B50.0/B50.8

\*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.2: Malaria, severe/complicated.

### Description

*P. falciparum* malaria with one or more of the following features:

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| 1. severe general body weakness (prostration)
 | 1. abnormal bleeding (e.g epistaxis)
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| 1. impaired consciousness
 | 1. convulsions
 |
| 1. renal dysfunction
 | 1. heavy parasitaemia (≥5%)
 |
| 1. repeated vomiting
 | 1. ARDS
 |
| 1. severe diarrhoea
 | 1. shock
 |
| 1. severe anaemia (Hb <6 g/dL)
 | 1. hypoglycaemia
 |
| 1. haemoglobinuria
 | 1. clinical jaundice
 |
| 1. acidosis (plasma bicarb <15 mmol/L)
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### General measures

Maintain hydration but avoid excessive fluid administration as this could contribute to the development of ARDS (especially in pregnancy).

Transfuse if haemoglobin <6 g/dL.

There is no convincing evidence of benefit for the use of exchange transfusion.

### Medicine treatment

Intravenous therapy:

**The preferred agent is parenteral artesunate:**

* Artesunate IV, 2.4 mg/kg at 0, 12 and 24 hours; then daily until patient is able to tolerate oral therapy.
* Administer at least 3 IV doses before switching to oral artemether/lumefantrine.

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| *LoE:Ia[[26]](#endnote-27)* |

Follow intravenous therapy with oral therapy:

* Artemether/lumefantrine 20/120 mg, oral, 4 tablets/dose with fat-containing food or full cream milk to ensure adequate absorption.
* Give the first dose immediately.
* Give the second dose 8 hours later.
* Then 12 hourly for another 2 days. (Total number of doses in 3 days = 6 doses; i.e. 24 tablets).

Monitor treatment response with regular blood smears.

An increase in parasitaemia may occur within 24 hours due to release of sequestrated parasites, but a reduction should be seen after 48 hours.

**Note**: Gametocytes may appear after this stage – this does NOT mean failure of therapy as gametocytes may persist for up to 2 weeks after successful therapy.

Only the reappearance of or failure to clear trophozoites means failure.

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| Consider concomitant bacteraemia in patients with severe malaria, especially if they have neutrophilia. |

### Referral

Patient in need of ventilation or dialysis if these are unavailable on site.

# 9.8 SCHISTOMIASIS

B65.0-3/B65.8-9

\*Notifiable medical condition.

**DESCRIPTION**

A parasitic infestation with:

1. *Schistosoma haematobium*: primarily involves the bladder and renal tract, or
2. *Schistosoma mansoni*: primarily involves the intestinal tract.

**DIAGNOSIS**

**Acute schistosomiasis syndrome**

1. Typically occurs in travellers to endemic areas with freshwater exposure 3-7 weeks before onset.
2. Clinical features include fever, rigors/chills, urticaria,angioedema, myalgias, arthralgias, dry cough, diarrhea, abdominal pain, and headache. Symptoms are usually relatively mild and resolve spontaneously over a period of a few days to a few weeks.
3. The eosinophil count is almost invariably markedly elevated.
4. Diagnosis is confirmed serologically – eggs are seldom seen in stool or urine.
5. Differential diagnosis includess urinary tract infection, glomerulo nephritis, HIV, gastroenteritis (Salmonella), hepatitis A, B and C, malaria.

**Chronic schistosomiasis**

1. Most individuals with schistosomiasis infection are asymptomatic.
2. *S. haematobium* may present with macroscopic haematuria and urinary symptoms. Chronic bladder involvement and urinary tract involvement may cause urinary incontinence and obstructive uropathy.
3. *S. mansoni* may present with chronic or intermittent dysentery. Periportal fibrosis and portal hypertension may occur.
4. Pulmonary hypertension and central nervous system involvement (particularly myelopathy) are uncommon complications.
5. Definitive diagnosis is by finding eggs in urine (*S. haematobium*), stool (*S. mansoni*), or on biopsy. Serology is usually positive.

**MEDICINE TREATMENT**

**Acute schistosomiasis syndrome**

* Corticosteroids (intermediate-acting) e.g.:
* Prednisone, oral, 40 mg daily for 5 days.

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| *LoE:IIIb[[27]](#endnote-28)* |

4-6 weeks later, after symptoms have resolved:

* Praziquantel, oral, 40 mg/kg as a single dose.

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| *LoE:IIIb[[28]](#endnote-29)* |

**AND**

* Corticosteroids (intermediate-acting)e.g.:
* Prednisone, oral, 40 mg daily for 5 days.

Optimum time for administration of praziquantel is uncertain but sufficient time is required for the worms to mature.

If in 4-6 weeks, eosinoplilia present and high antibody titres, repeat praziquantel treatment:

* Praziquantel, oral, 40 mg/kg as a single dose.

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| *LoE:IIIb[[29]](#endnote-30)* |

**Chronic schistosomiasis**

Manage as recommended in PHC STGs and EML, section 10.12: Schistosomiasis (bilharzia).

# 9.9 TETANUS

A35

\*Notifiable medical condition.

### DESCRIPTION

### Painful muscle spasms and rigidity following inoculation by trauma of *Clostridium tetani* spores, which germinate and produce toxins. The wound may be trivial and healing may have occurred before presentation. Incubation period is 3-21 days. Tetanus may be localised, with muscle spasms near the site of inoculation, or generalised, with spasm of the jaw muscles being a common presenting sign.

### General measures

These patients need to be managed in a high care setting where ventilation is available.

Maintain and protect airway.

Monitor ECG and blood pressure.

Maintain and replace IV fluids.

Wound management is essential with debridement and removal of any foreign bodies.

Alleviate fever with mechanical cooling methods.

### Medicine treatment

For rigidity, spasms: (R25.2)

* Diazepam, IV, 10 mg 4 hourly, for 24 hours, then consider oral route as high doses of parentral diazepam can cause an acidosis.

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| *LoE:IIIb[[30]](#endnote-31)* |

* Titrate to effect.
* Doses as high as 50–100 mg 2 hourly are sometimes required.
* Higher doses require monitoring for respiratory depression.

Use muscle relaxants sparingly as these may exacerbate autonomic instability.

Antibiotic treatment:

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| *LoE:IIIb[[31]](#endnote-32)* |

* Metronidazole, IV, 500 mg 8 hourly for 10 days.

For passive immunisation: (Z23.5)

* Tetanus immunoglobulin, IM, 3 000 units as a single dose.

For active immunisation of all patients:(as clinical tetanus does not always confer immunity) (Z23.5)

* Tetanus toxoid vaccine, IM, 0.5 mL, total of 3 doses:
* on admission,
* at 4 weeks, and
* at 6 months.
* Administer at a different site to that used for administering tetanus immunoglobulin.

For pain:

* Paracetamol, oral, 1 g 4–6 hourly when required.
* Maximum dose: 15 mg/kg/dose.

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| *LoE:IIa[[32]](#endnote-33)* |

* Maximum daily dose: 4 g in 24 hours.
* Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

For shock, dehydration, maintenance of hydration: R57.9+ (A35)

* IV fluids.

For prophylaxis for deep vein thrombosis: (Z29.2)

See section 2.14: Venous thrombo-embolism.

### Referral

All cases to a facility with resources for artificial mechanical ventilation.

# 9.10 TICK BITE FEVER

A93.8

### Description

Tick-borne infection due to *R. conorii*, acquired from dogs, or *R. africae*, acquired from cattle and game. The hallmark of tick bite fever is the eschar, a round black lesion ± 5 mm in diameter with an inflammatory halo, occurs in about two thirds of patients with *R. conorii* and in most cases of *R. africae* infection, where multiple eschars are common. A rash develops on about the third day of illness in about two thirds of patients with *R. conorii* and in fewer cases of *R. africae* infection. In *R. conorii* infection the rash is maculopapular and involves the palms and soles. In *R. africae* infection the rash is sparse and may be vesicular. Headache is a prominent symptom.

### medicine treatment

* Doxycycline, oral, 100 mg 12 hourly, for at least 3 days after the fever subsides with clinical improvement.
* Total duration of treatment is 7 days.

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| *LoE:IIIb[[33]](#endnote-34)* |

In pregnancy: O98.5+(A93.8)

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| LoE:IVb[[34]](#endnote-35) |

* Doxycycline, oral, 100 mg 12 hourly for 2 days.

Then switch to:

* Azithromycin, oral, 500 mg 12 hourly for 3 days.

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| *LoE:IIIb[[35]](#endnote-36)* |

For the rare patient unable to take oral therapy:

Total duration of therapy: 7 days.

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| *LoE:IIIb[[36]](#endnote-37)* |

* Ciprofloxacin, IV, 400 mg 8 hourly.

**Note**: This is inferior to doxycycline and oral doxycycline should be commenced as soon as possible.

**REFERRAL**
Tick bite fever responds rapidly to treatment and fever persisting for >48 hours after initiation of treatment should prompt consideration of an alternative or additional diagnosis***.***

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| *LoE:IVb[[37]](#endnote-38)* |

# 9.11 TYPHOID FEVER (ENTERIC FEVER)

A01.0-4

\*Notifiable medical condition (Typhoid fever).

**Description**

Systemic infection due to *S. enteritica* serotype Typhi or related organisms (e.g. *S. paratyphi*, *S. choleraesuis*). Initial symptoms are abdominal pain, headache, cough and fever, with diarrhoea developing after a few days. Bacteraemia is common in the first week of illness, subsequently stool culture has the highest yield.

### General measures

Transfusion is indicated for severe haemorrhage.

Replace fluid and electrolytes.

Contact isolation during acute phase of illness.

### medicine treatment

**Antibiotic therapy**

**Note: There is increasing resistance to ciprofloxacin in South Africa and it is important to send specimens for culture and sensitivity prior to commencing antibiotic therapy.**

Total duration of antibiotic therapy: 10 days.

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| *LoE:IIIb[[38]](#endnote-39)* |

* Ceftriaxone, IV, 2 g 12 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8oC for 24 hours, based on culture sensitivity results:

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| *LoE:IVb* |

* Ciprofloxacin, oral, 500 mg 12 hourly.

Stool cultures must be repeated at weekly intervals after convalescence to ensure that a carrier state has not developed. Two consecutive negative stool cultures are required to exclude carrier state. This is of vital importance in food handlers, who must not be permitted to return to work until stools are negative.

Chronic carriers: (Z22.0)

* Ciprofloxacin, oral, 500 mg 12 hourly for 6 weeks (if sensitive to ciprofloxacin).
* Advise strict hand washing.
* Avoid food preparation for others during severe illness.

**Referral**

Surgical consultation for complications such as intestinal haemorrhage, threatening bowel perforation or localisation with metastatic infection with or without abscess formation, and peritonitis.

Drug resistant organism: consult microbiology/infectious diseases services.

# 9.12 VARICELLA (chickenpox), COMPLICATED

B01.1† + (G02.0\*/G05.1\*+J17.1\*)/B01.8

### General measures

Cool, wet compresses or tepid water baths.

Body hygiene to prevent secondary infection.

Advise against scratching.

### medicine treatment

Antiviral therapy is required in complicated cases, e.g.:

1. chickenpox pneumonia,
2. pregnancy,
3. neurological involvement, and
4. chickenpox in immunocompromised patients.
* Aciclovir, IV, 10 mg/kg administrerd over one hour 8 hourly for 7 days.

The course can be completed with:

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| *LoE:IVb[[39]](#endnote-40)* |

* Antiviral, (active against varicella zoster), e.g:
* Aciclovir, oral, 800 mg five times daily.

Treat secondary bacterial infection if suspected.

For close contacts (household contacts or patients in adjacent beds in the same ward) who are severely immunologically compromised and are not immune (i.e. no history of chickenpox/shingles or negative VZV IgG), following a significant exposure (household contacts): (Z29.1)

* Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
* Maximum dose: 625 units.

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| *LoE:IVb[[40]](#endnote-41)* |

* Administer within 96 hours after significant exposure.

# 9.13 ZOSTER (SHINGLES)

B02.9

### description

Dermatomal eruption of vesicles on an erythematous base due to varicella-zoster virus (lies dormant in nerve ganglia following chickenpox).

### General measures

Isolate from immunocompromised or pregnant non-immune individuals (who may develop severe chickenpox).

Offer HIV test, especially in patients <50 years of age.

### medicine treatment

Antiviral therapy, for:

1. zoster in immunocompromised patients, provided that active lesions are still being formed, and
2. in immunocompetent individuals provided they present within 72 hours of onset of clinical symptoms.
* Antiviral (active against herpes zoster) e.g.:

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| *LoE:IVb[[41]](#endnote-42)* |

* Aciclovir, oral, 800 mg five times daily for 7 days (4 hourly missing the middle of the night dose).

For zoster with secondary dissemination or neurological/ eye involvement:

B02.7/B02.0-2†+(G02.0\*/G05.1\*/G53.0\*/G63.0\*)/ B02.3†+(H03.1\*/H13.1\*/H22.0\*/H19.2\*/ H19.0\*)

* Aciclovir, IV, 10 mg/kg administred over one hour 8 hourly for 7 days.
* The course can be completed with aciclovir, oral, 800 mg five times daily.
* Dose adjustment based on renal clearance (See Appendix IIfor guidance on prescribing and monitoring).

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| *LoE:IVb[[42]](#endnote-43)* |

**Secondary infection**

B02.8

This is seldom present and is over-diagnosed. The vesicles in shingles often contain purulent material, and erythema is a cardinal feature of shingles. If there is suspected associated bacterial cellulitis:

* Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

For pain:

Pain is often very severe and requires active control. Combination of different classes of analgesics is often necessary.

Recommended therapy for acute phase of infection, e.g.:

* Paracetamol, oral, 1 g 4–6 hourly when required.
* Maximum dose: 15 mg/kg/dose.
* Maximum daily dose: 4 g in 24 hours.

**AND/OR**

If pain is not adequately controlled:

* Tramadol, oral, 50–100 mg 4–6 hourly.

See chapter 26: Pain.

Post-herpetic neuralgia: B02.2+(G53.0\*)

Initiate treatment with adjuvant therapy early.

* Amitriptyline, oral, 25 mg at night.
* Titrate as necessary to a maximum of 75 mg.

See section 26.1.4: Neuropathic pain.

### Referral

Refer to an ophthalmologist if there is ocular involvement with ophthalmic zoster (if the tip of the nose is involved then ocular involvement is much more likely). See section 18.4: Herpes zoster ophthalmicus.

Patients who develop complications e.g. myelitis.

1. Clindamycin, oral: South African Antibiotic Stewardship Programme. A Pocket Guide to Antibiotic Prescribing for Adults in South Africa, 2015.http://www.fidssa.co.za/images/SAASP\_Antibiotic\_Gudidelines\_2015.pdf

 Clindamycin, oral: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022.

 Clindamycin, oral: Bouazza N, Pestre V, Jullien V, Curis E, Urien S, Salmon D, Tréluyer JM. Population pharmacokinetics of clindamycin orally and intravenously administered in patients with osteomyelitis. Br J ClinPharmacol. 2012 Dec;74(6):971-7.http://www.ncbi.nlm.nih.gov/pubmed/22486719 [↑](#endnote-ref-2)
2. Empiric parenteral antibiotic therapy (*S. aureus* infection): Chong YP, Moon SM, Bang KM, Park HJ, Park SY, Kim MN, Park KH, Kim SH, Lee SO, Choi SH, Jeong JY, Woo JH, Kim YS. Treatment duration for uncomplicated Staphylococcus aureus bacteremia to prevent relapse: analysis of a prospective observational cohort study. Antimicrob Agents Chemother. 2013 Mar;57(3):1150-6.http://www.ncbi.nlm.nih.gov/pubmed/23254436

 Empiric parenteral antibiotic therapy (*S. aureus* infection): Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW, Levine DP, Murray BE, J Rybak M, Talan DA, Chambers HF; Infectious Diseases Society of America. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 Feb 1;52(3):e18-55. http://www.ncbi.nlm.nih.gov/pubmed/21208910 [↑](#endnote-ref-3)
3. Empiric candidaemia therapy (duration of 2 weeks): Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE, Sobel JD. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016 Feb 15;62(4):e1-50. https://www.ncbi.nlm.nih.gov/pubmed/26679628

 Empiric candidaemia therapy (duration of 2 weeks): Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009 Jul 1;49(1):1-45. . Erratum in: Clin Infect Dis. 2010 Apr 1;50(7):1079. Dosage error in article text. Clin Infect Dis. 2010 Feb 1;50(3):457. https://www.ncbi.nlm.nih.gov/pubmed/19489710 [↑](#endnote-ref-4)
4. Vancomycin, IV: Reardon J, Lau TT, Ensom MH. Vancomycin loading doses: a systematic review. Ann Pharmacother. 2015 May;49(5):557-65. http://www.ncbi.nlm.nih.gov/pubmed/25712445

 Vancomycin, IV: Rybak M, Lomaestro B, Rotschafer JC, Moellering R Jr, Craig W, Billeter M, Dalovisio JR, Levine DP. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm. 2009 Jan 1;66(1):82-98. Erratum in: Am J Health Syst Pharm. 2009 May 15;66(10):887. http://www.ncbi.nlm.nih.gov/pubmed/19106348

 Vancomycin, IV: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-5)
5. Antibiotic therapy (candidaemia): Takesue Y, Ueda T, Mikamo H, Oda S, Takakura S, Kitagawa Y, Kohno S; ACTIONs Project. Management bundles for candidaemia: the impact of compliance on clinical outcomes. J AntimicrobChemother. 2015 Feb;70(2):587-93. http://www.ncbi.nlm.nih.gov/pubmed/25326087 [↑](#endnote-ref-6)
6. Amphotericin B, IV: Rex JH, Bennett JE, Sugar AM, Pappas PG, van der Horst CM, Edwards JE, Washburn RG, Scheld WM, Karchmer AW, Dine AP, et al. A randomized trial comparing fluconazole with amphotericin B for the treatment of candidemia in patients without neutropenia.Candidemia Study Group and the National Institute. N EnglJ Med. 1994 Nov 17;331(20):1325-30. http://www.ncbi.nlm.nih.gov/pubmed/7935701

 Amphotericin B, IV: Phillips P, Shafran S, Garber G, Rotstein C, Smaill F, Fong I, Salit I, Miller M, Williams K, Conly JM, Singer J, Ioannou S. Multicenter randomized trial of fluconazole versus amphotericin B for treatment of candidemia in non-neutropenic patients. Canadian Candidemia Study Group. Eur J ClinMicrobiol Infect Dis. 1997 May;16(5):337-45. http://www.ncbi.nlm.nih.gov/pubmed/9228472

 Amphotericin B, IV: Anaissie EJ, Darouiche RO, Abi-Said D, Uzun O, Mera J, Gentry LO, Williams T, Kontoyiannis DP, Karl CL, Bodey GP. Management of invasive candidal infections: results of a prospective, randomized, multicenter study of fluconazole versus amphotericin B and review of the literature. Clin Infect Dis. 1996 Nov;23(5):964-72. http://www.ncbi.nlm.nih.gov/pubmed/8922787

 Amphotericin B, IV: Takesue Y, Ueda T, Mikamo H, Oda S, Takakura S, Kitagawa Y, Kohno S; ACTIONs Project. Management bundles for candidaemia: the impact of compliance on clinical outcomes. J AntimicrobChemother. 2015 Feb;70(2):587-93. http://www.ncbi.nlm.nih.gov/pubmed/25326087

 Amphotericin B, IV: WHO. Diagnosis, Prevention and Management of Cryptococcal disease in HIV- infected Adults, Adolescents and children – 2011. Geneva: World Health Organization; 2011.http://www.who.int/en/

 Amphotericin B, IV: Atsmon J, Dolev E. Drug-induced hypomagnesaemia : scope and management. Drug Saf. 2005;28(9):763-88. http://www.ncbi.nlm.nih.gov/pubmed/16119971

 Amphotericin B, IV: WHO. Rapid advice: diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. 2011 [Online][Accessed June 2015] http://www.ncbi.nlm.nih.gov/books/NBK299520/pdf/Bookshelf\_NBK299520.pdf [↑](#endnote-ref-7)
7. Fluconazole, oral: Rex JH, Pappas PG, Karchmer AW. A randomized and blinded multicenter trial of high-dose fluconazole plus placebo versus fluconazole plus amphotericin B as therapy for candidemia and its consequences in nonneutropenic subjects. The National Institute of Allergy and Infectious Diseases Mycoses Study Group.Clin Infect Dis 2001; 36: 1221–8.http://www.ncbi.nlm.nih.gov/pubmed/12746765

 Fluconazole, oral: Edwards JE Jr, Bodey GP, Bowden RA, Büchner T, de Pauw BE, Filler SG, GhannoumMA, Glauser M, Herbrecht R, Kauffman CA, Kohno S, Martino P, Meunier F, Mori T, Pfaller MA, Rex JH, Rogers TR, Rubin RH, Solomkin J, Viscoli C, Walsh TJ, White M. International Conference for the Development of a Consensus on the Management and Prevention of Severe Candidal Infections. Clin Infect Dis. 1997 Jul;25(1):43-59. Review.http://www.ncbi.nlm.nih.gov/pubmed/9243032

 Fluconazole, oral: Andes D, van Ogtrop H. Characterization and quantitation of the pharmacodynamics of fluconazole in a neutropenic murine disseminated candidiasis infection model. Antimicrob Agents Chemother 1999; 43:2116–20.http://www.ncbi.nlm.nih.gov/pubmed/10471550 [↑](#endnote-ref-8)
8. Echinocandins (specialist motivation): National Institute for Communicable Diseases. The GERMS-SA Annual Report 2016. https://www.nicd.ac.za/wp-content/uploads/2017/03/GERMS-SA-AR-2016-FINAL.pdf

 Echinocandins (specialist motivation): National Department of Health: Essential Drugs Programme. Tertiary and Quaternary EML, June 2022. https://www.knowledgehub.org.za/elibrary/hospital-level-tertiary-and-quaternary-essential-medicines-list [↑](#endnote-ref-9)
9. Cefazolin, IV: McDanel JS, Perencevich EN, Diekema DJ, Herwaldt LA, Smith TC, ChrischillesEA, Dawson JD, Jiang L, Goto M, Schweizer ML. Comparative effectiveness of beta-lactams versus vancomycin for treatment of methicillin-susceptible Staphylococcus aureus bloodstream infections among 122 hospitals. Clin Infect Dis. 2015 Aug 1;61(3):361-7.https://www.ncbi.nlm.nih.gov/pubmed/25900170 [↑](#endnote-ref-10)
10. Flucloxacillin, oral (dose): South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-11)
11. Empiric antibiotic therapy (surgical wound infections): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. Erratum in: Clin Infect Dis. 2015 May 1;60(9):1448. Dosage error in article text.http://www.ncbi.nlm.nih.gov/pubmed/24973422 [↑](#endnote-ref-12)
12. Ertapenem, IV (severe penicillin allergy & confirmed Gram negative culture): An MM, Zou Z, Shen H, Zhang JD, Chen ML, Liu P, Wang R, Jiang YY. Ertapenem versus piperacillin/tazobactam for the treatment of complicated infections: a meta-analysis of randomized controlled trials. BMC Infect Dis. 2009 Dec 2;9:193. https://www.ncbi.nlm.nih.gov/pubmed/19951447

 Ertapenem (severe penicillin allergy & confirmed Gram negative culture): NICD AMR surveillance for ESKAPE, 1 January 2016 to 31 December 2016. [↑](#endnote-ref-13)
13. Vancomycin, IV: Reardon J, Lau TT, Ensom MH. Vancomycin loading doses: a systematic review. Ann Pharmacother. 2015 May;49(5):557-65. http://www.ncbi.nlm.nih.gov/pubmed/25712445

 Vancomycin, IV: Rybak M, Lomaestro B, Rotschafer JC, Moellering R Jr, Craig W, Billeter M, Dalovisio JR, Levine DP. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm. 2009 Jan 1;66(1):82-98. Erratum in: Am J Health Syst Pharm. 2009 May 15;66(10):887. http://www.ncbi.nlm.nih.gov/pubmed/19106348

 Vancomycin, IV: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-14)
14. Empiric antibiotic therapy (surgical wound infections): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. Erratum in: Clin Infect Dis. 2015 May 1;60(9):1448. Dosage error in article text.http://www.ncbi.nlm.nih.gov/pubmed/24973422

 Ceftriaxone, IV (Surgery on female uro-genital tract/ open GIT surgery): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. Erratum in: Clin Infect Dis. 2015 May 1;60(9):1448. Dosage error in article text.http://www.ncbi.nlm.nih.gov/pubmed/24973422

 Metronidazole, IV (Surgery on female uro-genital tract/ open GIT surgery): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. Erratum in: Clin Infect Dis. 2015 May 1;60(9):1448. Dosage error in article text.http://www.ncbi.nlm.nih.gov/pubmed/24973422 [↑](#endnote-ref-15)
15. Criterion for empiric antibiotic therapy for MDR-HAP and MDR-VAP: Meta-analysis in guideline - Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. https://www.ncbi.nlm.nih.gov/pubmed/27418577 [↑](#endnote-ref-16)
16. Duration of antibiotic therapy (7 days for VAP): Pugh R, Grant C, Cooke RP, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev. 2015 Aug 24;2015(8):CD007577. https://pubmed.ncbi.nlm.nih.gov/26301604/

 Duration of antibiotic therapy (7 days for VAP): Dimopoulos G, Poulakou G, Pneumatikos IA, Armaganidis A, Kollef MH, Matthaiou DK. Short- vs long-duration antibiotic regimens for ventilator-associated pneumonia: a systematic review and meta-analysis. Chest. 2013 Dec;144(6):1759-1767. https://pubmed.ncbi.nlm.nih.gov/23788274/

 Duration of antibiotic therapy (7 days for VAP/HAP): Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. Erratum in: Clin Infect Dis. 2017 May 1;64(9):1298. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161. https://pubmed.ncbi.nlm.nih.gov/27418577/ [↑](#endnote-ref-17)
17. Piperacillin/taxobactam and amikacin: Nau R, Kinzig-Schippers M, Sörgel F, Schinschke S, Rössing R, Müller C, Kolenda H, Prange HW. Kinetics of piperacillin and tazobactam in ventricular cerebrospinal fluid of hydrocephalic patients.Antimicrob Agents Chemother. 1997 May;41(5):987-91.http://www.ncbi.nlm.nih.gov/pubmed/9145857 [↑](#endnote-ref-18)
18. Cefepime, IV (2 g): NICD AMR surveillance for ESKAPE, 1 January 2016 to 31 December 2016.

 Cefepime, IV (2 g): South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-19)
19. Carbapenem (use of imipenem/cilastin and meropenem): South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-20)
20. Imipenem, IV: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022.

Imipenem, IV: NICD AMR surveillance for ESKAPE, 1 January 2016 to 31 December 2016. [↑](#endnote-ref-21)
21. Ciprofloxacin, oral: NHLS/NICD Communicable Diseases Surveillance Bulletin, April 2015 (Volume 13. No 1). http://www.nicd.ac.za/ [↑](#endnote-ref-22)
22. Pneumococcal vaccine (23 valent polysaccharide): ACIP Practice Guidelines - CDC. Morbidity and Mortality Weekly Report, October 12, 2012, Vol 61, No 40.http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm?s\_cid=mm6140a4\_w [↑](#endnote-ref-23)
23. Gentamicin: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-24)
24. Albendazole: Rigter IM, Schipper HG, Koopmans RP, van Kan HJ, Frijlink HW, Kager PA, Guchelaar HJ. Relative bioavailability of three newly developed albendazole formulations: a randomized crossover study with healthy volunteers. Antimicrob Agents Chemother. 2004 Mar;48(3):1051-4.http://www.ncbi.nlm.nih.gov/pubmed/14982808 [↑](#endnote-ref-25)
25. Albendazole plus PAIR surgery: Smego RA Jr, Bhatti S, Khaliq AA, Beg MA. Percutaneous aspiration-injection-reaspiration drainage plus albendazole or mebendazole for hepatic cystic echinococcosis: a meta-analysis. Clin Infect Dis. 2003 Oct 15;37(8):1073-83. http://www.ncbi.nlm.nih.gov/pubmed/14523772 [↑](#endnote-ref-26)
26. Artesunate, IV: Artesunate, parenteral: Sinclair D, Donegan S, Isba R, Lalloo DG. Artesunate versus quinine for treating severe malaria. Cochrane Database Syst Rev. 2012 Jun 13;6:CD005967.http://www.ncbi.nlm.nih.gov/pubmed/22696354 [↑](#endnote-ref-27)
27. Prednisone, oral: Grandière-Pérez L, Ansart S, Paris L, Faussart A, Jaureguiberry S, Grivois JP,Klement E, Bricaire F, Danis M, Caumes E. Efficacy of praziquantel during the incubation and invasive phase of Schistosoma haematobium schistosomiasis in 18 travelers. Am J Trop Med Hyg. 2006 May;74(5):814-8. https://www.ncbi.nlm.nih.gov/pubmed/16687686 [↑](#endnote-ref-28)
28. Praziquantel, oral: Grandière-Pérez L, Ansart S, Paris L, Faussart A, Jaureguiberry S, Grivois JP,Klement E, Bricaire F, Danis M, Caumes E. Efficacy of praziquantel during the incubation and invasive phase of Schistosoma haematobium schistosomiasis in 18 travelers. Am J Trop Med Hyg. 2006 May;74(5):814-8. https://www.ncbi.nlm.nih.gov/pubmed/16687686 [↑](#endnote-ref-29)
29. Praziquantel, oral (repeat dose): Grandière-Pérez L, Ansart S, Paris L, Faussart A, Jaureguiberry S, Grivois JP,Klement E, Bricaire F, Danis M, Caumes E. Efficacy of praziquantel during the incubation and invasive phase of Schistosoma haematobium schistosomiasis in 18 travelers. Am J Trop Med Hyg. 2006 May;74(5):814-8. https://www.ncbi.nlm.nih.gov/pubmed/16687686 [↑](#endnote-ref-30)
30. Diazepam, IV: Vassa NT, Doshi HV, Yajnik VH, Shah SS, Joshi KR, Patel SH. Comparative clinical trial of diazepam with other conventional drugs in tetanus. Postgrad Med J. 1974 Dec;50(590):755-8.http://www.ncbi.nlm.nih.gov/pubmed/4619836

 Diazepam, IV: Wilson KC, Reardon C, Theodore AC, Farber HW. Propylene glycol toxicity: a severe iatrogenic illness in ICU patients receiving IV benzodiazepines: a case series and prospective, observational pilot study. Chest. 2005 Sep;128(3):1674-81.http://www.ncbi.nlm.nih.gov/pubmed/16162774 [↑](#endnote-ref-31)
31. Metronidazole, IV: World Health Organisation. Technical note: Current recommendations for treatment of tetanus during humanitarian emergencies, January 2010. https://www.who.int/diseasecontrol\_emergencies/who\_hse\_gar\_dce\_2010\_en.pdf [↑](#endnote-ref-32)
32. Paracetamol (fever in tetanus): Lee BH, Inui D, Suh GY, Kim JY, Kwon JY, Park J, et al: Fever and Antipyretic in Critically ill patients Evaluation (FACE) Study Group. Association of body temperature and antipyretic treatments with mortality of critically ill patients with and without sepsis: multi-centered prospective observational study. Crit Care. 2012 Feb 28;16(1):R33. https://www.ncbi.nlm.nih.gov/pubmed/22373120 [↑](#endnote-ref-33)
33. Doxycycline, oral: Chapman AS, Bakken JS, Folk SM, Paddock CD, Bloch KC, Krusell A, et al: Tickborne Rickettsial Diseases Working Group; CDC. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis--United States: a practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep. 2006 Mar 31;55(RR-4):1-27. https://www.ncbi.nlm.nih.gov/pubmed/16572105 [↑](#endnote-ref-34)
34. Doxycycline (pregnancy – tick bite fever): Frean J, Grayson W. South African Tick Bite Fever: An Overview. Dermatopathology (Basel). 2019 Jun 26;6(2):70-76. https://pubmed.ncbi.nlm.nih.gov/31700846/

Doxycycline (pregnancy – tick bite fever): Cross R, Ling C, Day NP, McGready R, Paris DH. Revisiting doxycycline in pregnancy and early childhood--time to rebuild its reputation? Expert Opin Drug Saf. 2016;15(3):367-82. https://pubmed.ncbi.nlm.nih.gov/26680308/

Doxycycline (pregnancy – tick bite fever): McGready R, Prakash JA, Benjamin SJ, Watthanaworawit W, Anantatat T, Tanganuchitcharnchai A, et al. Pregnancy outcome in relation to treatment of murine typhus and scrub typhus infection: a fever cohort and a case series analysis. PLoS Negl Trop Dis. 2014 Nov 20;8(11):e3327. https://pubmed.ncbi.nlm.nih.gov/25412503/

Doxycycline (pregnancy – tick bite fever): South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

Doxycycline (pregnancy – tick bite fever): Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer SM, Gideon PS, et al. Antibiotics potentially used in response to bioterrorism and the risk of major congenital malformations. Paediatr Perinat Epidemiol. 2009 Jan;23(1):18-28. https://pubmed.ncbi.nlm.nih.gov/19228311/ [↑](#endnote-ref-35)
35. Azithromycin, oral (pregnancy): Cascio A, Colomba C, Antinori S, Paterson DL, Titone L. Clarithromycin versus

azithromycin in the treatment of Mediterranean spotted fever in children: a randomized controlled trial. Clin Infect Dis. 2002 Jan 15;34(2):154-8. http://www.ncbi.nlm.nih.gov/pubmed/11740701 [↑](#endnote-ref-36)
36. Ciprofloxacin, IV: Raoult D, Drancourt M. Antimicrobial therapy of rickettsial diseases. Antimicrob Agents Chemother. 1991 Dec;35(12):2457-62. http://www.ncbi.nlm.nih.gov/pubmed/1810178 [↑](#endnote-ref-37)
37. Treatment failure > 48 hours requiring referral: Chapman AS, Bakken JS, Folk SM, Paddock CD, Bloch KC, Krusell A, et al: Tickborne Rickettsial Diseases Working Group; CDC. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis--United States: a practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep. 2006 Mar 31;55(RR-4):1-27. https://www.ncbi.nlm.nih.gov/pubmed/16572105 [↑](#endnote-ref-38)
38. Ceftriaxone, IV: Acharya G, Butler T, Ho M, Sharma PR, Tiwari M, Adhikari RK, Khagda JB, Pokhrel B, Pathak UN. Treatment of typhoid fever: randomized trial of a three-day course of ceftriaxone versus a fourteen-day course of chloramphenicol. Am J Trop Med Hyg. 1995 Feb;52(2):162-5. http://www.ncbi.nlm.nih.gov/pubmed/7872445

 Ceftriaxone, IV: Smith MD, Duong NM, Hoa NT, Wain J, Ha HD, Diep TS, Day NP, Hien TT, White NJ. Comparison of ofloxacin and ceftriaxone for short-course treatment of enteric fever.Antimicrob Agents Chemother. 1994 Aug;38(8):1716-20. http://www.ncbi.nlm.nih.gov/pubmed/7986000

 Ceftriaxone, IV: Wallace MR, Yousif AA, Mahroos GA, Mapes T, Threlfall EJ, Rowe B, Hyams KC. Ciprofloxacin versus ceftriaxone in the treatment of multiresistant typhoid fever. Eur J ClinMicrobiol Infect Dis. 1993 Dec;12(12):907-10. http://www.ncbi.nlm.nih.gov/pubmed/8187784

 Ceftriaxone, IV: Islam A, Butler T, Kabir I, Alam NH. Treatment of typhoid fever with ceftriaxone for 5 days or chloramphenicol for 14 days: a randomized clinical trial. Antimicrob Agents Chemother. 1993 Aug;37(8):1572-5. http://www.ncbi.nlm.nih.gov/pubmed/8215265

 Ceftriaxone, IV: Lasserre R, Sangalang RP, Santiago L. Three-day treatment of typhoid fever with two different doses of ceftriaxone, compared to 14-day therapy with chloramphenicol: a randomized trial. J AntimicrobChemother. 1991 Nov;28(5):765-72. http://www.ncbi.nlm.nih.gov/pubmed/1778879

 Ceftriaxone, IV: Islam A, Butler T, Nath SK, Alam NH, Stoeckel K, Houser HB, Smith AL. Randomized treatment of patients with typhoid fever by using ceftriaxone or chloramphenicol. J Infect Dis. 1988 Oct;158(4):742-7. http://www.ncbi.nlm.nih.gov/pubmed/3171225 [↑](#endnote-ref-39)
39. Antiviral, oral (active against herpes zoster) therapeutic class: Tunbridge AJ et al; British Infection Society. Chickenpox in adults ‐ clinical management. J Infect. 2008 Aug;57(2):95‐102. https://pubmed.ncbi.nlm.nih.gov/18555533/ [↑](#endnote-ref-40)
40. Varicella-zoster immunoglobulin (VZIG), IM (indication of immunocompromised with no immunity): Centers for Disease Control and Prevention (CDC). Updated recommendations for use of VariZIG--United States, 2013. MMWR Morb Mortal Wkly Rep. 2013 Jul 19;62(28):574-6. https://pubmed.ncbi.nlm.nih.gov/23863705/ [↑](#endnote-ref-41)
41. Antivirals to treat herpes zoster (therapeutic class): Tunbridge AJ et al; British Infection Society. Chickenpox in adults ‐ clinical management. J Infect. 2008 Aug;57(2):95‐102. https://pubmed.ncbi.nlm.nih.gov/18555533/ [↑](#endnote-ref-42)
42. Aciclovir, IV - dose adjustment in renal impairment: South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022. [↑](#endnote-ref-43)