A POCKET GUIDE TO ANTIBIOTIC PRESCRIBING FOR ADULTS IN SOUTH AFRICA, 2015

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ON BEHALF OF THE SOUTH AFRICAN ANTIBIOTIC STEWARDSHIP PROGRAMME (SAASP)



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A pocket guide to antibiotic prescribing for adults in South Africa 2015 First published 2014 © Sean Wasserman, Tom Boyles, Marc Mendelson

GLOSSARY

Term	Definition		
Antibiogram	A list of antibiotics to which a cultured bacterium is		
	susceptible, intermediate or resistant		
BC	Blood culture		
BD	Twice daily		
Beta-lactam antibiotic	Antibiotic class containing a beta-lactam ring that inhibits		
	bacterial cell wall synthesis. Includes penicillins,		
	cephalosporins and carbapenems		
CA	Community-acquired		
САР	Community acquired pneumonia		
Cleaning solution	Antiseptic for hand hygiene, including 0.5% chlorhexidine		
	in 70% alcohol and iodine-based solutions		
Community-acquired (CA) infection	Illness starts prior to, or within 48 hours of admission		
CRB-65 score	A clinical prediction rule for mortality in community-		
	acquired pneumonia. The score is an acronym for		
	individual risk factors as follows:		
	Confusion of new onset		
	Respiratory rate ≥ 30 breaths per minute		
	Blood pressure < 90 mmHg systolic or < 60 diastolic		
	65 years or older		
	A single point is assigned to each risk factor.		
CRE	Carbapenem resistant Enterobacteriaceae		
CXR	Chest X-ray		
eGFR	Estimated glomerular filtration rate		
ESBL	Extended spectrum beta lactamase producing organism		
Health care associated infection (HCAI)	Any patient with a new infection starting \geq 48 hours after		
	admission and was not apparent at the time of admission,		
	or any catheter or line-associated infection irrespective of time of insertion.		
	The following factors increase risk:		
	Admission to an acute care hospital within 90 days of		
	the current presentation		
	 Resident of a nursing home or long-term care facility 		
	 Recent intravenous antibiotic therapy, chemotherapy or 		
	wound care within the past 30 days of the current		
	presentation		
	Patients attending a haemodialysis clinic		
НСАР	Health care associated pneumonia		
IPC	Infection prevention and control		
im	Intramuscular injection		
iv	Intravenous		
MRSA			
MRSA MSSA	Methicillin resistant Staphylococcus aureus		
MSSA	Methicillin resistant <i>Staphylococcus aureus</i> Methicillin sensitive <i>Staphylococcus aureus</i>		
	Methicillin resistant <i>Staphylococcus aureus</i> Methicillin sensitive <i>Staphylococcus aureus</i> Per os (oral)		
MSSA po	Methicillin resistant Staphylococcus aureus Methicillin sensitive Staphylococcus aureus Per os (oral) Treatment/therapy		
MSSA po Rx	Methicillin resistant <i>Staphylococcus aureus</i> Methicillin sensitive <i>Staphylococcus aureus</i> Per os (oral)		

Disclaimer

This document is provided as an information resource for all health care workers to assist in the appropriate prescribing of antibiotics. It attempts to summarise relevant information for clinicians from South African and International guidelines as well as reference to textbooks, key publications and expert opinion.

Recommendations change rapidly and opinion can be controversial. The authors do not warrant that the information contained in this booklet is complete and shall not be liable for any damages incurred as a result of its use.

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Chapter 1 Why do we need this guide?

The international community sits at the tipping point of a post-antibiotic era, where common bacterial infections are no longer treatable with the antibiotic armamentarium that exists. In South Africa, the identification of the first case of panresistant *Klebsiella pneumoniae* (Brink et al, J Clin Microbiol. 2013;51(1):369-72) marks a watershed moment and highlights our tip of the antibiotic resistance 'iceberg' in this country. Multi-drug resistant (MDR)-bacterial infections, predominantly in Gram-negative bacteria such as *Klebsiella pneumoniae*, *Escherichia coli, Pseudomonas aeruginosa* and *Acinetobacter baumannii* are now commonplace in South African hospitals. Whilst a number of expensive new antibiotics for Grampositive bacterial infections have been manufactured recently (some of which are licenced for use in South Africa), no new antibiotics active against Gram-negative infections are expected in the next 10-15 years. Hence what we have now, needs conserving.

The development of antibiotic resistance is a natural phenomenon. Drug-resistance mutations have been found in 30,000-year old ice blocks. In addition, bacteria may acquire antibiotic resistance mechanisms by horizontal gene transfer. There are over 1000 different naturally occurring enzymes that are produced by different bacteria, which inactivate antibiotics. The overuse of antibiotics is driving the selection of antibiotic resistance. Given the right circumstances, the resistant bacteria that are selected out can either colonize a patient (be present, potentially transmissible, but not cause clinical disease i.e. infection) or cause infection. It follows that the more antibiotics are used, the greater the likelihood of selecting out antibiotic resistance, and the broader the spectrum of antibiotic that is used, the greater the number of different types of resistant bacteria will be selected out. The fact that it is estimated that half of all antibiotics prescribed in human health are unnecessary e.g. for viral upper respiratory tract infections, demands our renewed efforts to make antibiotic prescribing appropriate. When it is indicated, an antibiotic must be the right choice at the right dose, dosing interval and route, and for the right duration, and when it is not indicated, that antibiotic must not prescribed.

Rather than be an exhaustive text on infectious diseases, microbiology or clinical pharmacology, the aim of this guide is to give you the practical information you need to perform antibiotic stewardship in an algorithmic manner, which mimics the day-to-day experience of the prescriber.

Chapter 2 Principles for rational antibiotic prescribing

1. Decide if an antibiotic is indicated: does the patient have a bacterial infection?



Targeted refers to specimen from site of infection e.g. urine for cystitis

2. Perform cultures <u>before</u> administering antibiotics in hospitalised patients or in outpatients with recurrent infections

This allows de-escalation to a narrow spectrum antibiotic once the antibiogram is available & is a cornerstone of antibiotic stewardship

3. Choose an appropriate empiric antibiotic:

- a. Target the most likely pathogen(s) for the site of infection This can be predicted by understanding the broad groups of pathogens that most commonly cause infections at various sites:
 - Skin and soft tissue: Gram positive cocci
 - Urinary tract: Gram negative bacilli
 - Intra-abdominal: Gram-negative, Gram-positive and anaerobic organisms
 - See chapters on specific infections for more details

An appropriate empiric antibiotic can then be selected by matching the narrowest spectrum antibiotic with the likely pathogens. Spectrums of activity of commonly used antibiotics are shown below

		Gram positive cocci				
	Clus	sters	Pairs/chains			
	MSSA	MRSA	<i>S. pneumoniae</i> Most other streptococci	E. faecalis	E. faecium	VRE
Amoxicillin/ampicillin	-	-	+	+	-	-
Cloxacillin	+	-	+/-	-	-	-
Clindamycin	+	+/-	+	-	-	-
Ceftriaxone	+	-	+	-	-	-
Co-amoxiclav	+	-	+	/	-	-
Vancomycin	/	+	/	/	+	-
Ertapenem	/	-	/	-	-	-
Moxifloxacin	/	+/-	+	/	+/-	-
Linezolid	/	/	/	/	/	+
Daptomycin	/	/	/	/	/	/

	Gram negative						
			Ba	ncilli			Cocci
	E. coli Klebsiella	Enterobacter spp.	ESBL	CRE	Salmonella spp.	Pseudomonas spp.	Neisseria meningitidis
	spp.				opp.		g.t.a.c
Amoxicillin/ampicillin	-	-	-	-	/	-	+/-
Penicillin	-	-	-	-	/	-	+/-
Cotrimoxazole*	+/-	+/-	+/-	-	+/-	-	-
Ceftriaxone	+	-	-	-	+	-	+
Co-amoxiclav	+	-	-	-	/	-	/
Ciprofloxacin	+	+	+/-	+/-	+	+	/
Aminoglycosides	+	+	+/-	+/-	-	+	-
Cefepime	/	+	-	-	/	+	/
Piptazobactam	/	+/-	-	-	/	+	/
Ertapenem	/	+	+	-	/	-	/
Imipenem	/	/	/	+/-	/	+	/
Meropenem	/	/	/	+/-	/	+	/

*Associated with much higher rates of toxicity than other antibiotics. Avoid using if a suitable alternative with a similarly narrow spectrum of activity is available



usually susceptible: recommended first line therapy while awaiting antibiogram

frequent resistance or poor clinical efficacy: do not use

variable susceptibility: only use with antibiogram result

usually susceptible but not first choice: do not use unless there is a compelling reason (e.g.

allergy, toxicity or resistance to first line drug or better outcomes for a particular site of infection)

b. Assess likelihood of antibiotic resistance

Risk factors include known colonisation with a resistant pathogen, HCAI, recent antibiotic exposure. Local resistance patterns inform prescribing.

c. Review potential contraindications

Allergy:

Clinicians should differentiate an immediate type 1 IgE mediated hypersensitivity reaction from other less dangerous types of hypersensitivity. Classical signs of type 1 hypersensitivity are anaphylaxis, angioedema, urticarial rash, and bronchospasm. If a type I hypersensitivity reaction to penicillin has occurred, then all β -lactam antibiotics should be avoided, unless there is no alternative drug available when penicillin desensitisation can be attempted as an inpatient.

Patients with other types of hypersensitivity reactions, usually a maculopapular rash to amoxicillin, should avoid all penicillins but may tolerate other β -lactam antibiotics like cephalosporins. The 1st generation cephalosporins should be avoided as they have a higher risk of cross-reactivity with penicillin, but this risk is much lower for second- or third-generation cephalosporins reported to be only 0.1%.

If the previous reaction to penicillin was a maculopapular rash, it is relatively safe to use $2^{nd}/3^{rd}$ generation cephalosporins and use would depend on the patient's social circumstances and access to follow-up. However, in patients with a remote history of a rash on penicillin it is often difficult to differentiate a maculopapular rash from an urticarial rash – all β -lactam antibiotics should be avoided if urticaria occurred on penicillins as this is a type 1 reaction. In this setting, skin testing before using a cephalosporin is recommended, as a positive reaction to penicillin indicates type 1 hypersensitivity.

Toxicity:

Antibiotics can cause direct dose-dependent toxicity and should be avoided in patients at high risk of developing organ damage with a specific agent. For example, do not use aminoglycosides in patients with renal impairment or hearing loss.

	CSF	Lung	Soft tissue	Urinary tract
Ampicillin	Good (in high doses)	Good	Good	Good
Cloxacillin	Inadequate data	Fair	Good	No data
Clindamycin	Poor	No data	Good	No data
Co-amoxiclav	Poor	Good	Good	Fair
Ceftriaxone	Good (in high doses)	Good	Good	Good
Aminoglycosides	Poor	Poor	Fair	Good (if normal GFR)
Ciprofloxacin	Good (in high doses)	Good	Good	Good
Co-trimoxazole	Good	Good	Good	Good
Ertapenem	Poor	Good	Good	Good
Meropenem	Good (in high doses)	Good	Good	Good
Imipenem	Good*	Good	Good	Good
Vancomycin	Poor	Fair	Poor	Good
Linezolid	Good	Good	Good	Good
Daptomycin	Poor	Poor	Good	Good

d. Choose drug with adequate target tissue penetration

*Associated with higher risk of seizures

e. Aim for a single drug with the desired spectrum of activity Monotherapy is preferred unless combination therapy is required for synergy (e.g. endocarditis) or extended spectrum beyond what can be obtained with a single drug (e.g. atypical pathogens in severe CAP).

4. Ensure correct dose and route of administration

The oral/enteral route is preferred whenever possible for patients with mild to moderate infections. Intravenous antibiotics should be reserved for severe infection or for certain sites such as the CSF, bacteraemia, endocarditis, bone and joint infections.

	Oral absorption (%)	Comments
Penicillin VK	Moderate	Take without food
Amoxicillin	Good	
Flucloxacillin	Good	Take on empty stomach
Clindamycin	Good	
Co-amoxiclav	Good	
Ciprofloxacin	Good	Do not give via NGT or with antacids
Doxycycline	Excellent	Take with food, do not co-administer with antacids
Azithromycin	Poor	Take without food
Metronidazole	Excellent	
Co-trimoxazole	Good	
Linezolid	Excellent	

- **5. Start the appropriate antibiotic rapidly in severe infections** Mortality increases by 8% for every hour antibiotic administration is delayed in

septic shock¹

6. Practice early and effective source control

Search for and remove any persistent foci of infection

7. Evaluate antibiotic appropriateness every day



¹ Kumar et al. Crit Care Med. 2006 Jun;34(6):1589-96.

Chapter 3 Interpreting test results

Non culture-based tests

Non culture-based tests such as urinary dipstick, peripheral white cell count (WCC), and C-reactive protein (CRP) confirm the presence of inflammation when positive but do not differentiate bacterial from non-bacterial causes. However, presence of nitrites on urine dipstick, high neutrophil count with left-shift and CRP >100 mg/ml all suggest bacterial infection. Negative results are generally good at excluding inflammation and therefore bacterial infection.

Procalcitonin (PCT) is more specific for bacterial infection than CRP or WCC but 10 times more expensive. There is high quality evidence for its use in a limited number of infections and its use should be limited to these indications. Specifically, low PCT safely excludes bacterial infection such that antibiotics can be withheld in meningitis, and acute exacerbations of chronic obstructive pulmonary disease (see later sections for details). PCT has no value in differentiating bacterial infection from tuberculosis and has very limited value in sepsis. Its price generally excludes its use in serial measurement to determine when to stop, although some evidence in ICU settings alone, exist.

Cultures

Does this positive culture represent infection, colonisation or contamination?

Infection = the presence of one or more microorganisms with an inflammatory response

Colonisation = the presence of microorganisms without significant inflammation.

Contamination = A culture that contains a microorganism(s) that did not originate from the intended anatomical site

Sterile sites

Normally sterile sites are CSF, lungs (below the glottis), urinary tract, biliary tract, and blood. Bacteria cultured from these sites are likely to be causing infection but still sometimes represent colonisation or contamination.

Finding bacteria in a sterile site is abnormal but may represent infection, or contamination. Organisms colonizing skin such as coagulase-negative staphylococci may cause contamination of sterile sites. Colonisation of urinary tract can occur without causing infection. If the organism corresponds with the clinical scenario then this should be considered to be causing infection

Non-sterile sites

Non-sterile specimens include sputum (as it must pass through the mouth), pus swabs from skin, GI tract and vagina. Specimens from these sites are **expected to culture bacteria** (unless growth is inhibited by laboratory techniques). Interpretation therefore depends on the organism(s) being compatible with the clinical scenario.

Cultures from non-sterile sites are often much harder to interpret and usually of less value.



Chapter 4

Correct techniques of microbiological sampling

Optimal sampling is very important to increase yields and decrease contamination rates (see boxes below). Surgical specimens from abnormal structures such as abscesses should usually be collected at the time of operation. Once surgical drains are placed they quickly become colonised with skin and environmental bacteria and culture results are not interpretable. Pus swabs collected outside of theatre are discouraged, as it is extremely rare for them to yield information that will change patient management.

Box 1. Correct technique for collecting mid-stream urine specimens

Instructions for collection of urine specimens Females

- Wash your hands
- Clean the vulva front to back with sterile gauze and sterile water
- Spread labia with fingers
- Void and collect urine mid-flow

Males

- Wash your hands
- Retract foreskin and wash glans with sterile gauze and sterile water
- Void and collect urine mid-flow

Box 2. Correct technique for collecting urine specimens from a catheter

- Use aseptic technique with sterile gloves and apron
- Clamp tubing just distal to sampling port
- Wait for urine to collect above clamp
- Wipe sampling port with cleaning solution
- Remove urine with a small gauge sterile needle and syringe
- Transfer urine to sterile container
- Clean port again
- Unclamp tubing

Box 3. Correct technique for performing a pus swab

- 1. Wounds with slough, necrotic tissue, or dried exudate should first be debrided
- 2. Wash the wound with sterile saline
- 3. If the wound is dry moisten the tip of the swab with sterile saline
- 4. Move swab tip across the wound surface in a zig-zag motion at the same time as being rotated between the fingers
- 5. Apply gentle pressure to release fluid from the base of the wound
- 6. Aim to include as much of the area of the wound as possible but avoid intact skin around the wound
- 7. Document clinical information on laboratory request form
- 8. Transfer to laboratory as soon as possible

Box 4. Correct technique for performing a blood culture

- 1. Verify the patient's identity and obtain verbal consent.
- 2. Assemble the correct materials required for blood culture:
 - blood culture bottle(s)
 - syringe (10 ml or more)
 - needle (22 gauge or more)
 - sterile gloves
 - tourniquet
 - adhesive strip
 - Cleaning solution*
 - sterile pack containing cotton/gauze swabs, sterile paper x2 and waste bag
 - patient labels
 - sharps waste disposal bin
- 3. Apply tourniquet and select a suitable vein
- 4. Wash hands and apply sterile gloves
- 5. Clean the puncture site with cleaning solution using aseptic technique and allow 30 seconds for the disinfectant to dry
- 6. Place green sterile cover with opening over site for blood culture
- 7. Collect 10ml of blood per bottle from adults
- 8. Release tourniquet and remove needle
- 9. If not using the vacutainer system, disinfect the top of the blood culture bottle before inoculating blood
- 10. Do not change needles between blood sample collection and inoculation of blood culture bottle
- 11. Always fill blood culture bottle before filling vials for other tests
- 12. Label the blood culture bottle making sure not to cover the bar code label or the bottom of the bottle
- 13. Complete a laboratory request form in full
- 14. If there is a delay in getting the sample to the laboratory, do not refrigerate the bottle; rather leave it at room temperature
- 15. Document in the notes, the date and time that the blood culture was taken

*Chlorhexidine-alcohol is recommended, but if using povidone iodine, it must be left to dry for at least 1 minute prior to performing culture

Chapter 5 Changing Antibiotics

Once antibiotics have been initiated the decision to change or stop therapy depends on the patient's clinical response and culture results (see algorithm).



Abx = Antibiotics, BSA = Broad spectrum antibiotics

Chapter 6 Infection prevention

The most important tools to prevent spread of infection are hand hygiene and contact precautions. Correct management of IV lines and urinary catheters are essential for reducing hospital-acquired infections.

Hand hygiene WHEN:



HOW:

Use alcohol-based solutions for routine hand decontamination.

Indications for soap and water:

- Hands visibly dirty
- Hands contaminated with body fluids
- After using the restroom or eating
- Exposure Clostridium difficile

Indications for gloves:

- Patient interactions that involve exposure to blood, mucous membranes or non-intact skin
- Suspected or proven C. difficile Always wash hands after glove use

<u>WARNING – STOP!</u> CONTACT PRECAUTIONS



ALL STAFF AND VISITORS GLOVES AND APRON FOR ALL PATIENT CONTACT DISINFECT/WASH YOUR HANDS BEFORE & AFTER PATIENT CONTACT

These should be implemented for any patient infected by or colonised with a drugresistant bacterial pathogen other than tuberculosis (which requires airborne precautions to prevent small droplet spread). Contact precautions involve the following:

- 1. Clear signage indicating that contact precautions are in place
- 2. Patient preferably placed in isolation
- 3. Hand disinfection prior to patient contact
- 4. Mandatory use of apron and gloves when entering the patient's room, before any contact with the patient or their surroundings and during examination
- 5. Remove apron first, followed by gloves
- 6. Hand disinfection after disposal of apron and gloves (use soap and water for *C. difficile* exposure)
- 7. Contact precautions remain in place even after treatment with antibiotics and for every hospital or nursing care re-admission for a period of 6 months. For patients with *C. difficile* associated diarrhoea contact precautions can be withdrawn after completion of treatment and resolution of diarrhoea.

Management of peripheral IV lines



Management of urinary catheters



Every time you see a patient you should be asking the questions:

- 1. Can I stop or de-escalate antibiotics?
- 2. Can I remove this urinary catheter?
- 3. Can I remove this IV line?

Chapter 7 Acute Upper Respiratory Tract Infection

Over-prescribing of antibiotics for upper respiratory tract infection (URTI) is a major driver of bacterial resistance in the community. URTI comprises three clinical syndromes depending on the site of infection; pharyngotonsillitis (sore throat), acute otitis media, and acute bacterial sinusitis.

Acute pharyngotonsillitis (sore throat)



Typical appearance of viral pharyngitis



Typical appearance of bacterial pharyngitis

Definition

• Acute inflammation of the pharyngeal wall and tonsils.

Likely pathogens

- Commonly respiratory viruses and Epstein-Barr virus. Around 5-30% caused by group A β-haemolytic streptococci (GABHS) (*S. pyogenes*).
- Viral and bacterial acute pharyngitis are self-limiting, including those caused by GABHS, hence, the primary reason for considering antibiotic therapy is to prevent Acute Rheumatic Fever (ARF)

Clinical features

- Sore throat
- It is possible to differentiate bacterial from viral causes on clinical grounds.



Penicillin allergy

Azithromycin 500 mg po daily for 3 days

Acute otitis media

Definition

Acute inflammation of the middle ear



Typical appearance of acute otitis media

Likely pathogens

• Haemophilus influenza, Streptococcus pneumoniae, Moraxella catarrhalis

Clinical features

- Ear pain and decreased hearing
- Reddened and bulging tympanic membrane, which may be draining pus.

Tests

• None required

Treatments

- Initially analgesics and decongestants only
- Antibiotics if febrile or symptoms do not settle within 48 hrs

First line

Amoxicillin 1g po 8-hourly for 5 days Alternative in beta-lactam allergic patients Azithromycin 500 mg po daily for 3 days

Acute bacterial sinusitis



Definition- Acute bacterial infection of para-nasal sinuses

Likely pathogens- Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis

Clinical features

- Often preceded by a viral URTI
- Fever, facial tenderness, dental tenderness, nasal discharge, nasal congestion and anosmia.

Tests

- Usually none
- If failure of initial therapy a CT scan, fibre-optic endoscopy with aspiration and culture of pus may be necessary

Treatments

- Symptomatic treatment: paracetamol, decongestant, nasal steroids perform better than antibiotics
- Antibiotics should be prescribed if any of the following are present-
 - Symptoms lasting > 10 days
 - \circ Fever >39°C
 - Purulent discharge
 - o Facial pain
 - Biphasic illness with sinusitis following typical viral URTI

First line

Amoxicillin 1g 8 hourly for 5 days po Alternative for beta-lactam allergy Azithromycin 500 mg po daily for 3 days

Chapter 8 Lower Respiratory Tract Infection

Acute bronchitis

Definition

Self-limited inflammatory process involving large and mid-sized airways

Common aetiologies

- Respiratory viruses (> 90%)
 - Influenza
 - Parainfluenza 3
 - Respiratory syncytial virus
 - Human metapneumovirus
- Non-viral (<10%)
 - Suspect if prolonged cough, longer incubation period, local outbreaks
 - Mycoplasma pneumoniae
 - Chlamydia pneumoniae
 - Bordetella pertussis
 - No association with *S. pneumoniae* or *H. influenzae* in patients without evidence of underlying lung disease

Tests

No investigations are required in the vast majority of cases:

- Gram stain not recommended
- Nasopharyngeal swab for influenza PCR not recommended for uncomplicated influenza-like illness

Diagnosis and management



Antibiotics not indicated

*Chest X-rays are not necessarily indicated for all patients with acute bronchitis and should be performed only if likely to influence management

Acute Exacerbation of COPD (AECOPD)

Definition

Acute increase in baseline dyspnoea, cough and/or sputum above the normal dayto-day variations, requiring a change in medication. Up to 80% of AECOPD have an infectious aetiology.

Common aetiologies

- Viral (up to 50%) more common in winter months
 - Rhinoviruses
 - Parainfluenza
 - Coronavirus
 - Influenza (in non-vaccinated)
 - RSV
- Bacterial
 - H. influenzae
 - S. pneumoniae
 - M. catarrhalis
 - Enterobacteriaceae (frequent hospitalisation and antibiotic use)
- Atypical bacteria are not implicated in AECOPD

Tests

Mild	Moderate (Requiring hospitalisation)	Severe (Requiring high
		care/ICU)
 Sputum culture not routine CRP or PCT (if available) Withhold antibiotics if negative 	 Sputum culture if frequent admissions or poor response to antibiotics CRP or PCT (if available) Withhold antibiotics if negative 	 Sputum culture Blood culture if pyrexial Nasopharyngeal swab for influenza PCR if in flu season

Diagnosis and management



COMPLETE A TOTAL OF 5 DAYS ANTIBIOTICS

Prevention

- Annual influenza vaccine recommended for all patients with COPD
- Pneumococcal polysaccharide (PPSV23) vaccine is recommended for all individuals over 65 years of age and anyone with COPD
- Antiviral chemoprophylaxis is not recommended

Pneumonia

Definition

Pneumonia is acute infection of lung parenchyma distal to the terminal bronchiole and causes consolidation.

САР		НСАР
Agent	Comments	Increased risk for infection with
S. pneumoniae	Most common cause	MDR pathogens
H. influenzae	More common in COPD	
Tuberculosis	More common in HIV	 Similar organisms to CAP
'Atypical organisms'	Not cultured	 Uncommonly
– M. pneumoniae	No specific clinical/	legionella or viruses
– Chlamydophilia	radiological features	 Gram negative bacilli
 Legionella spp. 	Suspect if risk factors or	 P. aeruginosa
	non-response to beta-	○ A. baumanii
	lactams	 Enterobacteriaciae
Oral anaerobes	Risk factors: alcoholism,	 S. aureus (including MRSA)
	aspiration, lung abscess	
P. jirovecii	HIV, bilateral infiltrates,	
	desaturation on minimal	
	exertion, poor response	
	to beta-lactams	
Respiratory viruses	Seasonal	
	Risk factors: pregnancy,	
	elderly, co-morbidities	

Common aetiologies of community acquired or health care associated pneumonia

Tests

16513			
САР	НСАР		
Only perform if likely to influence empiric management decisions	Always send specimens prior to initiation of empiric antibiotics		
Mild (CRB-65 score ≤ 2)	In all cases		
 Sputum culture and Xpert MTB/Rif if 	 Blood culture 		
failed outpatient Abx therapy	 Sputum Gram stain and culture 		
Severe (CRB-65 ≥ 3) or co-morbidities*			
 Sputum Gram stain and culture 			
Blood culture			
• Sputum for <i>P. jirovecii</i> DFAT if HIV +ve			
Urine Legionella antigen testing			
NP swab for influenza PCR if flu season			

NP = Nasopharyngeal, DFAT = direct fluorescent antibody test

* Chronic cardio-pulmonary disease, alcoholics, immune suppression (excluding HIV), CKD, cirrhosis

Diagnosis and management





- Send sputum GeneXpert MTB/rif
- Exclude empyema or lung abscess
- Add clarithromycin 500 mg 12-hourly (or azithromycin 500 mg daily)
- Send additional blood and sputum cultures

2. Health care associated pneumonia

- Send blood and sputum cultures prior to initiating broad spectrum antibiotics
- Consult microbiologist or infectious diseases specialist about choice of appropriate empiric antibiotic

3. Penicillin allergy

 Moxifloxacin 400 mg po/iv daily or levofloxacin 500mg po 12-hourly (750mg iv 12-hourly in severe pneumonia)

Chapter 9 Intra-abdominal infection

Definitions and causes

Infections in the abdomen can be divided into the following main groups:

- 1. Infections of the biliary system, including cholecystitis and cholangitis
- 2. Infections of the bowel, including appendicitis and diverticulitis
- 3. Intra-abdominal collections or abscesses
- 4. Peritonitis, including bowel perforations and spontaneous bacterial peritonitis (SBP) related to liver disease

Common aetiologies

Empiric antibiotic therapy for community-acquired intra-abdominal infections should cover all of the following organisms:

- Enteric gram-negative bacilli: E. coli, K. pneumoniae
- Anaerobic organisms
- Enteric streptococci

Other possible causes in health care-associated infections or severely ill patients include:

- Enterococci
- Candida
- MRSA

Tests

Most cases will require abdominal imaging (either ultrasound or CT), unless there is a clear indication for urgent laparotomy.

- Blood culture is recommended for patients with sepsis syndrome and suspected intra-abdominal infection.
- Culture of infected material is generally not helpful but is recommended in the following situations:
 - o HCAI
 - o SBP

 - o Re-do laparotomies

Diagnosis and management

1. Spontaneous bacterial peritonitis Diagnosis:

- Ascitic fluid aspirate with WCC > 250 cells/mm³
- Positive ascitic fluid culture (low sensitivity; high specificity if sample taken properly)

Management:

- Ceftriaxone 1 g IV daily for 5 days
- Add ampicillin 1 g QID in the following situations only:
 - Cholestatic liver disease
 - Fulminant liver failure (encephalopathy with coma)
 - Not responding to ceftriaxone after 48 hours

2. Most other intra-abdominal infections



Alternative antibiotic regimens

- Co-amoxiclav unavailable:
 - Ampicillin 1 g iv 6 hourly PLUS gentamicin 6 mg/kg/day PLUS metronidazole 500 mg iv 8-HOURLY

OR

- Ceftriaxone 1 g daily PLUS metronidazole 500 mg 8-hourly
- Severe Penicillin allergy:
 - Ciprofloxacin 400 mg iv 8-hourly PLUS metronidazole 500 mg iv 8-hourly

Chapter 10 Acute diarrhoea

Definition

Diarrhoea for < 2 weeks duration

Likely pathogens-

- Viruses (norovirus, rotavirus, adenoviruses, astrovirus),
- Bacteria (Salmonella, Campylobacter, Shigella, Enterotoxigenic *E. coli, C. difficile*) and bacterial toxins
- Protozoa (Cryptosporidium, Giardia, Cyclospora, Entamoeba)

Clinical features

- Stool taking the shape of its container > 3 times per day
- Blood in stool
- Fever

History

- Food exposure
- Illness among close contacts
- Recent travel
- HIV status
- Recent antibiotics

Tests (see algorithm)

The vast majority of episodes of diarrhoea DO NOT require antibiotics. Mild cases are usually self-limiting and require symptomatic treatment only. Moderate to severe cases require investigation +/- hospitalisation.

Diagnosis and management



Treatments

- Empiric:
 - Ciprofloxacin 500 mg po 12-hourly for 3 days pending results of culture and sensitivity
 - If bloody diarrhoea add empiric metronidazole 500 mg iv 8-hourly (or 400 mg po 8-hourly) for 5 days
- Definitive:
 - Based on culture results
- Clostridium difficile toxin or molecular test positive:
 - o See algorithm
 - Resolution of symptoms generally occurs within 5-7 days, but it is not unusual for symptoms to persist for the first 3-5 days
 - o 25% of patients with C. difficile will relapse

Management of C. difficile diarrhoea



Chapter 11 Urinary tract infections

Uncomplicated UTI

Definition

'Uncomplicated' refers to either a lower urinary tract infection or upper urinary tract infection (pyelonephritis) in non-pregnant women with structurally and neurologically normal genitourinary tracts. Acute uncomplicated cystitis is defined as:

• Symptomatic bladder infection characterised by a clinical syndrome of frequency, urgency, dysuria or suprapubic pain

Common aetiologies

Pathogens	Common contaminants of urine cultures
Enterobacteriaceae	Candida species
 – E. coli (most common) 	• Enterococcus spp.
– K. pneumoniae	Gardnerella vaginalis
 Enterobacter spp. 	Mycoplasma hominus
 Proteus spp. 	Ureaplasma urealyticum
Coagulase negative staphylococci	
– S. saprophyticus	
Group B streptococcus	
Enterococcus spp.	

Tests

- Urine culture only for:
 - Reinfection, persistent or recurrent cystitis
 - Symptoms with negative dipstick
- Do not perform follow-up cultures if symptoms have resolved
- Do not perform screening cultures in asymptomatic diabetics, elderly or patients with indwelling urinary catheters

Diagnosis and management

The diagnosis of urinary tract infection requires the presence of compatible symptoms plus bacteriuria (bacteria in the urine) or indirect evidence of infection, such as:

- Urine dipstick leucocyte esterase or nitrite positive
- Urine microscopy showing > 1+ leucocytes

Asymptomatic bacteriuria (a positive urine culture from patients without symptoms referable to the urinary tract) should not be treated, except in pregnant women and prior to invasive urological procedures.



Pyelonephritis



Complicated UTI

Definitions

A symptomatic urinary tract infection in:

- Individuals with functional or structural abnormalities of the genitourinary tract
- Men
- Pregnant women
- Patients with indwelling urinary catheters

Common infectious aetiologies

Caused by the same pathogens as uncomplicated UTIs. Infections in patients with indwelling urinary catheters more likely to be caused by drug resistant organisms.

Tests

Perform urine cultures in all of the above patient groups presenting with symptoms of UTI. In catheterised patients urine specimens should be obtained after catheter removal from a freshly placed catheter or voided midstream sample.

If fever/symptoms persist > 48 hours:

- Perform blood culture (in case of resistant bacteria)
- Image the urinary tract and abdomen to exclude collections
Catheter-associated UTI



NB: non-specific signs of CA-UTI include fever or rigors, altered mental state and unexplained lethargy

UTI in men



UTI in pregnancy

i. Asymptomatic bacteriuria

Pregnant women with asymptomatic bacteriuria are at increased risk of developing pyelonephritis. Therefore all pregnant women should be screened for bacteriuria.

Diagnosis:

• Any culture showing $\ge 10^3$ cfu/ml of a single organism (or any *E. coli*) in an asymptomatic pregnant woman

Management:

- Appropriate oral antibiotic for 5 days (see below)
- Perform follow-up urine culture to confirm sterility

ii. Cystitis and pyelonephritis

Diagnosis:

• As per uncomplicated UTI guidelines

• Always send urine culture

Management:

Ciprofloxacin is contraindicated in pregnancy. Therefore the following empiric antibiotics should be used, with de-escalation to narrower spectrum antibiotics once organism and sensitivities available:

- Cystitis or mild pyelonephritis:
 - Coamoxiclav 1 g po 12-hourly before the 3rd trimester.
 Cefuroxime 250 mg po 8-hourly is preferred in the 3rd trimester due to decreased risk of necrotizing enterocolitis
 - Duration 5 days for cystitis, 14 days for pyelonephritis
- Severe pyelonephritis
 - Treat as per uncomplicated UTI guidelines

Chapter 12 Sexually transmitted infections

Vaginal discharge

Definitions

Vaginal and occasionally cervical infection characterised by discharge, itching or odour.

Common aetiologies

- Bacterial vaginosis (BV): replacement of normal flora by polymicrobial overgrowth
- Trichomoniasis: *T. vaginalis*
- Candidiasis: Candida albicans
- Cervicitis: C. trachomatis and N. gonorrhoeae

Tests

No tests are necessary to confirm specific causes at the initial presentation. For recurrent or persistent symptoms, attempt to confirm diagnosis by office tests:

- Bacterial vaginosis
 - Clue cells on microscopy
 - pH of vaginal fluid > 4.5
 - Whiff test: fishy odour after addition of KOH to vaginal fluid
- Trichomoniasis
 - Wet prep slide to visualise motile organisms (sensitivity 70%)
- Candidiasis
 - Wet prep slide with KOH demonstrating yeasts and pseudohyphae

Diagnosis and management



Penicillin allergy (severe)

Omit ceftriaxone and increase azithromycin: 2 g po single dose

Urethritis

Definition

Urethral inflammation from infectious and non-infectious causes

Common aetiologies

- Gonococcal urethritis (*N. gonorrhoeae*)
- Non-gonococcal urethritis (NGU)
 - Chlamydia (*C. trachomatis*)
- Non-chlamydial NGU: usually no pathogen found

Tests

Usually requires no special investigations.

Diagnosis and management



Genital ulcer syndrome (GUS)

Definition

New genital, anal or perianal lesion after recent sexual activity.

Common aetiologies

Sexually transmitted

- HSV and syphilis most common
- H. ducreyi (chancroid)
- C. trachomatis (LGV)

Non-sexually transmitted

- Infectious: folliculitis, candida, tuberculosis
- Non-infectious: trauma, malignancy, eczema, psoriasis, contact dermatitis (latex allergy), aphthous ulcers

Diagnosis

It is not possible to distinguish the causes on clinical grounds alone. Do not diagnose a venereal cause of GUS if no sexual activity in the past 3 months (except for reactivated HSV).

Recurrent	Herpes simplex reactivation	
Painless	Primary syphilis	
	Lymphogranuloma venerum (LGV)	
Painful	Herpes simplex (HSV)	
	Chancroid	
Lymphadenopathy	Syphilis	
	HSV	
	LGV (massive, often unilateral)	
	Chancroid	

Tests

Usually requires no investigations.

Management



Chapter 13 Acute meningitis

Definition

• Acute inflammation of the meninges of <7 days duration.

Likely pathogens

- Common Various bacteria, viruses. TB meningitis can present acutely. Rare
 fungi, protozoa and helminths
- Common bacterial pathogens are *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae* and *Listeria monocytogenes* (in immunocompromised and elderly patients).

Clinical features

- Any 2 of the 4 cardinal features; headache, fever > 37.5°C, neck stiffness and altered mental status
- Supporting features are photophobia, blanching or purpuric rash and vomiting

Tests

• See algorithm for lumbar puncture and CT brain



Management

General principles:

- Patients with suspected bacterial meningitis should receive ceftriaxone 2 g iv immediately. The dose for continued treatment is 2 g iv 12-hourly
- Penicillin allergy is not a contra-indication to use of ceftriaxone, unless the allergy was life threatening
- Blood culture and lumbar puncture should be performed before administration of antibiotics ONLY if this does not cause significant delay
- If bacterial meningitis is strongly suspected on the basis of clinical and CSF findings and all cultures are negative give ceftriaxone for 10 days
- Steroids are not recommended

Specific therapy:

- *S pneumoniae*: duration 10 days
 - If MIC unknown or > 0.1 microg/ml: ceftriaxone 2 g iv 12-hourly
 - If MIC < 0.1 microg/ml: penicilin G 4 mU ivi 4-hourly or ampicillin 2 g iv 4-hourly
- N meningitidis: duration 7 days
 - Ceftriaxone 2 g iv 12-hourly
- *L monocytogenes*: duration 21 days
 - Ampicillin 2 g iv 4-hourly
- Gram-negative infection: duration 21 days
 - Community-acquired: cefepime 2 g iv 8-hourly or ceftazidime 2 g iv 8-hourly
 - Health care associated: meropenem 2 g iv 8-hourly



⁹Opening pressure, protein, total WCC and % neutrophils reduced. % lymphocytes & CSF/serum glucose increased

Chapter 14 Peripheral line sepsis

Peripheral line-related infections increase morbidity, mortality, antibiotic usage and length of stay. PREVENTION BY EARLY REMOVAL OF LINES IS THE KEY INTERVENTION. By definition these are healthcare associated infections (HCAI) with a high risk of resistant pathogens.

Likely pathogens

Staphylococcus aureus (MSSA/MRSA), Coagulase negative staphylococci, Streptococcus spp.

Diagnosis and management



Exclude or drain collections Ensure adequate vancomycin trough

levels (15 - 20 mg/mL) Repeat blood cultures

Chapter 15 Staphylococcus aureus bacteraemia

Staphylococcus aureus (*S. aureus*) bloodstream infection carries a high mortality rate. It is commonly introduced by vascular line infections or other health-care associated interventions, but can result from invasive *S. aureus* at any site. *S. aureus* bacteraemia can disseminate to any organ including heart valves, bone and lungs, and therefore requires prolonged intravenous therapy with higher doses of appropriate antibiotics.

Definitions and dosing

Methicillin sensitive S. aureus (MSSA)

- Sensitive to anti-staphylococcal beta-lactam antibiotics
- Cloxacillin is the treatment of choice:
 - Initial dose 2 g 6 hourly IV
 - Use 3 g 6 hourly for endocarditis, prosthetic heart valves or other endovascular material, meningitis and osteomyelitis

Methicillin resistant *S. aureus* (MRSA)

- Resistant to beta-lactam antibiotics
- Vancomycin is the treatment of choice:
 - Loading dose 25 30 mg/kg slow infusion
 - Thereafter 15-20 mg/kg BD (will require lower doses and/or less frequent intervals in renal impairment)
 - Measure trough levels before the 4th dose and aim for a target of 15 20 mg/L

Management



Clinical features of complicated *S. aureus* bacteraemia include persistent fever, bone pain, new murmur or peripheral manifestations of endocarditis or focal neurological signs. Patients with these problems require directed investigations for source control and should be discussed with an infectious diseases specialist.

Chapter 16 Skin and soft tissue infections

Cellulitis

Definition

Acute infection involving skin and subcutaneous tissue

• Commonly precipitated by minor trauma or underlying skin lesion

Diagnosis (Image: http://treatmentofcellulitis.net)

Clinical only:

• Redness, tenderness, local heat, non-raised edges

Differentiate from:

Infections	Non-infectious	
Erysipelas	DVT	
Necrotising fasciitis	Insect bites	
Gas gangrene	Fixed drug reaction	

Common aetiologies

- Streptococci (usually S. pyogenes)
- S. aureus

Tests

None recommended

- Blood cultures are rarely positive and not generally helpful unless extensive or severe infection.
- Superficial pus swabs are not helpful and should NOT be performed



Management



Cutaneous abscess

Definition

Deep inflammatory nodule extending into subcutaneous tissue that develops from preceding folliculitis

Common aetiologies

S. aureus

Tests

None

Management

All cases require surgical drainage.

Uncomplicated cases

• No antibiotics required

Complicated cases (surrounding cellulitis, located on face, systemic symptoms)

- Flucloxacillin 500 mg po 6-hourly for 5 days or co-amoxiclav 1g po 12-hourly
- In penicillin allergy use clindamycin 450 mg po 8 hourly

Diabetic foot

Definition

Chronic foot infections in diabetics

- Mild: limited to skin/superficial subcutaneous tissue < 2 cm beyond ulcer margin
- Moderate: cellulitis > 2 cm, deep fascial involvement, gangrene, abscess, osteomyelitis
- Severe: systemic complications

Common aetiologies

- Mild infections or previously untreated
 - S. aureus
 - Streptococci
- Chronic lesions or previously treated
 - Above plus
 - Enterobacteriaceae
- Chronic, refractory or prolonged broad spectrum antibiotics
 - Above plus
 - Pseudomonas
 - Anaerobes
 - Enterococci

Tests

None required in mild or previously untreated infections. Tissue cultures are recommended in all other scenarios. It is essential to clean and debride the lesion before obtaining specimens for culture. Blood cultures should be performed in severe infections.

Diagnosis and management



Penicillin allergy:

- Mild/moderate infections: Clindamycin 450 mg po 8-hourly (add ciprofloxacin 500mg po 12-hourly if requires admission)
- Severe infections: Clindamycin 600 mg iv 8-hourly PLUS ciprofloxacin 400 mg iv 8-hourly

Wound management

Optimal wound care is essential. Surgical consultation is recommended for the following problems:

- Deep abscess
- Bone or joint involvement
- Crepitus
- Gangrene
- Necrotising fasciitis
- Severe vascular insufficiency

Necrotising fasciitis

Definition (image: http://medicatoz.com/news/view?id=57)

Acute severe infection involving subcutaneous soft tissues including the fascial layers. Usually precipitated by trauma, surgery, peri-rectal abscess, bedsores or bowel perforation.



Common aetiologies

Usually polymicrobial infections:

- Streptococci
- Enterobacteriaceae
- Anaerobes

Tests

Blood cultures and surgical tissue specimens.

Diagnosis and management

Necrotising fasciitis is commonly associated with systemic toxicity manifested by fever, leukocytosis and possibly organ dysfunction. It rapidly progresses to cutaneous gangrene. Management involves the following:

- 1. Early and aggressive surgical debridement
- 2. Co-amoxiclav 1.2 g IV continued until clinical resolution

Alternative antibiotic regimens

- If co-amoxiclav unavailable: ampicillin 1 g 6-hourly PLUS metronidazole 500 mg 8-hourly PLUS gentamicin 6 mg/kg/day, all iv
- For refractory infections and in penicillin allergy: clindamycin 600 mg 8-hourly PLUS ciprofloxacin 400 mg 8-hourly, both iv

Chapter 17 Bone and joint infections

SEPTIC ARTHRITIS

Definition

Bacterial joint infection, usually due to haematogenous spread.

Common aetiologies

- Non-gonococcal
 - *S aureus* most common
 - Streptococcus spp. (S pyogenes, S pneumoniae, S agalactiae)
 - Gram-negative organisms (elderly, immunocompromised, comorbidities)
- N gonorrhoeae

Tests

In all cases:

- Joint aspirate BEFORE ANTIBIOTICS
 - o Cell count plus differential: high neutrophil count in most cases
 - o Gram stain and culture
 - Microscopy for crystals
- Plain X-ray

Diagnosis and management



OSTEOMYELITIS

Definition

Bacterial infection of bone due to contiguous spread from soft tissues, haematogenous seeding, or direct inoculation.

Common aetiologies

- Common
 - Saureus
 - Coagulase-negative staphylococci
- Occasional
 - Streptococci
 - Enterococci
 - Gram-negative bacilli
- Other
 - M tuberculosis
 - Fungal infections

Tests

- Always send specimens for culture
 - Deep tissue specimen: open surgical procedure or guided needle aspiration
 - Blood culture
- Imaging
 - Plain X-ray in all cases
 - May require other modalities such as bone scan, CT or MRI
- CRP may be useful to monitor response to therapy

Diagnosis and management



Notes:

- May need to continue IV therapy for 6 weeks or longer
- Do not add rifampicin in cases without foreign material
- Consider tuberculosis if culture-negative or no clinical improvement
- Vancomycin is used for health care-associated osteomyelitis or confirmed MRSA (loading dose 23 – 30 mg/kg followed by 15 – 20 mg/kg 12-hourly; maintain trough levels 15 – 20 mg/mL)
- See Chapter 18 for management of open fractures
- Infections associated with prosthetic material should be discussed with an expert

Chapter 18 Prophylaxis

Surgery

Surgical prophylaxis aims to prevent infection following a predictable exposure to bacteria. Antibiotics are only required **during** exposure and a single dose taken preoperatively is usually sufficient. A repeat dose should only be given if surgery is prolonged or there is massive blood loss. Choice of antibiotic depends on which bacteria are likely to be introduced by the operation, usually normal colonisers of skin or bowel. Examples are given below but refer to local policies for guidance.

Type of surgery	Prophylaxis	
Cardiothoracic	Cefazolin 2g iv	
Upper Gl		
Neurosurgery		
Orthopaedic (elective non-trauma)		
Lower limb amputation	Cefazolin 2g iv	
Colorectal	Plus	
Biliary	Metronidazole 500mg iv	
Pelvic		
ENT		
Ophthalmic	Chloramphenicol 0.5% drops	
ERCP with obstruction	Ciprofloxacin 500mg po 2h prior to the	
	procedure or cefuroxime 1.5g iv or	
	PIP/TZ 4.5g iv, both 1h prior to the	
	procedure	
Surgery for the implantation of any	Cefazolin 2g iv or cefuroxime 1.5g iv or	
permanent prosthetic material	vancomycin 1g iv as single dose	
Penetrating abdominal trauma or open	Cefazolin 2g iv + metronidazole 500mg IV	
fracture	and second dose if procedure > 3h	

Head injuries

Closed head injuries with non-penetrating wounds **do not** require antibiotic prophylaxis even if there is a CSF leak. Compound depressed skull fractures and penetrating spinal cord injuries do require prophylaxis/pre-emptive treatment e.g. ceftriaxone plus metronidazole for 5 days.

Open long bone fractures

If early (< 5 hours) washout and debridement, provide prophylaxis with cefazolin 1g iv 12-hourly for 48 hours only. If long delay to washout or significant contamination, treat with coamoxiclav 1.2 g ivi 12-hourly for 5 days.

Infective endocarditis

The evidence base is weak and guidelines are largely based on expert opinion, which differs between countries and region. In general only those at the highest risk of

infective endocarditis should be offered prophylaxis and then only when the risk of bacteraemia from the procedure is high.

Conditions requiring prophylaxis

- Significant congenital or acquired cardiac abnormalities
- Prosthetic valves or valvular repair utilising prosthetic material
- Previous infective endocarditis

Procedures requiring prophylaxis

• Dental procedures involving manipulations if the gingival or perapical region of the teeth or perforating the oral mucosa.

Examples of regimens are given in the table.

Procedure	Regimen	Alternative
Dental, oral or upper	Amoxicillin 3g po	Clindamycin 600mg iv
respiratory tract		
Genitourinary,	Ampicillin 2g iv	Vancomycin 1g iv
gastrointestinal or	Plus gentamicin 1.5mg/kg	Plus gentamicin 1.5mg/kg
biliary		

Rheumatic fever

• Secondary prophylaxis should be prescribed for all patients following rheumatic fever to prevent recurrences

Duration

- Without carditis 5 years after last attack or 21 years (whichever is longer)
- With mild carditis 10 years after last attack or 21 years (whichever is longer)
- With carditis and residual heart disease 10 years or until age 40 (whichever is longer). Sometimes life-long prophylaxis.

Regimen

• Benzathine penicillin 1.2MU IM every 3-4 weeks or penicillin V 250mg po 12hourly. If penicillin allergic azithromycin 250mg daily.