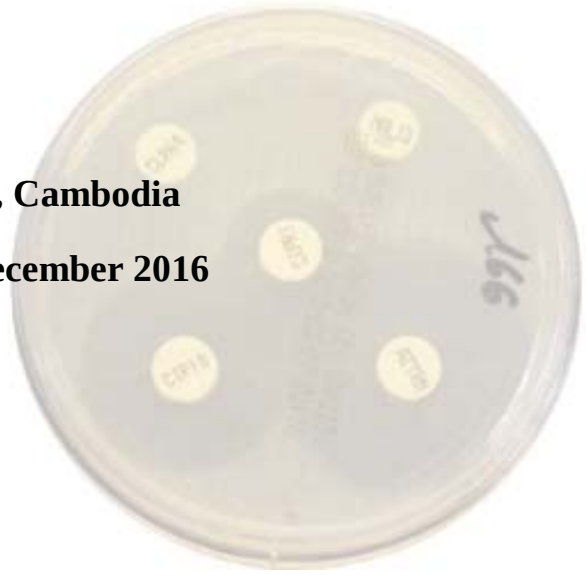
Clinical Practice Guidelines

Standard antibiotic treatment guidelines

for

Sihanouk Hospital Center of HOPE (SHCH) and HOPE Medical Centers (HMC)



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Preface

Guidelines are an important way to improve and standardize our antibiotic prescription (antibiotic stewardship). These clinical practice guidelines on standard antibiotic treatment version 2.0 are a revision of the original practice guidelines, which were issued in September 2011. These are a result of the fruitful collaboration between the Sihanouk Hospital Center of HOPE (SHCH)/HOPE Medical Centers (HMC) and the Institute of Tropical Medicine (ITM), Antwerp (Belgium) with the financial support from the Belgian Directory General of Development Cooperation (DGDC).

They remain based on local microbiology surveillance data, on published evidence from researches performed in the Southeast Asian region and on already existing international treatment guidelines.

They have been written as a consensus after many meetings and discussions among the members of the antibiotic committee from SHCH and HMC with the antibiotic coordination team and experts from ITM.

We have adapted our guidelines and revisions with a clear instruction on ANNOTATION that will make it easy for you to see what has changed, and what is new. Moreover, we included a number of new chapters. A detailed overview of the changes can be found on page 2.

Guidelines are always in evolution because of new surveillance data, changing scientific insights, differences in drug availability or local circumstances.

We always welcome your suggestions to adapt and improve our guidelines and hope they might be of help during your clinical practice!

Please contact or send your comments or suggestions to our antibiotic coordinating team:

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We would like to thank Dr **Thai Sopheak**, director of SHCH, A. Prof **Tan Kim Meng**, executive director of HMC, Prof **Lut Lynen**, Department of Clinical Sciences, ITM, for their guidance and continuous support for the guidelines revision.

Phnom Penh December 22, 2016.
The antibiotic team

List of abbreviations

AFB	Acid-Fast Bacilli
ARDS	Acute Respiratory Distress syndrome
BP	Blood Pressure
BS	Blood Sugar
BSI	Blood Stream Infection
BUN	Blood Urea Nitrogen
CAP	Community Acquired Pneumonia
CBC	Complete Blood cell count
CFU	Colony Forming Unit
COPD	Chronic Obstructive Pulmonary Disease
CPG	Clinical Practice Guideline
Cr Cl	Creatinine Clearance
CSF	CerebroSpinal Fluid
CVP	Central Vein Pressure
CXR	Chest X Ray
DBP	Diastolic Blood Pressure
DIC	Disseminated Intravascular Coagulation
DKA	Diabetes Keto-Acidosis
DM	Diabetes Mellitus
ECG	Electrocardiogram
ELISA	Enzyme-linked Immunosorbent Assay
ENT	Ear Nose Throat
ESBL	Extended-Spectrum Beta-Lactamase
ESR	Erythrocyte Sedimentation Rate
GCS	Glasgow Coma Scale
HAP	Hospital/Health-care Acquired Pneumonia
HCO3	Bicarbonate
HIV	Human Immunodeficiency Virus
I&D	Incision and Drainage
ICP	Intra Cranial Pressure
ID	Infectious Disease (Department/Doctor)
IE	Infective Endocarditis
IV	IntraVenous
IVP	IntraVenous Pyelography
LFTs	Liver Function Tests

LP	Lumbar Puncture
LR	Lactate Ringer
MAP	Mean Arterial Pressure
MAT	Micro agglutination test
MIC	Minimum Inhibitory Concentration
MRSA/E	Methicillin Resistant Staphylococcus Aureus/Entoerococcus
MSSA	Methicillin Susceptible Staphylococcus aureus
NSS	Normal Saline Solution
SaO2	Oxygen Saturation
OP	Opening Pressure
PCP	Pneumocystis Carinii (Jiroveci) pneumonia
PE	Pulmonary Embolism
PMN	Polymorphonuclear
PO	Per Os
q4h, q6h, q8h, q12h	Every 4 hours, every 6 hours, every 8 hours, every 12 hours
qd or QD	Every day
RBC	Red Blood Cell Count
SBP	Spontaneous Bacterial Peritonitis
SD	Single Dose
AST or SGOT	Aspartate Aminotransferase
ALT or SGPT	Alanine Aminotransferase
SIRS	Systemic Inflammatory Response Syndrome
SOP	Standard operating Procedure
Sp	Species
SSTI	Skin and Soft Tissue Infections
STD	Sexually Transmitted Diseases
TB	Tuberculosis
UA	Urine Analysis
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infection
VDRL	Venereal Disease Research Laboratory
WBC	White Blood Cell Count

Guideline outline

Introduction

These clinical practice guidelines (CPG) on standard antibiotic treatment version 2.0 are a revision of the original practice guidelines, which were issued in September 2011. These are a compilation of several 'Clinical Practice Guidelines' which have been composed by the different Guidelines'Groups in SHCH/HMC which were initially done between 2008 and 2011.

After being in use for several years, the original guidelines needed revision. New scientific evidence emerged; we encountered diseases in our clinical practice that were not covered in the original guidelines, the surveillance data showed emerging trends and local circumstances and practices changed. In this new guideline, we added a number of new chapters and we updated the existing guidelines (for a detailed overview of the changes see page 2).

The problem of antibiotic resistance in SHCH/HMC is not isolated and is a reflection of the bigger public health problem in Cambodia. Awareness of this problem is increasing slowly, also at the level of the Ministry of Health.

The guidelines are based upon (inter)national literature and local surveillance data. They reflect good consensus among all opinions. In all antibiotic choices listed in these guidelines, care was given to the optimal balance between effectiveness, toxicity, cost and further induction of resistance.

In most guidelines, and also in ours, there is a strong focus on "empiric" antibiotics, meaning antibiotics that can be given based on clinical presentation and/or while awaiting the culture results. Before starting any antibiotic, it is very important to question whether an antibiotic is really necessary, and if so, if the necessary cultures have been taken. In settings where microbiological laboratory diagnosis is available, the antibiotic treatment needs to be reviewed and adapted according to the Gram stain and culture results.

The first aim of these guidelines is 'guiding' the diagnostic and therapeutic choices, but they cannot replace careful assessment and critical judgment of the individual patient's problem. This means that exceptions are possible on a case by case basis and after discussion with members of the antibiotic team.

On the other hand, these guidelines are also meant to streamline and rationalize the hospital's antibiotic use in a context of quickly emerging antibiotic resistance. This is a very important tool in the containment of antibiotic resistance, together with surveillance and infection control.

Therefore, the SHCH/HMCs antibiotic team highly appreciates and recommends the use of these guidelines in your clinical practice, and we are welcoming all your questions, remarks and additions for the next version!

What is new in this revised Antibiotic Clinical Practice Guidelines V 2.0?

The major changes include:
(for details, please see full text in separate chapters)

1- New chapters with guidelines on:

   a. Spontaneous bacterial peritonitis (SBP) (chapter 9 – page 48) together with SOP of paracenthesis (page 72).
   b. Leptospirosis (based on clinical suspicion with clinical criteria and scoring: Faine's Criteria for the Diagnosis of Leptospirosis) (chapter 10 – page 52).
   c. Rickettsial diseases (chapter 11 – page 57)
   d. Short note on management of patients suspicion of tetanus (page 65)

2- Chapter 1: Sepsis guidelines (page 4):
   a. Adjustment of treatment of melioidosis (see more detail in chapter 8):
      - Ceftazidim dose increased to 2g q6-8h;
      - No more doxycycline required for eradication phase
   b. In case of suspicion of rickettsiosis or scrub typhus, add doxycycline 100 mg q12h PO for 5 - 10 days.
   c. Add note:
      - **Amikacin or gentamycin should not be used alone**;
      - **No need to add amikacin on meropenem use.**

3- Chapter 2: Pneumonia (page 11):
   a. Adaption of the empiric treatment for lung abscess :
      - No ciprofloxacin but first choice: amoxicillin/clavulanic acid, alternative: ceftriaxone + metronidazole.
      - In case of severe sepsis or septic shock, add amikacin
   b. Added note for PCP: avoid high flow >10 L/mn oxygen after 48-72 hours because of risk of oxygen toxicity.

4- Chapter 3: UTI (page 19): added note:
   a. Clinical symptoms should be evaluated carefully; repeat sampling through a clean catheter if highly suspicion of contamination.
   b. Cultures from contaminated samples often grow multi-drug resistant pathogens, for which unnecessary antibiotics may be prescribed.
   c. A high epithelial cell counts suggests a bad sampling (= chance to find the true bacteria causing UTI is less) => reject sample and need to repeat sample before making decision to treat.

5- Chapter 7: Bacterial meningitis (page 37):
   a. Note on empirical treatment: Consider adding doxycycline high dose (200 mg q12 for 10 d) for presumed rickettsiosis/scrub typhus.
   b. Removed aminoglycoside coverage for *Listeria monocytogenes*

6- Chapter 8: melioidosis (page 42):

a. Acute phase: ceftazidim dose is increased to 2 g IV **q6-8h**

b. Reduced dose of cotrimoxazole (trimethroprim/Sulphamethoxazole:TMP/SMX): according to body weight 6/30 mg/kg q12h PO for 3-6 months

Weight	Dose TMP/SMX
<40 Kg (children)	160/800 mg q12h PO
≤ 60 Kg	240/1200 mg q12h PO
> 60 Kg	360/1600 mg q12h PO

c. Consolidation phase: treatment with cotrimoxazole only; **NO MORE DOXYCYCLINE**

- Alternative for cotrimoxazole in case of contra-indications or toxicity: Augmentin 20/5 mg up to 1000/250 mg q8h PO or doxycycline 100mg q12h PO

d. A renal dose adjustment of ceftazidim/meropenem and cotrimoxazole according to creatinine clearance and patient's body weight (*please also see page 76 for additional explanation on renal insufficiency).*

	CrCL 31 – 50	CrCL 15 – 30	CrCL <15	Hemodialysis
Ceftazidime				after each dialysis
> 60 Kg	2 g q8h	2 g q12h	2 g q24h	add 2g
≤ 60 Kg	1 g q8h	1 g q12h	1 g q24h	add 1g
Meropenem	1 g q12h	1 g q12h	1 g q24h	1 g dose after each dialysis
Cotrimoxazole				After each dialysis
> 60 Kg	1920 mg q12h	1920 mg q24h	1920 mg q24h	Add 1920 mg
≤ 60 Kg	1440 mg q12h	1440 mg q24h	1440 mg q24h	Add 1440 mg

Creatinine clearance (CrCL): calculated by Cockroft-Gault method (see page 76)

*Adapted from Jabbar Z, Currie BJ. Melioidosis and the kidney. Nephrology 2013.

7- Chapter 12: Surgical prophylaxis (page 59): added to note: ceftriaxone 2g IV single dose for surgical prophylaxis may be used in case no cefazolin available.

1. Sepsis

1. Case Definition:

- **SIRS criteria:** (Systemic Inflammatory Response Syndrome): two or more of:

  - Temperature > 38°C or < 36°C
  - Heart rate > 90 beats/min
  - Respiratory rate > 20 breaths/min
  - WBC > 12,000/mm^3 or < 4,000/mm^3

  SIRS can be caused by an infection or another type of inflammation (burns, trauma…)

- **Sepsis:** = presence of SIRS-criteria due to either a culture-proven infection or an infection identified by clinical examination

- **Severe sepsis:** = sepsis + at least one of the following signs of organ hypoperfusion or dysfunction:

  - Areas of mottled skin
  - Capillary refilling requires ≥ 3 seconds
  - Urine output < 0.5-1 ml/kg/h for at least one hour, or need for renal replacement therapy
  - Abrupt change in mental status
  - Platelet count < 100,000 platelets/ml
  - Disseminated intravascular coagulation
  - Acute lung injury or acute respiratory distress syndrome (ARDS)
  - (Cardiac dysfunction, as defined by echocardiography)

- **Septic shock:** = sepsis (see above) + hypotension:

  - MAP < 60 mmHg (or < 80 mmHg if patient has hypertension) despite adequate fluid resuscitation.
  - OR dopamine > 5 µg/kg/min is required to maintain MAP ≥ 60 mmHg (or ≥ 80 mmHg if patient has hypertension)

  * Note: MAP= (Systolic BP + 2 Diastolic BP)/3

2. Most frequent etiological agents in SHCH :

- *Staphylococcus aureus* (rarely non-aureus staphylococci)
- Streptococci (pneumococcus and other)
- *E. coli* and other *Enterobacteriaceae* (*Klebsiella* sp., *Enterobacter* sp.)
- *Burkholderia pseudomallei*
- Salmonella Typhi/Paratyphi A and non-typhoid Salmonella

3. Differential diagnosis:

- Cardiogenic shock
- Hypovolemic shock
- Anaphylactic shock

- Neurogenic shock
- Addisson crisis
- Intoxication

4. Diagnostic procedures:

4.1. Clinical arguments:

i. Predisposing conditions: underlying diseases that cause immune deficiency (diabetes, HIV, steroid use, liver cirrhosis, chronic renal failure, malignancy, chemotherapy…)

ii. Clinical symptoms/signs: see case definition

4.2. Technical procedures:

4.2.1. Baseline lab:

- Blood culture two bottles (see SOP)
- CBC, creatinine, BUN, electrolytes, transaminase, blood sugar, HCO_3
- Urine analysis. If UA (+), urine microscopic and culture
- Chest radiography
- Pregnancy test if applicable

4.2.2. Additional lab:

- CSF Gram stain and culture if suspicion of meningitis
- Pus Gram stain and culture, if abscess or wound present
- Malaria smears
- Serum amylase (if suspicion of acute pancreatitis)
- HIV test
- ECG if indicated
- Abdominal ultrasonography
- Heart ultrasound (if suspicion of endocarditis)

4.2.3. Clinical procedure as indicated (see SOP for specific procedures):

- Lumbar puncture, thoracocentesis, arthrocentesis, paracentesis, abscess aspiration, bone marrow biopsy….
- Pelvic and rectal exam

5. Therapeutic approach:

5.1. Stabilize the patient

5.1.1. Stabilize the patient according to ABC (Airway, Breathing, Circulation)

5.1.2. IV fluid resuscitation: IV bolus NSS or Ringer Lactate

- 20-30 ml/kg, if severe sepsis or septic shock can be repeated several times up to 40 to 60 ml/kg in first 6 hours, or more in some patients (estimate around 4-6 liters over 24 hours)
- Consider to start dopamine 5µg/kg/min (max 20µg/kg/min) after unsuccessful IV challenge of at least 3-4 liters IV fluids in the first 1-2 hours (or 1-2 liters in case of congestive heart failure (CHF) or advanced heart disease).

- The goal of fluid resuscitation is:
  - Improved vital signs
  - Urine output ≥ 0.5-1 ml/kg/h
  - CVP 8-10 cm H_2O (normal CVP 3-9 cm H_2O = 2-7 mmHg)

5.2. Empirical treatment:

- Sepsis from respiratory focus: amoxicillin-clavulanic acid 1000/250 mg IV q4-6h or 1000/250 mg PO q8h

* Alternative: ceftriaxone 2 g IV qd (amoxicillin-clavulanic acid preferred over ceftriaxone because of its anti-melioidosis activity).

* If severe sepsis or ARDS: add amikacin 20 mg/kg IV qd

- Sepsis from soft tissue focus: cloxacillin 2 g IV q6h

* Alternative (in case of penicillin allergy): lincomycin 600 mg IV q8h

* If suspicion of melioidosis: ceftazidime 2 g IV q6-8h + cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd

* Early surgical consultation as needed

- Sepsis from necrotizing fasciitis: penicillin 4 MIU IV q4h + lincomycin 600 mg IV q8h+ amikacin 20 mg/kg IV qd

* Please perform here besides blood cultures also Gram stain and culture on wound/pus/tissue

- Sepsis from abdominal source (eg. deep organ abscess, peritonitis…):

- Ceftriaxone 2 g IV qd + metronidazole 500 mg IV q8h
- OR: amoxicillin-clavulanic acid 1000/250 mg IV q4-6h
- **If suspicion of typhoid fever**: ceftriaxone 2 g IV qd
- **If severe sepsis or septic shock**: add amikacin 20 mg/kg IV qd (should be discussed with ID-team doctor).
- Early surgical consultation as needed

- Sepsis from SBP: ceftriaxone 2 g IV qd (criteria to treat: PMN > 250cells/ml in ascites fluid)

- Sepsis from urinary focus: ceftriaxone 2 g IV qd

- **If severe sepsis, septic shock** or if no improvement within 48 hours: add amikacin 20 mg/kg IV qd (should be discussed with ID-team doctor).

- Sepsis due to multifocal infections (more than 2 infection sites) with risk factors of melioidosis : ceftazidime 2 g IV q6-8h and cotrimoxazole 6/30 mg/kg IV/PO q12h *plus* folic acid 5 mg PO qd (need to discuss with antibiotic committee)

- Sepsis from meningitis: ceftriaxone 2 g IV q12h (+ ampicillin 2 g IV q4h in very young or very old patients and immunocompromised patients).
Add dexamethasone (8-10 mg IV q8h for 5 d).

- **Suspicion of leptospirosis**: ceftriaxone 2g IV qd. If ricketiosis or scrub typhus cannot be ruled out, need to add doxycycline 100 mg q12h PO for 5-10 days

5.3. Directed treatment (if result available from blood or other relevant culture)

- *Staphylococcus aureus:*

- If oxacillin S: cloxacillin 2 g IV q6h x 14 d (PO treatment not effective enough if blood stream infection)

* It is advised to perform echocardiography to look for endocarditis. If endocarditis found: cloxacillin 2 g IV q4h for 6 weeks *plus* gentamicin loading dose 3 mg/kg IV then 1mg/kg IV q8h (see endocarditis guideline)

- If MRSA: vancomycin 1 g IV q12h is preferable

If not available: cotrimoxazole 5/25 mg/kg IV/PO q12h or lincomycin 600 mg IV q8h for 2 weeks (only if proven susceptibility from antibiogram).

- *Streptococcus pneumoniae:*

- If penicillin S or I: penicillin G 4 MIU IV q6h x 10 d (when afebrile may be switched to amoxicillin 1 g PO q6h)
- If meningitis: penicillin G 4 MIU IV q4h OR ceftriaxone 2 g IV q12h x 14 d

- *Escherichia coli* and other *Enterobacteriaceae*

If ceftriaxone resistant: meropenem 1 g IV q8h x 14 d (run over 3 hours IV) (only after discussion with ID team). PO treatment depending on antibiogram results

- *Salmonella* sp.:

- If ciprofloxacine S: ciprofloxacin 500 mg PO q12h x 10 d
- If ciprofloxacine R: ceftriaxone 2 g IV qd or azithromycin 500 mg PO qd x 10 d

* In case blood cultures are sterile and still strong suspicion of infection due to S*almonella* sp.:

- For non-immunocompromised or suspicion of typhoid fever (Salmonella Typhi), ceftriaxone can be switched to azithromycin 500 mg PO qd to complete 10 d
- For immunocompromised patients or suspicion of non-typhoid salmonella (e.g. *S. Choleraesuis*): ceftriaxone can be switched to ciprofloxacin 500 mg PO q12h

- *Burkholderia pseudomallei*: (see specific guideline on melioidosis for details)

- **Attack phase:** ceftazidime 2 g IV q6-8h + cotrimoxazole 6/30 mg/kg PO q12h for 10-14 d *plus* folic acid 5 mg PO qd.
- **Eradication phase**: cotrimoxazole 6/30 mg/kg PO q12h (3-6 months) *plus* folic acid 5 mg PO qd for 3-6 months.

5.4. Monitoring:

5.4.1. Clinical monitoring: every hour for the 1st 24 hours

- Urine output
- Vital signs, consciousness-level
- Blood sugar q1h for the first 24 hours if known BS > 150 mg (finger stick)

5.4.2. Laboratory monitoring

- BS (goal is < 150 mg/dl)
- Hematocrit should be at least around 21-27%.
- After the result of Gram stain and culture with AB-sensitivity test is available, please change the antibiotic accordingly.

* **General remarks**: Repeat the blood cultures if patient does not improve on the current empiric schedule and in all cases of bacteraemia by *Staphylococcus aureus* (at day 3), *Candida* species (at day 5) and *Burkholderia pseudomallei* (at day 5).
* Repeat the baseline lab at day 2 and day 5 or as needed.

Note

* Please aim for tight blood sugar control if BS > 200 mg/dl:

- Start short acting insulin according to the formula: **IV Actrapid = (current BS-100):40**.
- If persistent high > 400 mg/dl- insulin drip should be considered after the 1st 2-4 hours or started immediately in DKA. *Insulin drip 0.1 IU/kg/hours or 2-5 IU/hour*.
- Do not start long acting insulin in the first 48 hours.

* Empirical antibiotic choice is based on local microbiological patterns, severity of illness, age, clinical features, co-morbidities, exposure, (other medication).

* Switch IV to PO antibiotics (after 72 hours) when hemodynamically stable, clinically improving, able to ingest medications and have normally functioning GI tract.

* For melioidosis, cotrimoxazole should be very high dose: 6/30 mg/kg PO q12h

* If gentamicin is indicated as single dose, it is 6 mg/kg IV

* Amikacin or gentamycin should not be used alone

* No need combine amikacin with meropenem

* For streptococcal infection (e.g. pneumococci…): need to look at the MIC (Minimum Inhibitor Concentration)

* ESBL (Extended Spectrum Beta Lactamase) used for Gram negative bacilli (Enterobacteriacae group: *E. coli, Klebsiella* sp, *Salmonella* sp, *Enterobacter* sp. It is not used for non-fermentive Gram-negative such as *Pseudomonas* sp, *Burkholderia pseudeomallei, Acinetobacter* sp…)

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2. Pneumonia

1. Case Definition:

2.1 General Definition:

Pneumonia is an infection of the pulmonary parenchyma and surrounding tissues.

2.2 Diagnostic criteria: at least 2 of the following:

i. Symptoms
   a- Fever, rigors
   b- New cough +/- sputum production or chronic cough with change in color of sputum
   c- Chest pain and /or shortness of breath.
ii. Auscultatory findings consistent with pneumonia (e.g. localized crackles)
iii. Chest X-ray: new opacity or infiltrate

2.3 Types: pneumonia can be broadly categorized as:

i. *Community-acquired pneumonia=CAP* (including atypical pneumonia): Pneumonia acquired outside of hospitals or ≤ 48 hours of admission.
ii. *Hospital acquired pneumonia (HAP):* Pneumonia acquired in a hospital setting > 48 hours or previous hospitalization in the last 3 months.
iii. *Aspiration Pneumonia*: pneumonia secondary to abnormal entry of endogenous secretions or exogenous substances into the lower airways.
iv. *Pneumonia in the immune compromised host including HIV/AIDS*

2. Etiology

2.1 Community acquired pneumonia (CAP):

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- Other Gram negative bacteria *(E. coli, Klebsiella* sp. …)
- *Burkholderia pseudomallei* (melioidosis)
- Agents causing atypical *(Leptospira sp.,* scrub typhus, *Mycoplasma pneumoniae, Legionella sp),* viral *(influenza, parainfluenza,…)* or fungal *(Cryptococcus, Histoplasma,…)* pneumonia
- *Mycobacterium tuberculosis*

2.2 Hospital acquired pneumonia (HAP):

- *Enterobacteriaceae (Klebsiella* sp.*, Enterobacter* sp.*, Proteus* sp.*)*
- *Streptococcus pneumoniae and Haemophilus influenzae*
- *Staphylococcus aureus*
- *Pseudomonas aeruginosa, Acinetobacter* sp.

2.3 Respiratory infection in immuno-compromised and HIV patients (see also HIV guidelines)

- HIV+; CD4 ≥ 200: usual causes of CAP + *Mycobacterium tuberculosis*
- HIV+; CD4 < 200: agents above *plus* PCP, disseminate fungal infection, non-tuberculosis mycobacteria, *Pseudomonas* sp., *Nocardia* sp.,..
- Other immunocompromized hosts: same as above *plus Burkholderia pseudomallei*, *Strongyloides* hyperinfestation,…

2.4 Aspiration pneumonia:

- Aspiration of bacteria colonizing the upper airway: *S. pneumoniae*, *H. influenzae*, Gram negative bacilli, anaerobic bacteria and *S. aureus*.

2.5 Lung abscess

- *Staphylococcus aureus*
- Anaerobic infections +/- co-infection with other Gram positive or negative bacteria
- *Mycobacterium tuberculosis*
- *Burkholderia pseudomallei* (melioidosis)
- *Nocardia* sp.
- Deep fungal infections

3. Differential diagnosis

3.1 Infectious:

- Acute bronchitis, acute exacerbations of chronic bronchitis
- Infectious exacerbation of bronchiectasis
- Pulmonary TB

3.2 Non-infectious:

- Congestive heart failure/pulmonary edema: cough, dyspnea but no fever
- Pulmonary embolism: fever, dyspnea, tachycardia, usually no lung infiltrate
- Pulmonary carcinoma: often with atelectasis or space occupying lesion
- Non-infectious pneumonitis, alveolitis, lung fibrosis: often longstanding lesion, may present acutely without fever
- Acute respiratory distress syndrome (ARDS)

4. Diagnostic procedures

4.1 - Predisposing conditions:

- Smoking
- Comorbid condition: asthma, lung cancer and other malignancy, COPD, diabetes, alcoholism, chronic renal/liver diseases, congestive heart failure (CHF), chronic corticosteroid use, malnutrition or acute/chronic weight loss, HIV, asplenia. bronchiectasis

- Hospitalization in the past 3 months
- Risk factors for meliodosis: diabetes, steroid use, alcoholism, liver cirrhosis near-drowning, rainy season, farmer, fisher, etc.

4.2 - Clinical arguments:

- Fever +/- chills, onset of cough +/- productive
- Pleuritic chest pain
- Tachypnea (respiratory rate > 25/ minute)
- Signs of consolidation: decreased breath sounds , localized crackles, localized dullness

4.3 - Paraclinical and laboratory procedures

i. **Routinely** (these might be not necessary if symptoms are mild)
- CBC, creatinine, BUN
- Chest X Ray

ii. **Additional investigations (** for severe or atypical presentation)
- Blood cultures (according to sepsis guideline)
- Sputum exam (AFB smear)
- Electrolytes, SGOT, SGPT
- HIV test and malaria smear if suspected
- Thoracocenthesis (pleural fluid examination) if indicated

We do not recommend sputum Gram stain and culture as routine lab examination in case of pneumonia because of its limited added value and risk of wrong interpretation of results.

5. Treatment

5.1 Supportive treatment:

- Oxygen therapy (titrated and aim for oxygen saturation > 90%)
- Adequate hydration
- Antipyretics/analgesics (for fever and pain)
- Cough suppression <u>not commonly recommended</u>
- Drainage (aspiration once or repeated; chest tube drainage) in case of
  - Significant pleural effusion (> 10 mm on lateral decubitus)
  - Empyema
  - See the SOP of chest tube

5.2 - Empirical Antibiotic Management

5.2.1. Empiric treatment of CAP:

<u>Management of out-patients:</u>

a. **No comorbidity**: amoxicillin 1 g PO q8h x 7 d
b. **Comorbidity and/or age ≥ 65 years**:
   - Mild disease: amoxicillin 1 g PO q8h x 7 d

- Sick patient: amoxicillin-clavulanic acid (Augmentin) 1000/250 mg PO q8h x 7 d
  - Alternative: cefuroxime 500 mg PO q8h x 7 d

c. In case of penicillin allergy (type I) ONLY

- Levofloxacin 750 mg PO qd x 5 d
  * In general, quinolones are not recommended since they are part of the second line (multidrug-resistant) TB treatment

d. 'Atypical pneumonia':

* Please discuss with AB team (may be TB, melioidosis, PCP…)

- **Not suspect for PCP:**
  - Amoxicillin-clavulanic acid 1000/250 mg PO q8h (or cefuroxim 500 mg PO q8h) *plus* clarithromycin 500 mg PO q12h x 14 d or azithromycin 500 mg PO qd for 7-10 d.
  - If strong suspicion of rickettsiosis/scrub typhus: replace clarithromycin by doxycycline 100 mg q12h x 5-10 d.
- **Suspect for PCP:**
  - Cotrimoxazole 5/25 mg/kg IV/PO q6h x 21d
  - If hypoxia (SaO2 <90%): prednisolone 40 mg PO q12h for 5 d, then 40 mg qd for 5 d, then 20 mg qd for 11 d, hospitalization indicated.
  - If severe hypoxia: dexamethasone 10 mg IV q6h for 3 d, then prednisolone 40 mg PO q12h for 3 d, then 40 mg qd for 5 d, then 20 mg qd for 10 d, hospitalization indicated.

  * Note: Avoid high flow oxygen >10 L/mn after 48-72 hours because of risk of oxygen toxicity.
- Suspicion of *Strongyloides stercoralis*: albendazole 400 mg PO q12h for 7 d

* Discontinuation of therapy: treat for minimum of 5 d, if afebrile for 48-72h and no sign of clinical instability

Management of hospitalized patients:

a. **First choice**: amoxicillin-clavulanic acid 1000/250 mg IV q4-6h (2-3d then switch to PO 1 g q8h to complete 7 d course).
b. **Second choice**: ceftriaxone 2 g IV qd or cefuroxime 1,5 g IV q8h (2-3 d then switch to amoxicillin-clavulanic acid 1000/250 mg PO q8h or cefuroxim 500 mg PO q8h if available).
c. **In case of penicillin allergy ONLY**: levofloxacin 750 mg PO QD x 7 d
   * Please discuss with AB team (restricted use).
d. **If suspicion of melioidosis**: ceftazidime 2 g IV q6-8h + cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd (see Sepsis and Melioidosis guideline).

5.2.2. Management of Nosocomial Pneumonia:

Mild or moderately severe, early onset (≤ 5th hospital day), no high risk factors:

- Ceftriaxone 2 g IV qd (2-3 d then switch to amoxicillin-clavulanic acid PO) or amoxicillin-clavulanic acid 1000/250 mg PO q8h x 7 d.
- In case of penicillin allergy ONLY: levofloxacin 750 mg PO or IV qd x 7d.

Severe, onset > 5th hospital day, or high risk:

- Amoxicillin-clavulanic acid 1000/250 mg IV q4h + amikacin 20 mg/kg IV qd (switch amoxicillin-clavulanic acid to PO after 2-3 d to complete 7 d course). Amikacin may be stopped after 3-5 d.

5.2.3. Management of aspiration pneumonia:

- Aspiration pneumonia presumed to be due to effect of gastric acid or other irritant: wait 24 h (effective treatment chest physiotherapy and/or incentive spirometer); if symptoms persist, give antibiotic therapy:
- **Mild or moderately severe**: amoxicillin-clavulanic acid 1000/250 mg PO q8h x 7 d.
- **Severe**: ceftriaxone 2 g IV qd with or without lincomycin 600 mg IV q8h (2-3 d then switch to PO if possible).

5.2.4. Lung abscess:

- Think of TB, melioidosis, *Staphylococcus aureus*,…
- **Empiric treatment**: amoxicillin-clavulanic acid 1000/250 mg IV q4h; OR Ceftriaxone 2 g IV qd + metronidazole 500 mg q8h IV are alternative. In severe septic cases, add Amikacin 20 mg/kg IV qd.
- Switch to PO amoxicillin-clavulanic acid 1000/250 mg q8h to complete 4-6 weeks, except amikacin (reassess after 3 to 5 days)
- **If blood cultures grow *S. aureus***: switch to cloxacillin 2 g IV q4-6h for 4-6 weeks (may be switched to PO 1 g q6h if afebrile for 5 d).
- **If strong suspicion of melioidosis**: ceftazidime 2 g IV q6-8h + cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd (see also melioidosis guideline)
- **If suspicion of Nocardia infection**: cotrimoxazole 10/50 mg/kg PO q12h *plus* folic acid 5 mg PO qd for 3-6 months. If severe, add ceftriaxone 2 g IV q12h for 2-4 weeks.

5.2.5. Pleural empyema:

- Chest tube drainage. Collect sample for AFB, Gram stain and culture (besides routine cell count and chemistry). Also do blood culture.
- Empirical antibiotic treatment as for CAP in hospitalized patients.
- Switch antibiotics according to isolate and antibiogram or follow the CAP treatment for 4-6 weeks.
- **Sufficient pain medication**

5.2.6. Other neglected disease:

- Add doxycycline 100 mg q12h PO for 5 – 10 days if suspicion of rickettsiosis or scrub typhus

5.3 - Directed treatment

- As soon as blood culture result and antibiogram available, switch according to the result.
- See sepsis guideline for directed treatment of specific bacteria

*** Note:**

1- Proportion amoxicillin/clavulanic acid=1000 mg/250 mg (maximum dose of clavulanic acid=1500 mg/24h).

2- In the first 24 hours there is no need to adjust the dose of antibiotics according to renal function (see Annexes for adjustment renal dose after 24 hours)

5.1 - Follow-Up/monitoring

- If no clinical improvement: control chest X-ray at day 3. If clinical improvement, no need for repeat CXR within the first 4-6 weeks.
- Chest X-ray after insertion of chest tube (to check its position).

Failure of therapy:

1. **Definition:**
   - **a.** Persisting sepsis signs or
   - **b.** Clinical deterioration after 72 hours of antibiotic therapy or
   - **c.** No improvement or early recurrence of symptoms after completion of antibiotic therapy.
2. **Consider:**
   - **a.** Patient-related factors:
     - i. Adrenal crisis (to add hydrocortisone 100 mg IV q8h for 3-5 d)
     - ii. Non-infectious pulmonary pathology
     - iii. Immunosuppression
   - **b.** Pathogen-related factors:
     - i. Antibiotic resistance
     - ii. Non-bacterial etiology: viruses, *Mycobacterium* sp., fungi,…
   - **c.** Drug related factors:
     - i. Non-compliance
     - ii. Malabsorption
     - iii. Drug-drug interaction
     - iv. Drug fever

6. Complications

Common complications of severe pneumonia include:

- Respiratory failure, ARDS
- Shock and multi-organ failure/possible DIC
- Exacerbation of comorbid illnesses
- Pleural effusion, empyema
- Metastatic infection, lung abscess
- Atelectasis (need incentive spirometer to prevent this)

Note:

Assess the severity of the pneumonia : CURB-65 score parameters:

- **C**onfusion (acute mental status: AMS)
- **U**rea (BUN) > 7 mmol/l,
- **R**espiratory rate ≥30/min
- **Blood pressure**: systolic ≤ 90 mmHg, diastolic ≤ 60 mmHg
- Age ≥ 65 years old.

1 point for the presence of each criterion. Mortality increases if the total score increases: 0 (0.7%) ; 1 (3.2%) ; 2 (13.0%) ; 3 (17.0%) ; 4 (41.5%); 5 (57.0%)

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3. Urinary Tract Infections (UTI)

1. Case definition

- Uncomplicated lower urinary tract infection (UTI): cystitis
- Uncomplicated upper UTI: pyelonephritis +/- urosepsis
- Complicated UTI (lower or upper caused by abnormal anatomy)
  - Including recurrent UTI (occurrence of UTI >3 times/year)
- Special types: may be STD related: prostatitis, epididymitis, orchitis, urethritis

2. Frequent etiological agents

2.1 - In normal host:

- *Escherichia coli* (80 %) and other *Enterobacteriaceae* (*Klebsiella pneumoniae, Enterobacter* sp.*…)*
- *Staphylococcus saprophyticus* 5-15%
- *Enterococcus* sp.

2.2 - In immunocompromised host: as above, *plus*:

- *Pseudomonas aeruginosa*
- *Burkholderia pseudomallei* (melioidosis)
- *Candida* sp..

3. Differential diagnoses

3.1 For presumed diagnosis of cystitis:

- Neurological bladder
- Bladder cancer
- Mucosa irritation by foreign body, chemical substance
- Women: vaginitis/cervicitis due to Candida, STD (*Trichomonas vaginalis*, gonorrhea/Chlamydia/herpes), other gynaecological pathology
- Men: urethritis/balanitis due to Candida or STD (idem)

3.2 For presumed diagnosis of pyelonephritis:

- Obstructive uropathy (stone, compression)
- Glomerulonephritis

3.3 For presumed diagnosis of complicated UTI:

- Uninfected stone
- Cancer
- TB
- Prostate hyperplasia

3.4 For presumed diagnosis of STD :

- Cancer
- Stone or foreign body
- TB

4. Diagnostic procedures

4.1 Clinical arguments:

4.1.1. Predisposing conditions include:

- Women are always anatomically more predisposed!
- Underlying urological structural abnormality, nephrolithiasis, benign prostatic hyperplasia
- Underlying immune depressed status: HIV, diabetes, immunosuppressive medication, pregnancy, elderly…
- Recent hospitalization or urologic tract manipulation (eg. Foley catheter)

4.1.2. Signs and symptoms:

a. **Lower UTI symptoms:** dysuria, urinary frequency and urgency, sometimes with suprapubic pain/pressure, rarely with hematuria (no fever)

b. Upper UTI symptoms

- Fever (sometimes with chills) with or without signs of shock
- Flank pain/kidney percussion pain
- Lower tract symptoms (may or may not be clearly present)
- Severe pain (colicky) with radiation into the groin (if renal calculus)

c. **UTI in older adults:** mostly asymptomatic, but can present with frequency, dysuria, hesitancy, and incontinence

- Abdominal pain
- Altered mental status (AMS)
- Shock/sepsis of unknown source

4.2 Technical procedures

4-2-1. Baseline lab:

a. <u>Urine analysis (UA, dipstick):</u>

- WBC > 2+, with or without positive Nitrite (if positive is strongly indicated)
- If dipstick is negative but UTI symptoms: do microscopic examination and urine culture (depends on presence of WBC on microscopy).

b. <u>Microscopic examination of the urine:</u>

- Pyuria: clean-catch mid-stream urine specimen: ≥ 10 WBC/mm3
- Asymptomatic bacteriuria: presence of a significant number of bacteria in the urine without symptoms
- Sterile pyuria: presence of significant number of WBC in urine with repeatedly negative culture (without antibiotic)

- RBC: can be present in UTI. If gross/persistent hematuria rule out stones, tumors, vasculitis, glomerulonephritis, renal tuberculosis (≥ 5 RBC/mm3)
- Epithelial cells: moderate or many epithelial cells indicate a bad sampling method
- Casts: consider other causes (eg. glomerulonephritis)

c. **Urine culture (if complicated UTI)** → See SOP of urine sampling (nurse)
- Urine culture done only if positive dipstick or urine microscopic ≥ 10 WBC/mm3
- Midstream clean catches (if necessary through catheterization).
- ≥ 10^5 cfu/ml (colony forming unit)
- Can be false negative if exposure to antibiotics

* **Note**: - clinical symptoms should be evaluated carefully or repeat a sample by clean catheter if suspicion of contamination. The contaminated samples often grow multi-drug resistant bacteria for which unneccesary antibiotics are being prescribed.
- A high epithelial cell counts suggestbad sampling (= chance to find the true bacteria causing UTI is less) => reject sample and need to repeat sample before making decision to treat.

4-2-2. Additional investigations (in serious condition):

- CBC, creatinine, BUN
- Ultrasonography of bladder and kidneys
- Radiography: supine abdominal X-Ray, IVP (intravenous pyelography)
- Blood culture (follow the sepsis guideline)

5. Therapeutic approach

5.1 **Supportive treatment**: abundant drinking (2-2.5 liters extra) to increase urine flow

***** In "renal colic", no abundance water intake within the first 12 hours

5.2 Empirical treatment:

5-2-1. Uncomplicated lower UTI: cystitis

- **First choice**: nitrofurantoin 100 mg PO q8h for 7 d
  * Contraindication if creatinine clearance < 40 ml/min
- **Second choice**
  - Ciprofloxacin 500 mg PO q12h for 3 d
  - Amoxicillin-clavulanic acid 500/125 mg PO q8h for 5 d

5-2-2. Uncomplicated upper UTI (pyelonephritis +/- urosepsis):

- Perform urine and blood cultures
- Ceftriaxone 2 g IV qd +/- amikacin 20 mg/kg IV qd (see CPG on Sepsis)
- Adapt antibiotic therapy with the result of urine/blood culture and antibiogram. If result negative, stop ceftriaxone and amikacin, and switch to ciprofloxacin 500 mg PO bid
- Total duration of treatment is 10-14 d

5-2-3. Complicated UTI

- Ceftriaxone 2 g IV qd
  - If sepsis: add amikacin 20 mg/kg IV qd (see CPG sepsis).
  - If sepsis and renal failure (Cr Cl< 30ml/min): switch to meropenem (adapted dose).
  - If abscess or hydronephrosis with/without stone: use meropenem 1 g IV q8h.
    - Amikacin has reduced penetration efficacy in abscess due to low pH. Beware that amikacin can be nephro-toxic.
    - **Discuss with AB team**
    - Discuss with surgeon for necessity of drainage or decompression
- Adapt all antibiotic therapy with the result of urine/blood culture and antibiogram. If result negative, stop IV empiric therapy, and switch to ciprofloxacin 500 mg PO bid.
- Total treatment duration depends on clinical evolution: 2 weeks; longer for abscesses (4-6 weeks)

5-2-4. Recurrent UTI:

- Episodic treatment of acute-recurrent UTI (nitrofurantoin)
- If permanent catheter in place (Foley or suprapubic):
  - Most patients have bacterial colonization of urinary tract, often with very resistant bacteria.
  - Try to remove or replace the catheter. If impossible, consider bladder irrigation with betadin solution 1% (flash 200ml of betadin solution once or twice daily).
  - Treat with antibiotic only in case of fever and/or sepsis signs.
- AB prophylaxis is not recommended because of increased risk of resistance.

5-2-5. Special situations:

a. Urethritis: ceftriaxone 250 mg IM single dose (for gonorrhea) +/- doxycycline 100 mg PO q12h for 7 d (for Chlamydia)

For pregnancy or breast feeding: ceftriaxone 250 mg IM single dose + erythromycin 500 mg PO q6h for 7d

b. Acute Prostatitis, Epididymitis, Orchitis:

- Ciprofloxacin 750 mg PO q12h *plus* doxycycline 100 mg PO q12h for 4w
- Ceftriaxone 2 g IV qd (then switch to ciprofloxacin PO) + doxycycline 100 mg PO q12h + amikacin 20 mg/kg IV qd for sepsis cases. The duration is 4 weeks except for amikacin (stop/adapt according to culture result)

* **Note**: - Should think of melioidosis, mumps
- The sexual partner should be treated as well in case of STD

c. UTI in pregnancy

Asymptomatic bacteriuria/cystitis is treated with a 10-day course based on sensitivity testing.

- Nitrofurantoin 100 mg PO q8h 1st and 2nd trimester
- Amoxicillin-clavulanic acid 500/125 mg PO q8h in 3rd trimester

d. If urine culture positive with urine WBC < 20 cells/ml, suggest to repeat urine microscopy before deciding to treat according to previous antibiogram (discuss with AB team).

5.3 Monitoring:

- Clinical and laboratory monitoring: necessary for complicated UTI/hospitalized patients: creatinine, CBC
- If no improvement after 72 hours: repeat blood and urine culture +/- abdominal ultrasound

6. Complication

- Renal failure
- Sepsis
- Urinary stricture
- Urine incontinence

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4. Infective endocarditis

1. Case Definition

1.1 General definition:

Acute inflammation of the cardiac valves (endocardium, endothelium) by micro-organisms (mostly bacterial)

1.2 General diagnostic criteria (Duke Criteria):

The diagnosis of infective endocarditis can be made in the presence of one of the following combinations of clinical findings:

- Two major clinical criteria or
- One major and three minor criteria or
- Five minor criteria

Major diagnostic criteria (adapted from Durack):

- Typical microorganism for IE from 2 separate blood cultures (mostly staphylococci and streptococci)
- Repeated positive blood culture results from:
  - Blood cultures taken on intervals of more than 12h (see lab section)
- All or most of blood cultures grow the same bacteria
- Signs of endocardial infection on echocardiogram:
  - Vegetation on valve or supporting structure, OR
  - Abscess OR
  - New valvular regurgitation

Minor Diagnostic Criteria

- Predisposing heart condition or intravenous drug use
- Prolonged fever with temperature > 38.0° C (100.4° F)
- Vascular abnormality: eg. arterial emboli, pulmonary infarcts, mycotic (infection-related) aneurysms, conjunctiva hemorrhages, Janeway lesions
- Immunologic abnormality: glomerulonephritis, Osler nodes, Roth spots
- Microbiological evidence: positive blood culture with less typical bacteria
- Echocardiographic findings: other findings suggestive for IE but not as defined in Major

2. Frequent etiological agents:

- *Streptococcus* and *Enterococcus* sp.
- *Staphylococcus aureus*
- Rarely: Gram negative bacteria, fungal infection,…

3. Differential diagnoses

- Other endovascular infections eg. septic thrombophlebitis
- Marantic (non-infectious) vegetations
- Libman sacks endocarditis (SLE vegetation)
- Non-infectious causes of acute valve insufficiency
- Other causes of prolonged fever e.g.malignancies, auto-immune diseases,..

4. Diagnostic procedures

4.1 Clinical arguments

4.3.1 Predisposing conditions

- IV drug abuse
- Presence of non-drained abscesses, osteomyelitis, untreated blood stream infection
- Underlying heart disease, especially rheumatic heart disease

4.3.2 Clinical symptoms/signs.

- Prolonged or relapsing fever
- New heart murmur, new heart failure
- Sometimes shock
- Sometimes signs of source or metastatic infection (septic arthritis, osteomyelitis and deep organ abscess)
- Skin and mucosal signs (see Duke Criteria)

4.2 Technical procedures

- Echocardiography
- ECG
- CXR (sometimes you can see signs of heart failure, diffuse multiple patches infiltrates…).

4.3 Laboratory exams

4.3.1 Routine laboratory:

- Blood cultures:
  - Day 1: 2 times blood culture (1 hour interval) before empiric antibiotic treatment
  - Day 2, 3 and 5: 1 time blood culture per day
- CBC, ESR, creatinine, urea and urine analysis

4.3.2 Additional investigation:

- HIV test if suspected
- Abdominal ultrasonography

- Pregnancy test if applicable

5. Therapeutic approach

5.1 Supportive treatment

- O_2 and IV fluids if needed
- Follow up of signs of heart failure
- I & D of underlying or metastatic abscesses (eg *Staphylococcus aureus*)

5.2 Empirical treatment:

Empiric treatment should be started as soon as possible.

- Cloxacillin 2 g IV q4h *plus*
- Ampicillin 2 g IV q4h (or penicillin 4 MIU IV q4h) *plus*
- Gentamicin loading dose 3 mg/kg IV then 1 mg/kg IV q8h

* Ampicillin is preferred as it also covers enterococci, but if the culture arrives – can change to Penicillin

5.3 Directed treatment

Therapy is modified based on results of blood culture and antibiogram:

Duration of treatment (in general): 6 weeks

Pathogens	AB recommended	Duration
Streptococci susceptible (MIC ≤ 0.1 µg/ml) or intermediately susceptible (MIC: 0.1- 0.5 µg/ml) to penicillin	Penicillin 4 MIU IV q4h *plus* gentamicin 1 mg/kg IV q8h	4 weeks for penicillin 2 weeks for gentamicin
Streptococci resistant to penicillin (MIC > 0.5 µg/ml) Enterococci	Penicillin 4 MIU IV q4h *plus* gentamicin 1 mg/kg IV q8h	4-6 weeks for both
Methicillin-susceptible Staphylococcus aureus (MSSA)	Cloxacillin 2 g IV q4h *plus* gentamicin 1mg/kg IV q8h	4-6 weeks for cloxacillin 3 d for gentamicin
Methicillin-resistant Staphylococcus aureus (MRSA)	Vancomycin loading dose 1 g IV run over 2 hours, then drip 30 mg/kg over 24 hours	4-6 weeks

* Penicillin can be switched to ceftriaxone 2 g IV qd after 2 weeks in case of need (need to discuss with antibiotic team).
* Penicillin allergy: try to desensitize, under cover of vancomycin.
* Vancomycin drip should be prepared every 12 hours (solution is not stable for longer than 12 hours).

5.4 Monitoring

5.3.1 Clinical monitoring

- Clinical symptoms and signs: vital signs (temperature evolution) and urine output

5.3.2 Laboratory monitoring

- Blood culture (see lab section)
- CBC, creatinine, urea on day 3, 5 and 7 then every week
- Echocardiogram repeated on week 2 and 4

* If at week 4 the vegetation is still present on echocardiography, ideally we have to remove the vegetation surgically if affordable.

6. Complications

- Heart failure
- Sepsis
- Septic embolism (pulmonary embolism, stroke, seizure…)
- Haemolytic anemia
- Mitral or aortic regurgitation
- Ventricular or atrial septal defect (VSD or ASD)
- Metastatic abscess

7. Prophylaxis

- Dental procedure needs prophylaxis: amoxicillin 2 g PO single dose one hour before procedure (50 mg/kg for children). Alternative is azithromycin 500 mg PO single in case of penicillin allergy.

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5. Septic arthritis

1. Definition:

- 'Septic arthritis' is inflammation of the joint(s) due to infection, mainly due to bacteria, but also mycobacteria, spirochaetes and fungi are possible causes.
- Septic arthritis involves often only one joint (monoarthritis) but infection of several joints is also possible (oligoarthritis). Most often the knee (> 50% of the cases) is involved.
- Septic arthritis may present as acute (< 4 weeks) or subacute (4-6 weeks) infection.

2. Etiology (adults):

- More than 80% of all causes:
  - *Staphylococcus aureus* (most common cause in all age groups)
  - Streptococci
- Others:
  - *Mycobacterium tuberculosis* and other mycobacterial species
  - *Burkholderia pseudomallei*
  - *Neisseria gonorrhoeae*
  - Gram negative bacteria e.g. *Haemophilus influenzae*, *E. coli*, *Klebsiella* sp., *Salmonella* sp.
  - Fungi (e.g. *Histoplasmosis*, *Penicillium*, *Cryptococcus* sp.)

3. Differential diagnosis:

- Other infection or post-infection
  - Reactive arthritis
  - Bursitis
  - Cellulitis
- Non-infectious
  - Cristal-arthropathy (gout, pseudogout)
  - Rheumatoid arthritis, sarcoidosis, SLE,…
  - Trauma +/- hemarthrosis

4. Diagnostic procedures:

4.1 Predisposing condition

Old age, diabetes, rheumatoid arthritis, recent joint trauma or surgery, alcoholism, previous intra-articular steroid injection, drug abuse, skin ulcer or infection

4.2 Clinical arguments:

Patients need a complete physical exam with special attention to other joints and bones, and also possible signs of sepsis or endocarditis.

Symptoms and signs suggestive of septic arthritis:

- A warm, swollen and painful joint(s) with restricted movements
- With or without fever
- Presence of increased synovial fluid

4.3 Paraclinical and laboratory investigation:

4-3-1. Routine laboratory

- Arthrocenthesis/investigation of synovial fluid
  - The synovial fluid must be aspirated prior to starting antibiotics and sent fresh to the laboratory.
  - Synovial analysis: Cell count, Gram stain, AFB, bacterial culture

  * Note: - WBC in synovial fluid > 50.000/mm3 increases the likelihood of septic arthritis.
    - Absence of organisms on Gram stain or/and sterile culture of synovial fluid does not exclude the diagnosis of septic arthritis.
- CBC, creatinine
- Blood cultures
- X-ray of the affected joint for finding complications and alternative diagnosis, (e.g. osteomyelitis)

4-3-2. Additional investigations

- Chest X Ray in case of suspicion of tuberculosis
- Cardiac ultrasound if suspicion of endocarditis

5. Therapeutic approach

5.1 Antibiotic treatment of septic arthritis

- Start the treatment immediately after sending blood and joint fluid for culture.
- There is no evidence on which to advise the optimal duration of IV or oral antibiotics. Conventionally, they are given IV for up to 1-2 weeks or until signs improve, followed by PO treatment for 4 weeks or longer depending on the clinical evolution.
- Symptoms, signs and acute phase responses are all helpful in guiding the decision to stop antibiotics.
- A possibly infected prosthetic joint should be referred to an orthopedic surgeon with multidisciplinary discussion.
- Encourage patient to gently move the involved joint to avoid frozen joint.

5.2 Joint drainage and surgical options

Septic joints should ALWAYS be aspirated to dryness as often as required. A 16-18 gauge needle is required (see SOP of arthrocentesis).

5.3 Empirical treatment (before culture result is known):

* Please send sample for culture if possible before start of antibiotics.

- **If no organism seen in Gram stain and culture still pending:**
    - Ceftriaxone 2 g IV qd *plus* cloxacillin 1 g PO or 2 g IV q6h. If septic shock, add amikacin 20 mg/kg IV qd.
    - If presence of risk factors of melioidosis with systemic infection (atypical chest X-ray or deep organ abscess): ceftazidime 2 g IV q6-8h *plus* cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd (discuss with AB team)
- **If Gram stain shows "Gram positive cocci":**
    - Cloxacillin 2 g IV q4-6h or 1-2 g PO q6h
        - If suspicion of MRSA: vancomycin 500 mg IV q6h (need AB team discussion). Cotrimoxazole 160/800 mg PO/IV q8h can be used if not life threatening.
        - If penicillin allergy: lincomycin 600 mg IV q6h or clindamycin 900 mg IV q8h
        - If suspicion of pneumococcus: ceftriaxone 2 g IV qd
- **If Gram stain shows "Gram negative bacilli/cocci"**
    - Ceftriaxone 2 g IV qd (if suspicion of gonococcus: 1 g)
        - If suspicion of multidrug resistant organism or severe sepsis: add amikacin 20 mg/kg IV qd.
        - If suspicion of melioidosis: ceftazidime 2 g IV q6-8h + cotrimoxazole 6/30 mg/kg IV/PO q12h for 2 weeks, then cotrimoxazole 6/30 mg/kg PO q12h (for 6 months) *plus* folic acid 5 mg qd for 6 months

5.4 Directed treatment (when culture result is known):

- Duration of treatment: 1-2 weeks IV then 2-4 weeks orally or longer in some cases (6 months for melioidosis/TB)
    - Staphylococci (oxacillin sensitive): cloxacillin 2 g IV q4h for 2 weeks then 1 g PO q6h for 4 weeks
    - Pneumococcus and other streptococci: ceftriaxone 2 g IV qd for 2 weeks (or ampicillin 2 g IV q4-6h or benzylpenicillin or penicillin G 4 MIU IV q4-6h) then amoxicillin 1 g PO q6h for 4 weeks
    - Gonococcus: ceftriaxone 1 g IV qd for 10 d or in mild cases amoxicillin-clavulanic acid 1 g PO q8h x 10 d

5.5 Monitoring:

- Clinical monitoring: decrease of fever (if present), joint inflammation signs and movement of the joint.
- Laboratory monitoring: After result of Gram stain, cell count and culture with susceptibility test, please switch antibiotic accordingly.

6. Complications:

- Destruction of articular cartilage
- Deformity and disability/osteomyelitis, frozen joint
- Bacteraemia
- Endocarditis (especially in case of staphylococcal infection)

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6. Skin and soft tissue infection (SSTI)

1. Definition:

- Skin and soft tissue infections (SSTIs) are microbial invasions of the epidermis, dermis and subcutaneous tissues.
- They cause induration, redness, warmth, and pain or tenderness.
- Patients may also have systemic signs and symptoms e.g. fever, chills, malaise and sometimes hypotension.
- SSTIs can sometimes lead to disseminated infection via the circulatory and lymphatic systems, especially in patients with immune suppression.
- Clinical presentation varies from very limited infection (impetigo, lymphangitis, cellulitis, erysipelas) to abscesses (pyomyositis) and necrotizing fasciitis and gangrene.
- Chronic SSTI may be seen in diabetics (so called 'diabetic foot')

2. Frequent etiological agents

- *Staphylococcus aureus*
- *Streptococcus pyogenes* and other streptococci
- *Burkholderia pseudomallei*
- *Pseudomonas aeruginosa* (often in chronic lower extremity infections)
- Other Gram negative bacteria *(e.g. E. coli, Klebsiella* sp.*)*
- *Clostridium perfringens*

3. Diagnostic procedures:

3.1 Clinical arguments:

3.1.1. Predisposing factors:

Certain conditions increase the risk of developing cellulitis/SSTI e.g.:

- Recent injury to the skin (e.g. wound, cut, bite …)
- Chronic skin conditions (e.g. eczema, psoriasis,…)
- Chronic oedema of the limbs
- Obesity
- Neutropenia, asplenia, diabetes, other immune depressing conditions

* However, SSTI can also develop in people who have no known risk factors.

3.1.2. Signs and symptoms:

Danger signs:

- Very severe pain not in proportion to the physical findings

- Blisters with dark fluid
- Cutaneous hemorrhage
- Skin peeling, skin anesthesia
- Rapid progression and gas in the tissue
- Low blood pressure, unstable vital signs
- **These signs and symptoms often appear late in the course of necrotizing infections.**

3.2 Laboratory workup

3.2.1. Routine lab

- CBC, creatinine
- Pus aspiration whenever possible, otherwise pus or tissue culture from operation room
- Blood culture if sepsis signs

3.2.2. Additional investigation

- HIV test if suspected
- Ultrasound of limb (to look for drainable collection)
- X-Ray (to look for foreign body or gas in tissue)
- Chest X ray and abdominal ultrasound if suspicion of melioidosis
- Echocardiography if suspicion of endocarditis

4. Therapeutic approach

4.1 Surgical intervention

- For closed abscess: incision and drainage
- For open wound: debridement
- Immediate and very extensive debridement needed in gangrene/necrotizing fasciitis

* NB: Send all samples to lab for Gram stain, AFB smear and bacterial culture.
* A surgical consultation should be requested for inspection, exploration, and/or drainage before planned admission.

4.2 Empirical treatment

The treatment is usually 1-2 weeks but can be longer with complicated SSTI.

- **For stable patients:**
  - **In healthy afebrile patient:** usually cloxacillin 500 mg PO q6h for 1 week (if penicillin allergy: clindamycin 600 mg PO q8h)
    NB: If completely debrided or drained, no need to give antibiotic.

- **In healthy febrile patient with or without co-morbidity or closed abscess**: cloxacillin 1 g IV/PO q6h with or without ciprofloxacin 500 mg PO q12h
- **Diabetic gangrene**: ciprofloxacin 750 mg PO q12h *plus* lincomycin 500 mg PO q8h. If severe sepsis or septic shock, add amikacin 20 mg/kg IV qd. Should work-up for other infection source for possible diagnosis of melioidosis.
- **If suspicion of melioidosis**: amoxicillin-clavulanic acid 1000 mg/250 mg PO q8h for 2 weeks *plus* cotrimoxazole 6/30 mg/kg PO q12h and folic acid 5 mg PO qd for 3-6 months.

- **Patient with sepsis or septic shock -/+ closed abscess**:
  - cloxacillin 2 g IV q4-6h +/- amikacin 20 mg/kg IV qd
  - **If suspicion of necrotizing fasciitis:** penicillin G 4M IV q4h *plus* lincomycin 600 mg IV q8h (or clindamycin 900 mg IV q8h) *plus* amikacin 20 mg/kg IV qd
  - **If suspicion of melioidosis:** IV ceftazidime *plus* cotrimoxazole (see above)
  - **Diabetic gangrene**: ciprofloxacin 400 mg IV q12h *plus* lincomycin 600 mg IV q8h *plus* amikacin 20 mg/kg IV qd. Should work-up for other infection source for possible diagnosis of melioidosis

* Hospitalization should be considered and a definitive etiologic diagnosis pursued aggressively by means of procedures such as Gram stain and culture of needle aspiration or punch biopsy specimens.

* Should avoid steroid injection in any cases suspected to have septic arthritis

4.3 Direct treatment

See sepsis guideline for specific microbial agents.

- Therapy may be discontinued upon the resolution or marked improvement in the clinical signs and symptoms of inflammation.
- Most cases of uncomplicated SSTI can be successfully treated for 1–2 weeks.

4.4 Adjunctive treatment

- Pain killer
- Well wound dressing (see nursing procedure)
- Stabilized vital signs (oxygen, IV fluids) and co-morbiditiy (glycaemia control: BS < 150 mg/dl)
- Encourage the high protein nutrition if possible.
- Immobilize the infected limb in a splint and elevate.

5. Monitoring:

- Clinically: vital signs, wound or swelling, erythema and indurations of the lesion
- BS should be controlled below 150 mg/dl

* Ideally, hemoglobin should be above 9 g/dl for diabetic patients or patients with co-morbidity, to achieve better wound healing.

6. Complications

- Gangrene
- Osteomyelitis
- Sepsis
- Endocarditis

7. Prevention

About 20% of patients with a first episode of SSTI will develop subsequent episodes. Therefore, measures should be considered to prevent recurrence:

- Underlying conditions that predispose to SSTI must be addressed, and patients should be advised on proper skin and nail care.
- Topical antifungal agents, topical steroids and skin lubricants may be indicated in patients with tinea pedis, eczema and dry, cracked skin, respectively.

Annex:

Classification: SSTIs can be divided into four classes according to the severity of signs and symptoms of infection, and the presence of co-morbidities.

a. **Class 1**: Cellulitis without fever and healthy patient. No sign or symptom of systemic toxicity. Can be usually treated with oral antimicrobials as outpatient.
b. **Class 2**: Febrile and ill appearing, but no unstable co-morbidities
c. **Class 3**: Toxic appearance, or at least one unstable co-morbidity, or a limb-threatening infection that may interfere with their response to treatment.
d. **Class 4**: Sepsis syndrome or life-threatening infection, e.g. necrotizing fasciitis

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7. Bacterial meningitis

1. Case definition/diagnostic criteria:

- Clinical triad (headache, fever and neck stiffness) *plus* abnormal finding in cerebro-spinal fluid (CSF) analysis.
- Signs of severity:
  - Decreased consciousness, seizures
  - Focal neurologic deficit
  - Other signs of raised intracranial pressure (ICP) e.g. vomiting, papilledema, increased opening pressure on LP

2. Frequent etiological agents:

- *Streptococcus pneumoniae* and other streptococci *(e.g. Streptococcus suis)*
- *Neisseria meningitidis* (meningococcus)
- *Haemophilus influenzae*
- *Leptospirosis, rickettsia*, scrub typhus
- Rarely: *Listeria monocytogenes*, Gram negative bacilli (e.g. *E. coli, Klebsiella* sp.), *Staphylococcus aureus* in case of foreign material in situ or post-surgery.

3. Differential diagnosis

- Severe or cerebral malaria
- Other causes of meningitis (TB, viral, fungal (Cryptococcus), syphilis …)
- Encephalitis (mostly viral, especially herpes simplex)
- Localised intracranial infections: brain abscess, sphenoidal sinusitis
- Non infectious: stroke, malignancy, connective tissue diseases

4. Diagnostic procedures

4.1 Clinical arguments

4-1-1. Predisposing conditions

- Infections spreading to the meninges regionally (ENT infection: otitis, sinusitis, tooth abscess) or via blood stream infection (e.g. pneumonia, endocarditis…)
- Immunocompromised patients: post-splenectomy, HIV, steroid use, diabetes, alcoholism, liver cirrhosis, cancer, elderly
- Head trauma with/without CSF leakage

4-1-2. Clinical symptoms/signs

- *Classic triad:* fever, headache, neck stiffness
- Brudzinski's sign, Kernig's sign (sensitivity = 30%; specificity = 70%).
- *Other signs and symptoms can also be present:*
  - Nausea, vomiting
  - Photophobia

- Altered mental status: assessed by Glasgow Coma Scale (GCS)
- Seizures (at least 1 in 3 patients)
- Focal neurologic deficit (especially if *S. pneumoniae*)
- Shock, purpura (esp. if meningococcal),
- Other infection (e.g. pneumonia)

* About 25% have symptoms that develop over 24h.

* In immunocompromised host or old age, the typical clinical triad may not be seen.

4.2 Technical procedures

- **Blood cultures: positive in 50-75% of cases; always to be taken before AB**
- **Lumbar puncture** (see LP procedure: 3 tubes of CSF to be collected)
  - Is indicated for every patient with suspicion of meningitis
    - Opening pressure (normal: < 20 cmH_2O)
  - But it is not safe in case of:
    - Increased intracranial pressure
      - Papilledema, focal neurologic symptoms
    - Soft tissue infection near the puncture site
    - Coagulation disorders (severe DIC, platelets < 20.000/mm^3)
  - The decision to perform LP or not should NOT delay the start of antibiotic treatment if there is a strong suspicion of bacterial meningitis!

4.3 Laboratory exams

4-3-1. Routine laboratory:

- **CSF analysis**:
  - Macroscopic aspect (normal CSF is clear)
  - Microscopic analysis:
    - Gram stain: sensitivity 50-90%, specificity 99%
      - May be false negative (e.g. antibiotic exposure before LP)
    - WBC (may be falsely low if Abx exposure before LP)
    - AFB
    - Biochemistry: glucose, protein.
    - Culture: may be false negative due to exposure to antibiotics before.

    * Abnormal CSF value for bacterial meningitis (see table in appendix):

    - WBC ≥ 50/mm^3 with (predominance of polymorphonuclear). **If WBC between 5-50 cells/mm3, and clinically suspected of bacterial meningitis, please discuss with supervisor.**
    - Protein > 0.5 g/l
    - Glucose < 60% of serum glucose.
- Blood culture before AB administration
- Full blood count, creatinine, electrolytes, random blood sugar.

4-3-2. Additional investigations (as indicated):

- HIV test, malaria smear, transaminase

- VDRL, India ink (cryptococcal antigen if India ink staining is negative)
- Chest radiography
- Leptospira IgM if strong suspicion of leptospirosis (see *Faine's Criteria for the Diagnosis of Leptospirosis- page 54)*
- Pregnancy test, abdominal ultrasonography, urine analysis
- CT scan of the brain with contrast in case of focal neurologic deficit
- INR/PT before LP in case of suspicion of bleeding disorder

5. Therapeutic approach

5.1 Empirical treatment:

Empiric treatment should be started as soon as possible.

- Ceftriaxone 2 g IVq12h (while CSF culture results are pending)
- Ampicillin 2 gIVq4h, can be added for those at risk of listeriosis (diabetes, alcoholism, pregnancy, elderly (>50 years)

* Note: Consider adding doxycycline high dose (200 mg q12 for 10 d) for presumed rickettsiosis/scrub typhus if Gram stain does not show organisms and cultures remain negative.

5.2 Directed treatment

Therapy is modified based on results of CSF/blood culture and antibiogram. Please discuss with infectious diseases team in case of resistance.

* **Table for recommended treatment**

Pathogens	Antibiotic recommended	Duration
Neisseria meningitidis *Streptococcus pneumoniae* other streptococci	- Penicillin sensitive (MIC ≤ 0.064µg/ml): benzylpenicillin 4 MIU IV q4h - Penicillin resistant (MIC > 0.064µg/ml): ceftriaxone 2 g IV q12h	10 days
Streptococcus suis	- First choice: Penicillin G 4M IU IV q4h - Second choice: Ceftriaxone 2 g IV q12h Note: use ceftriaxone after penicillin at least for 2 weeks.	Minimum 3 weeks. Extend to 4-6 wks based on clinical evolution (LP: ideally WBC decreased at least 80% from peak)
Haemophilus influenza	- Ceftriaxone 2 g IV q12h	7-10 days
Staphylococcus aureus	- MSSA: cloxacilline 2 g IV q4h - MRSA: vancomycin 500 mg IV q6h OR drip 2 g over 24 hours after loading dose 1 g IV run over 2 h. - In case vancomycin is not available: cotrimoxazole 5/25 mg/kg IV/PO q12h	21 days

Gram negative bacilli (except *Pseudomonas* sp)	- Ceftriaxone 2 g IV q12h	21 days
Pseudomonas aeruginosa	- Ceftazidime 2 g IV q6h *plus* aminoglycoside (gentamicin 5 mg/kg IV qd or amikacin 25 mg/kg IV qd	21 days (1 week for aminoglycoside)
Listeria monocytogenes	- Ampicillin 2 g IV q4h	21-28 days (follow-up LP to see WBC decrease)

* Note: - Fluoroquinolones (eg. gatifloxacin) are preserved for TB, and not mentioned here. However, if required, case-by-case discussion can be done with supervisor.

- Vancomycin drip should be prepared for every 12 hours (solution is not stable for longer than 12 hours). Vancomycin use should be discussed case by case.

- Listeria meningitis: clinical improvement is very slow, usually occurs 3-4 days after the correct treatment (from our observation).

- S*treptococcus suis*: hearing loss might occur or improve (if patient already has this symptom) after 48 hours of starting the treatment (from our observation).

- ***Cryptococcal meningitis management:***
  Amphotericine-B infusion 0.7 mg/kg IV qd (starting 0.3 mg/kg at day 1) plus fluconazole 800mg qd for 14 d then fluconazole 400 mg PO qd for 8 weeks then secondary prophylaxis with fluconazole 200 mg PO qd until CD4 > 100 cells/mm^3.
  If non-HIV patient, no need to give secondary prophylaxis.

5.3 Adjunctive treatment

- Dexamethasone 8-10 mg IV q8h, for 5 d for all patients **except** known or suspected HIV status or pulmonary tuberculosis. Preferably to be given before the first dose of antibiotic.
- Seizure precaution
- Chest physiotherapy and contracture prevention
- Bedsore prevention and oral hygiene
- Restrict IV fluid (< 2000ml/24h) except in dehydration or sepsis.
- Pain killers (see pain management guideline)

5.4 Monitoring

i. Clinical monitoring: clinical symptoms and signs:
   - GCS q6-12h
   - Vital signs q1-2h for the first 24 h
   - Urine output q1-2h for the first 24 hours (goal 20ml/kg/h)

ii. Laboratory monitoring
   - CBC, electrolyte, creatinine: at 12-24h after admission, then D5 and D7
   - Blood sugar every 1 hour for the first 12 hours if known BS > 150 mg (BS goal is < 150 mg/dl)
   - Repeat LP:

- If no clinical improvement after 72 hours
- In case of cryptococcal meningitis (follow-up of intracranial pressure). If opening pressure (OP) > 25cmH_2O, drain 30 cc of CSF and repeat daily until OP < 25 cmH_2O. Repeat LP later on if patient's headache increases again.

6. Complications

The complications of bacterial meningitis include:

- Seizures
- Focal neurologic deficits (e.g, cranial nerve palsy, hemiparesis, hearing loss)
- Cerebrovascular abnormalities
- Intellectual impairment
- Sepsis, DIC

7. Prophylaxis for presumed meningococcal infection:

- General precaution: wear face mask (patient, carers and staff) for the first 24 hours.
- Isolate the patient if possible for the first 24 hours.
- Prophylaxis for careers and staff in close contact with patient highly suspect of meningococcal infection in the first 24 hours: ciprofloxacin 500 mg PO single dose.

Appendix: Table of CSF result in central nervous system infection

Cerebrospinal fluid analysis in central nervous system infection

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/µL)		
	<10*	10-45●	>250△	50-250◇	>1000	100-1000	5-100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Lyme disease Neurosyphilis	Bacterial meningitis	Bacterial or viral meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCM)	TB meningitis		Some cases of mumps and LCM	Encephalitis	Encephalitis

LCM: lympocytic choriomeningitis virus.
* <0.6 mmol/L.
● 0.6-2.5 mmol/L.
△ >2.5 g/L.
◇ 0.5-2.5 g/L.

* **Extract from** UpToDate Version 19.1

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8. Melioidosis

1- Case definition

- Melioidosis is an infectious disease caused by *Burkholderia pseudomallei.*
- It causes a wide spectrum of clinical presentations, ranging from asymptomatic infection over SSTI, pneumonia to life-threatening septic shock.
- It can present as an acute or chronic disease.

* Note: treatment of melioidosis has been changed in line with new evidence

2- Etiology

Burkholderia pseudomallei is a Gram negative non fermentative bacillus.

It is distributed widely in the soil and water of the tropics of mostly South (East) Asia and Northern Australia.

Melioidosis has been described in Cambodia in several publications including in SHCH.

3- Differential diagnosis

- **Skin infection:** pyogenic skin abscesses due to *S. aureus,…*
- **Lung infection:** CAP due to other causes, TB, lung cancer, pulmonary metastasis
- **Blood stream infection:** sepsis due to other causes
- **Deep organ abscess:** amoebic liver abscess, other pyogenic abscesses, HCC,…

4- Clinical presentation/form

4.1 Acute form of infection

- Initial infection through skin trauma or inhalation is often asymptomatic. Soft tissue infections are usually symptomatic, but have a good outcome.
- In contrast, when presenting with a systemic illness like pneumonia, liver/kidney and/or spleen abscesses mortality is >50%. In case of overwhelming blood stream infection case fatality rates can be up to 90% with death occurring within 24-48 hours if left untreated.
- In melioidosis septicemia, high fevers and rigors are present. These findings may be accompanied by confusion, dyspnea, abdominal pain, muscle tenderness, pharyngitis, diarrhea, and jaundice.
- While the typical foci in these severe cases begin from the skin or the lungs, metastasis (to liver, spleen, kidney, brainstem, parotid gland) may occur.
- Clinical presentation is non-specific and diagnosis in endemic regions is often based on a strong clinical suspicion. This is particularly true for patients with predisposing co-morbidities, such as diabetes mellitus, chronic renal failure, and alcoholism.

4.2 Chronic form

- The chronic form involves multiple abscesses. The chronic form can reactivate many years after the primary infection. Latent infection (10%) with reactivation can mimic TB ("TB look–alike").

5- Diagnostic Work-up

5.1. Risk Factors

- Diabetes mellitus (especially dysregulated patients with HbA1c > 9%)
- Metabolic syndrome
- Alcohol excess
- Chronic steroid use
- Chronic disease: lung, kidney and liver

* Note: A cut-off of HbA1c > 9% is based on experience only

5.2. Investigations

5.2.1. Baseline lab:

- Two blood culture
- Gram stain and culture of any open wound and urine
- Complete blood count
- Renal function tests
- Blood sugar

5.2.2. Additional investigations:

- Alkaline phophatase, bilirubin, transaminases
- Chest radiography: 80% of CXR may demonstrate bilateral bronchopneumonia, miliary nodules, segmental or lobar infiltrate, diffuse nodular shadowing.
- Abdominal ultrasound (look for deep organ abscesses in liver and spleen)
- HbA1c if random blood sugar is high or if high suspicion of metabolic syndrome/diabetes

6- Management

Ampicillin, ceftriaxone, ciprofloxacine (and other fluoroquinolones) and aminoglycosides (gentamicine, amikacine) are not effective antibiotics to treat melioidosis.

Drugs of choice are ceftazidime, meropenem, cotrimoxazole (SMX/TMP) and amoxicillin-clavulanic acid.

<u>Intensive phase:</u> for at least 10-14 days

- **First choice:**

- Ceftazidime 50 mg/kg (max 2g IV q6-8h) OR meropenem 25mg/kg (1g IV q8h.)
- *Plus* cotrimoxazole 6/30 mg/kg PO q12h (max 320/1600 mg q12h – see table below related with dosage and body weight)
- *Plus* folic acid 5 mg PO qd

- **Second choice:** if no ceftazidime available or stable patient without deep organ abscesses: amoxicillin-clavulanic acid 1g IV q4h (20/5 mg/kg) OR 20/5 mg/kg PO q8h (max 1500/375 mg PO q8h) *plus* cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd. Realize that the use of amoxicillin-clavulanic acid instead of ceftazidime is associated with increased risk of failure and relapse.

  * **NOTE**: amoxicillin-clavulanic acid around 1 g IV q4h because of half-life of clavulanic acid

- **Eradication phase: for 3 - 6 months**
  - **1st choice**: cotrimoxazole 6/30 mg/kg PO q12h *plus* folic acid 5 mg PO qd

Dose of cotrimoxazole (TMP/SMX) according to body weight:

Weight	Dose TMP/SMX
<40 Kg (for children)	160/800 mg q12h PO
≤ 60 Kg	240/1200 mg q12h PO
> 60 Kg	360/1600 mg q12h PO

  - **2nd choice**/alternative: in case of intolerance to cotrimoxazole, use amoxicillin/clavulanic acid 20/5 mg/kg up to 1000/250 mg q8h PO OR Doxycyclin 100mg bid PO

  * **Note**: 3 months for soft tissue infection without osteomyelitis.

Dose adjustment of antibiotic in case of renal impairment

(*Please also see page 76 for detail on instruction related with renal insufficiency)*

	CrCL 31 – 50	CrCL 15 – 30	CrCL <15	Hemodialysis
Ceftazidime > 60 Kg ≤ 60 Kg	 2 g q8h 1 g q8h	 2 g q12h 1 g q12h	 2 g q24h 1 g q24h	after each dialysis add 2g add 1g
Meropenem	1 g q12h	1 g q12h	1 g q24h	1 g dose after each dialysis
Cotrimoxaozle > 60 Kg ≤ 60 Kg	 1920 mg q12h 1440 mg q12h	 1920 mg q24h 1440 mg q24h	 1920 mg q24h 1440 mg q24h	After each dialysis Add 1920 mg Add 1440 mg

Creatinine clearance (CrCL): calculated by Cockroft-Gault method (see page 76)

*Adapted from Jabbar Z, Currie BJ. Melioidosis and the kidney. Nephrology 2013.

- **Supportive treatment**
  - Tight control of blood sugar (goal BS < 150 mg/dl)
  - Fluid management
- **Monitoring**

1. Repeat blood culture on Day 5
2. Liver and splenic abscesses: discuss management with surgeon and antibiotic team before admission:
   - Large abscesses: aspiration under ultrasound guidance
   - Multiple smaller abscesses: conservative treatment is preferred.
   - Monitoring for abscess by abdominal ultrasound: D0, D7, D14, M3 OR M6
3. Resolution of fever may take up to 7-10 d (spiking fever within the first week of treatment).
4. Reactivated arthritis may occur after 3 days of treatment (Advise to do arthrocenthesis to confirm *B pseudomallei* from synovial fluid culture)
5. In case of pneumonia: CXR on admission and at the end of eradication treatment (month 6)

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9. Spontanous Bacterial Peritonitis (SBP)

Phe Thong, Lim Kruy, Erika Vlieghe, Janneke Cox, Jan Jacobs
Version 1.0

1. Definition:

SBP is defined as an ascitic fluid infection without an evident perforation or inflammation of an intra-abdominal organ (this is called a secondary peritonitis).

It primarily occurs in patients with advanced liver cirrhosis.

SBP occurs rarely in patients with ascites secondary to other causes: nephrotic syndrome, malignancy or cardiopathy.

2. Clinical presentation:

a. Evident ascites
b. SIRS signs (see Sepsis guidelines in chapter 1, page 2)
c. Variety of clinical presentation:
    i. severe sepsis or septic shock (see sepsis guideline for definitions)
    ii. Diffuse abdominal pain, sign of paralytic ileus,
    iii. Altered mental status: from infection and/or hepatic decompensation
d. Complication:
    i. metabolic acidosis, and azotemia
    ii. Hepato-pulmonary syndrome.
    iii. Hepato-renal syndrome
    iv. Upper gastro-intestinal bleeding (perform rectal examination).

* Note that patients with SBP may have very mild or no clinical signs with or without fever.

3. Etiology:

SBP is mostly caused by bacteria from the gut.

a. Gram negative pathogens: mostly *Escherichia coli*
b. Gram positive pathogens: Streptococcus sp., Enterococcus sp.

4. Risk factors:

a. Advanced cirrhosis (Child Pugh Score)
b. Prior episode of SBP
c. Upper gastro-intestinal hemorrhage
d. Malnutrition
e. Use of proton pump inhibitors
f. Nephrotic syndrome

5. Diagnostic evaluation:

a. A "clinical diagnosis" of SBP with result of ascites fluid examination.
b. Do paracenthesis: draw at least 40 ml of ascites fluid for analysis (see annex on paracenthesis procedure)
    i. PMN count ≥ 250 cells/mm3 OR
    ii. Ascitic fluid bacterial culture (+) (note that approximately 60% has negative culture results) AND

iii. Other causes of peritonitis are excluded

c. Do blood culture (2 bottles) as part of sepsis guideline although patient has no fever.

d. Additional Based line lab:
   i. CBC, Liver function test, renal function test
   ii. Optional: INR/PT, albumin/protein, bilirubin

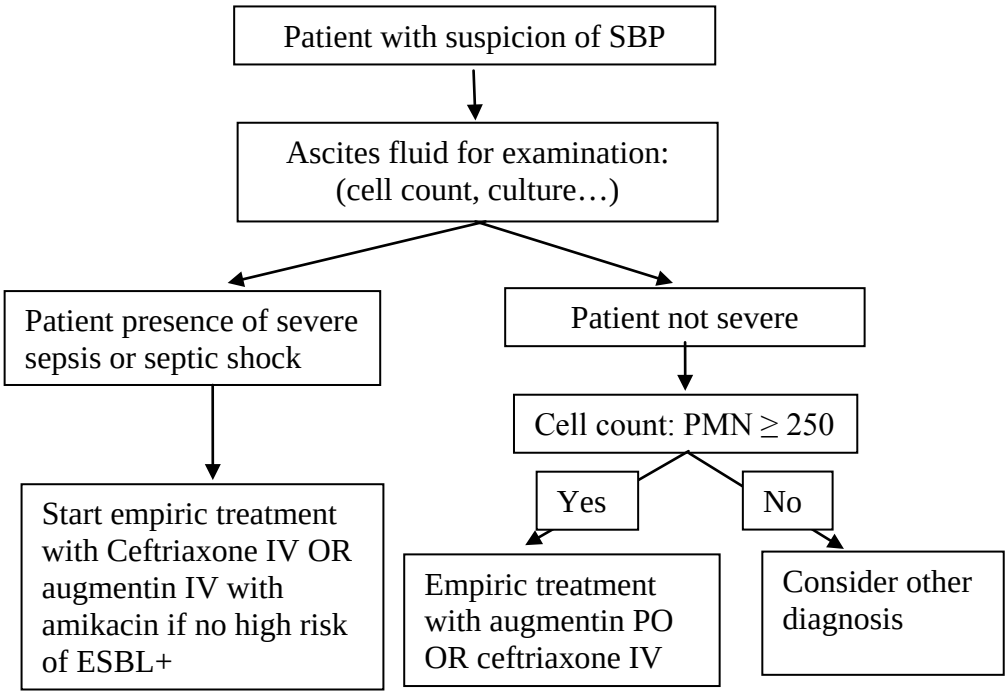
*** Please note:**

In case of bloody ascites, need to do a correction of the PMN count as follows:
PMN count = absolute PMN count - 1 PMN for every 250 red cells/mm3.

6. Treatment approach:

Start empiric treatment as soon as ascitic fluid and blood have been obtained for culture and analysis.

Besides antibiotics, fluid management should be aggressive even big ascites to prevent hepato-renal syndrome



a. Empirical treatment (7 to 10 days):

i. Non severely ill SBP: amoxicillin/clavulanic acid 1g/250mg q8h PO OR Ceftriaxone 2g IV qd

ii. Severely ill (presence of severe sepsis or septic shock):
   1. Ceftriaxone 2 g IV q24h OR amoxicillin/clavulanic acid 1g/250mg q4h IV with amikacine 20 mg/Kg IV qd (for 3-5 days).
   2. FOR ESBL suspicious Meropenem 1g q8h IV (Always discuss with AB team)

b. **Direct treatment:** Adapt the antibiotic according to the result of ascitic fluid/blood culture and drug susceptibility result. Duration of therapy: (to complete 7 - 10 days).
c. Monitoring:

- Fever, abdominal pain, abdominal circumference and
- Vital signs and **urine output (important**)
- Clinical assessment after 72 hours of SBP treatment
    - If clinical not improve or getting worse within 48 hours: Repeat paracentesis and work up other cause: if ascitis fluid not significantly reduction (PMN drop less than 25%) consider change Antibiotic (Discussed with your team)

7. Prevention/Prophylaxis:

- Add spironolactone to decrease ascites volume may help prevent SBP.
- Early recognition and aggressive treatment of localized infections, *e.g*, cystitis and cellulitis, can also help to prevent bacteremia and SBP in these immunocompromised patients.
- No recommendation for routine use of antibiotic prophylaxis, but can discuss case by case in patients with repeated SBP many times.
- If SBP occurs more than 3 times with in the first 3 months, consider antibiotic prophylaxis which depends on the results of antibiotic susceptibility (discuss with AB committee team)

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10. Leptospirosis

1. Definition:

Leptospirosis is a zoonotic disease that can affect a variety of animal species, but the rat is the main host and reservoir.

It is caused by leptospira, a spirochete which has a preference for the liver and kidneys causing hepatitis and nephritis.

The clinical course is variable and can vary from mild, self-limiting disease to severe, fatal disease. It has an incubation period of 2-26 days (average 10 days). It is difficult to diagnose because of aspecific symptoms and low sensitivity of diagnostic tests.

2. Etiology:

- Leptospira are Gram-negative obligate aerobe spirochetes that is excreted by infected animals in their urine.
- They can survive for several months in water and soil
- There are 24 serogroup with more than 250 serovars.

3. Transmission:

- Leptospira enter the body through transcutaneous penetration (wound) or mucous membranes after immersion in contaminated water (pool, canals, rivers) or through close animal contact.
- Rats, dogs and livestock are the most common source of human infection. These animals can be healthy carriers for many years.
- Risk factors: farmers, veterinarian, slaughter, garbage man
- Following infection, leptospiraemia develops and the spirochetes spread to multiple organs.
- Clinical manifestation of leptospirosis are the result of direct effect of leptospires and/or host immune responses to infection.

4. Differential diagnosis:

- First phase: Dengue + + + (initial phase), flu, viral infection
- Second phase: Malaria, Hepatitis, cholangitis,
- Severe cases:
  - Typhoid fever, scrub typhus, rickettsia,
  - Meningitis, pyelonephritis
  - Non-infectious: vasculitis

5. Clinical presentation:

- Clinical features vary from subclinical infection with a self-limiting febrile illness to potentially lethal multi-system illness with jaundice, renal failure and pulmonary haemorrhage (Weil's syndrome)
- Clinical disease occurs 1 – 3 weeks post-infection.
- Two phase manifestation:
  - First phase/ invasive stage (1 – 5 days): flu-like syndrome, sudden onset, non-specific: fever 39-40°C, chill, malaise, headache, myalgia – usually self-limiting
  - Second phase/ polyvisceral localization (4-7 days later):
    - Persisting systemic infectious signs,
    - Icterus that rapidly and gradual increases
    - Bilateral redness of the conjunctiva +++ (conjunctival suffusion)
    - Hemorrhage: purpura, epistaxis
    - Pseudo-surgical abdominal pain
    - Kidney involvement: oliguria and albuminuria with risks of renal failure
    - Lung involvement: cough, lung hemorrhage with haemoptysis in severe disease
    - Meningeal syndrome: presence as aseptic meningitis
- Death due to multi-organ failure or pulmonary hemorrhage.

*** <u>Different form of leptospirosis:</u>**

- Anicteric form: « summer flu », more frequent in children, difficult diagnosis
- Classic Weil's disease: febrile hepato-nephritis
- Severe forms: often brutal, dramatic
  Alert signs: cardiac, pulmonary, encephalitis, hemorrhage, thrombocytopenia
- Meningeal form (rare) except with certain serotypes

6. Diagnostic evaluation:

- Clinical diagnosis of leptospirosis (see the table of scoring below)

  - Early clinical diagnosis is difficult in septicemic phase (week 1) due to non-specific signs and symptoms.
  - In week 2: immune phase with signs of icterus and complications: diagnostics are based on immune-responses
  - The spirochete is very difficult to culture and diagnostic tests have a very low sensitivity. Therefore, a high clinical suspicion and a low threshold for empiric treatment in case of severe diseases is important.

- **Laboratory work-up**

  - Baseline laboratory tests:
    - CBC (WBC >10,000/mm3; platelet < 100 K to rule out hepatitis),
    - ALT, AST

- UA (proteinuria/albuminuria)
- Renal function test: creatinine, BUN

- **Specific test**: Serology leptospira: ELISA IgM to be requested if fever more than 5 days of fever.
- Blood culture is negative (in normal culture media as in our laboratory)
- Additional laboratory tests:
  - Bilirubine
  - Abdominal ultrasound (liver and kidney are normal) to rule out other diseases

* **Note**: ELISA IgM is the only test available test in Cambodia, which can be used for the diagnosis of leptospirosis. It is expensive and needs to be done only on strongly suspected cases. It becomes positive only after day 5.

Score to diagnosis leptospirosis: Modified Faine's Criteria 2012 for the Diagnosis of Leptospirosis

	Score
Part A: Clinical data	
Fever	***2***
Headache	***2***
Temperature > 39 °C	***2***
Myalgia	***4***
Conjunctival suffusion	***4***
Meningism	***4***
Conjunctival suffusion + Meningism + Myalgia	***10***
Jaundice	***1***
Albuminuria or elevated BUN	***2***
Part B: Epidemiological factors	
Rainfall	***5***
Contact with contaminated environment	***4***
Animal contact	***1***
Part C: Bacteriological and Laboratory Findings	
Isolation of leptospira in culture – Diagnosis certain PCR	***25***
Positive serology	
ELISA IgM positive	***15***
SAT (Slide Agglutination Test) positive	***15***
Other rapid tests	***15***
MAT(Microscopic Agglutination Test) – single positive in high titer	***15***
MAT – Rising titer / seroconversion (paired sera)	***25***

*** Presumptive diagnosis** of leptospirosis is made of:

- Part A or part A+B with a score ≥ 26
- Part A+B+C ≥ 25 (with ELISA IgM for our setting)

*** Possible diagnosis** of leptospirosis : score A+B= 20 – 25

* Note:

1- For laborotory test, use only once score if more than one test is done.
2- Culture and MAT are available only in very specialized laboratory. ELISA IgM is adequate and available in our country.

7. Treatment approach:

a- **Antibiotic therapy (duration 7 days)**:

- For mild form: Doxycycline 100mg bid PO or erythromycin 500mg q8h PO or amoxicillin 1g q8h PO
- For moderate or severe form: Penicillin G 2 M IU IV q6h or Ampicillin 2 g IV q6h or Ceftriaxone 2 g IV qd.

* **Note:** Jarisch -Herxheimer reactions (redness, fever, blood pressure drop) may occur after the start of antimicrobial therapy and should not be confused with allergic reactions.

b- **Supportive or symptomatic treatment**:

- Paracetamol for fever (no aspirin due to risk of hemorrhage)
- In severe case, hemodialysis and organ support may be required.

c- Monitoring:

- Fever, vital signs, urine output, general condition
- Complication signs: hemorrhage, hepato-renal syndrome

8. Prevention/Prophylaxis:

Protection with water exposure and animal products: boots, gloves, clothing.

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11. Rickettsial diseases

1. Definition:

- Infectious diseases caused by *Rickettsia sp*. are transmitted by arthropod vectors (e.g. fleas, ticks, mites, lice).
- There is a wide variety of diseases and clinical features that can be caused by *Rickettsia sp*. In Asia, there are two common rickettsial diseases:
  - **Scrub typhus** caused by *Orientia tsutsugamushi* which are transmitted by mites and
  - **Murine typhus** caused by Rickettsia typhus and transmitted by fleas.
- In this guideline, we will only discuss these 2 conditions.

2. Etiology and contamination:

- Gram negative bacilli, strictly intracellular
- Reservoirs: rats, wild rodents, rabbits, pigs.
- Contamination through bites from :
  - Mites (scrub typhus)
  - Rat fleas (murine typhus)

3. Differential diagnosis:

- Dengue + + + (initial phase)
- Malaria
- Leptospirosis
- Typhoid fever
- Secondary syphilis
- Viral hepatitis
- Brucelosis
- (non-infectious) Vasculitis
- Drug allergy

4. Clinical presentation:

- High fever of acute onset, chills, myalgia
- Intense headache, typhoid state, nausea
- Macular or maculo-papular rash in 50 % of the patients, mainly localized on trunk, but may involve extremities
- **Black eschar** (papule at the site of infection becomes necrotic) is a **pathognomonic sign (but not always present!)**
- Hepato-splenomegaly with or without general lymphadenopathy
- May complicate with atypical pneumonia, meningitis, shock,…
- When antibiotic treatment is initiated, fever disappears within a few days.

5. Diagnostic evaluation:

- Clinical diagnosis

- Laboratory work-up
  - Baseline lab:
    - CBC (leucopenia or normal with thrombocytopenia or normal),
    - ALT, AST, creatinine
  - Blood culture is negative (in normal culture media as in our lab)
  - Confirmation laboratory test:
    - Serology rapid test rickettsia: IgM + (not available yet in Cambodia)

Note: the diagnosis of rickettsial disease is difficult and should rely on clinical suspicion as laboratory diagnositics are not available and/or have very low sensitivity and/or become positive only after a long period of time.

6. Treatment approach:

a- **Antibiotic therapy**:

- Doxycycline 100 mg q12h PO for 5-10 days (10 days for severe cases, and 200 mg q12h for meningitis cases) OR
- Clarithromycin 500 mg q12h PO for 5 days OR
- Azithromycin 500 mg PO qd for 5 days

b- Supportive or symptomatic treatment:

- Paracetamol for fever (no aspirin due to risk of hemorrhage)

c- Monitoring:

- Fever, VS, urine output, general condition

7. Prevention/Prophylaxis:

- Eliminate fleas.
- Wear long clothes, covering the whole body when going into the forest or in the bush.

References

1. Michael Eddleston et al. Oxford handbook of Tropical Medicine, 3rd edition 2011
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4. Botelho-Nevers E1, Socolovschi C, Raoult D, Parola P. Treatment of Rickettsia spp. infections: a review. Expert Rev Anti Infect Ther. 2012 Dec;10(12):1425-37.
5. Sabine Dittrich, Sayaphet Rattanavong. Orientia, rickettsia, and leptospira pathogens as causes of CNS infections in Laos: a prospective study. Lancet Glob Health 2015; 3: e104-12

12. Surgical antibiotic prophylaxis

1. Introduction

Relationship between risk factors and incidence of postoperative infection

Type	Conditions	Risk of postoperatieve infections without prophylaxis	Prophylaxis warranted?
Clean surgery	• No traumatic wounds • No inflammation • No hygiene errors during intervention • Intact mucosa	< 2%	No (except in placement of prosthetic material)
Clean contaminated surgery	• Small hygienic errors • Opening mucosa without major spillage: procedures in urology, gynecology, upper gastrointestinal tract, lung, ENT	10%	Yes in patients with risk factors
Contaminated surgery	• Fresh trauma • Important spillage • Inflamed non-purulent tissue • Lower gastrointestinal tract	20%	Yes
Dirty surgery	• Dirty/old wound • Bite wounds • Fecal contamination • Foreign bodies • Necrotic or purulent tissue • Compound fracture • Perforated viscus	> 30%	Rather consider therapeutic antibiotics

2. General recommendations

a. **Prophylaxis should be started preoperatively, ideally within 60 minutes** before skin incision. However, when ciprofloxacin or vancomycin is indicated, the infusion should begin within 120 minutes before incision to prevent antibiotic-associated reactions. There is no consensus that the infusion must be completed before incision.

Exceptions:

- When a tourniquet is required, the IV antibiotic needs to be completely infused before inflation of the tourniquet to ensure that the necessary tissue concentration is achieved.
- Antibiotics should also be administered immediately after unexpected contamination of the tissues, if no antibiotic has been given preoperatively

Example:

- Decision intraoperatively to do an appendectomy when an ovariectomy was planned.
- Injury of bowel/bladder in hernia repair
- Suddenly decision to use implant: If tourniquet used, release tourniquet first, inject antibiotic and apply tourniquet again 10 minutes after the antibiotic is completely infused.

b. Antibiotic prophylaxis should be limited to the peri-operative period:

In most of the cases, a single shot prophylaxis is recommended. In operations with huge blood loss (> 1,500 cc) a second dose should be given q 1,500 cc of blood loss.

In operations of longer duration (> 3 hours), a second dose should be given (see 'Appendix' for re-dosing schedule). Postoperative doses of antibiotic for prophylaxis should only be given exceptionally. Presence of catheters or drains after surgery is no reason to prolong prophylaxis.

If antibiotics have to be given > 48 hours (for curative reasons), specimen (fluid, urine, tissue, bone and others) for Gram stain and culture need to be taken in OR, for open fractures at the first exploration of the fracture site.

c. Alternatives in patients with penicillin/ betalactam allergy

Replace cephalosporins by lincomycin or clindamycin.

d. Nonantimicrobial methods of preventing infection.

3. Recent data suggest that attention to intraoperative temperature control and supplemental oxygen administration along with aggressive fluid resuscitation may reduce infection rates. Additional research is required before definitive recommendations can be made. There is considerable evidence that aggressive perioperative control of blood sugar with intravenous insulin for patients undergoing cardiac operations reduces SSI rates. The risk of SSI appears to be related to the presence of hyperglycemia rather than to a diagnosis of diabetes mellitus (see reference 4).

4. Guidelines for specific situations

	Antibiotic	**Duration**
Head and Neck surgery		
Clean: thyroid and parotis	No antibiotics	
Radical neck	Cefazolin 2 g IV	Single shot
Contaminated: Tracheotomy, operation involving mouth	Lincomycin 600 mg IV	Single shot
General surgery		

Hernia repair without mesh	No antibiotics	
Hernia repair with mesh	Cefazolin 1 g IV	Single shot
Strangulated hernia	Cefazolin 2 g + metronidazole 500 mg IV	• Single shot • If gangrene or necrotizing fasciitis: continue 7 - 10 days with ceftriaxone 2 g IV qd + metronidazole 500 mg IV q8h (+amikacin 20 mg/kg IV qd if septic), switch to appropriate antibiotic as soon as culture result and antibiogram
Mastectomy/ axillary clearance (cancer without wound)	Cefazolin 1 g IV	Single shot
Mastectomy/ axillary clearance (cancer with wound)	According to culture result	5 days treatment
Plastic surgery		
Reconstruction with flaps or skin graft, if contaminated and AB sensitivity known	According to sensitivity	Five days as treatment
Reconstruction with flaps, Skin graft, soft tissue release if not contaminated only for: • Reconstructive surgery on the lower extremities or groin • Wedge excisions of the lip and ear, skin flaps on the nose • Skin grafts • Patients with extensive inflammatory skin disease • Burn contracture	Cefazolin 1 g IV	• Single shot • For skin graft after contracture surgery continue with cloxacillin for 5 days. (No evidence-based recommendation concerning duration available)
Skin laceration	No antibiotics needed Cleaning and debridement If in doubt, no closure.	
Bites (Incl. snake bites)	Amoxicillin-clavulanic acid 500/125 mg PO q8 h Cleaning and excision Secondary closure	5 d
Abdominal surgery		
Laparotomy for acute abdomen, bowel obstruction, division of adhesions	Cefazolin 1 g + metronidazole 500 mg	Single shot
Colorectal		

Resection in prepared colon	Cefazolin 2 g + metronidazole 500 mg	Single shot
Resection in unprepared colon	Cefazolin 2 g + metronidazole 500 mg	• Single shot • If severe contamination, continue ceftriaxone + metronidazole 5 d
Colostomy/colostomy Closure	Cefazolin 2 g + metronidazole 500 mg	• Single shot • If severe contamination. continue ceftriaxone + metronidazole 5 d
Appendectomy	Cefazolin 2 g + metronidazole 500 mg	Single shot
Gastric operations	Cefazolin 2 g + metronidazole 500 mg	Single shot
Hepatobiliary and pancreatic surgery		
Cholecystectomy	Cefazolin 2 g	Single shot
Biliary tree surgery Pancreatic surgery	Cefazolin 2 g + metronidazole 500 mg	Single shot
Necrotizing pancreatitis	Ceftriaxone 2 g + metronidazole 500 mg	7-14 d
Small bowel surgery	Cefazolin 2 g + metronidazole 500 mg	Single shot
Obstetrics & gynaecology		
Hysterectomy	Cefazolin 2 g	Single shot
Rectocele repair	Cefazolin 2 g + metronidazole 500 mg	Single shot
Difficult D&C	Cefazolin 2 g + metronidazole 500 mg	Single shot
Orthopedic surgery		
Partial hip replacement Femur or tibia nailing Spine surgery	Cefazolin 2 g	Maximum 24 hours
Open reduction and internal fixation (ORIF), not nailing	Cefazolin 2 g	One shot preoperatively and one shot 6 hours later
Open fracture 1st and 2nd degree (< 24 hours after trauma)	Cloxacillin 1 g IV q6h + gentamicin 6 mg/kg IV qd	24 hours > 24 h: If bone not covered by soft tissue: continue till soft tissue coverage, but switch to PO amoxicillin-clavulanic acid 500/125 mg q8h as soon as possible
Open fracture 3rd degree or any open fracture with	Cloxacillin 1 g IV q6h + gentamicin 6 mg/kg IVqd	At least five to seven days or until bone covered by soft tissue but

severe contamination (< 24 hours after trauma)	+ metronidazole 500 mg IV q8h	switch to PO amoxicillin-clavulanic acid 500/125 mg q8h as soon as possible
Amputation/Stump revision		
Not infected	Cefazolin 1 g	Single shot
Infected	Ciprofloxacin 400 mg IV q12h + lincomycin 600 mg IV q8h	As treatment 7 - 10 d. Switch to PO as soon as possible
Urology		
With sterile urine	Cefazolin 2 g IV	Single shot
Preoperative bacteriuria	According to culture result	Till catheter removed or maximum 10 d. PO antibiotics as soon as possible
Vascular surgery		
abdominal and lower limb surgery	Cefazolin 2 g	24 hours
Neurosurgery		
Craniotomy VP shunt Laminectomy	Cefazolin 2 g	Single shot
Open skull fracture	Closure of wound after debridement Ceftriaxone 2 g + lincomycin 600 mg IV q8h	48 hours
Basal fracture with CSF leak	Cefazolin 2 g IV q6h	7 to 14 days according to neurosurgeon
Basal fracture no CSF leak	No AB	
Maxillofacial fracture with laceration of mucosa	Lincomycin 600 mg IV q8h	5 d

* Note: If cefazolin is not available, cefuroxime 1.5 g IV OR ceftriaxone 2 g IV may be used as alternative.

Appendix: Re-dosing schedule adapted with creatinine clearance

Antibiotic	Renal half-life, normal kidney function (h)	Renal half-life, end stage kidney disease (h)	Standard dose	Re-dosing interval in normal kidney function (h)[a]
Cefazolin	1.2 – 2.5	40 – 70	1 – 2 g iv	2 – 5
Cefuroxime	1 – 2	15 – 22	1.5 g iv	3 – 4
Clindamycin	2 – 5.1	3.5 – 5	600 mg iv	3 – 6
Lincomycin			600 mg iv	8
Ciprofloxacin	3.5 – 5	5 – 9	400 mg iv	4 – 10
Gentamycin	2 – 3	1- - 70	5 mg/kg iv	Not required
Metronidazole	6 – 14	7 – 21	500 mg iv	6 – 8

[a] *Redosing interval*: For procedures of long duration, antibiotics should be re-administered at intervals of 1-2 times the half-life of the drug.

* *Table adapted from Antimicrobial Prophylaxis for Surgery (Reference 4)*

References:

1- Giorgio Zanetti, Richard Giardina, Richard Platt, Intra-operative Redosing of Cefazolin and Risk for Surgical Site Infection in Cardiac Surgery**,** CDC, Emerging infectious diseases, Vol. 7, No 5, Sept – Oct 2001

2- Recommendation American Academy of Orthopedic surgeons June 2004 http://www.aaos.org/about/papers/advistmt/1027.asp

3- Antibiotic prophylaxis in surgery, Revised 2006 http://www.surgicalcriticalcare.net/Guidelines/antibiotic_prophylaxis.pdf

4- W. Bratzler Dale, M. Houck Peter, Antimicrobial Prophylaxis for Surgery: An Advisory Statement from the National Surgical Infection Prevention Project Clinical infectious diseases, 2006, Volume 38, Issue 12, p. 1706-1715

13. Short note on management of patients with suspicion of tetanus

- Wounds must be cleaned, disinfected and treated surgically if appropriate.
- Equine tetanus antitoxin (antitetanic serum): total dose 50,000 – 100,000 IU IV
  - Initial dose: 20,000 IU IV over 30 mn (15 amp of 1,500 UI)
  - 4 hours later: 30,000 IU IV (20 amp)
  - 4 hours later: 30,000 IU IV (20 amp)
- Antibiotics for 10 days:
  - First choice: metronidazole 500 mg IV q6h
  - Second choice: penicillin 3M IU IV q4h.
- Diazepam adapted dose to achieve spasm control but be aware of excessive sedation and hypoventilation: start 10 to 20 mg IV q2h up to 7 days. Increase dose with 5 mg until adequate effect is reached (Max 20 mg/kg/day).
- Antitetanus vaccine 0.5 ml SC at days 3, repeat at M1, M6, M18, M30 (follow national protocol). Optional boosting at year 5 and year 10.
- Patient need to be in dark room.

Appendix: Guide for Tetanus vaccine booster and immunoglobulin

History of tetanus vaccination		Type of wound	Tetanus vaccine booster	Tetanus immunoglobulin
3 or more doses	< 5 years since last dose	All wounds	NO	NO
	5-10 years since last dose	Clean minor wounds	NO	NO
		All other wounds	YES	NO
	> 10 years since last dose	All wounds	YES	NO
< 3 doses or uncertain		Clean minor wounds	YES	NO
		All other wounds	YES	YES

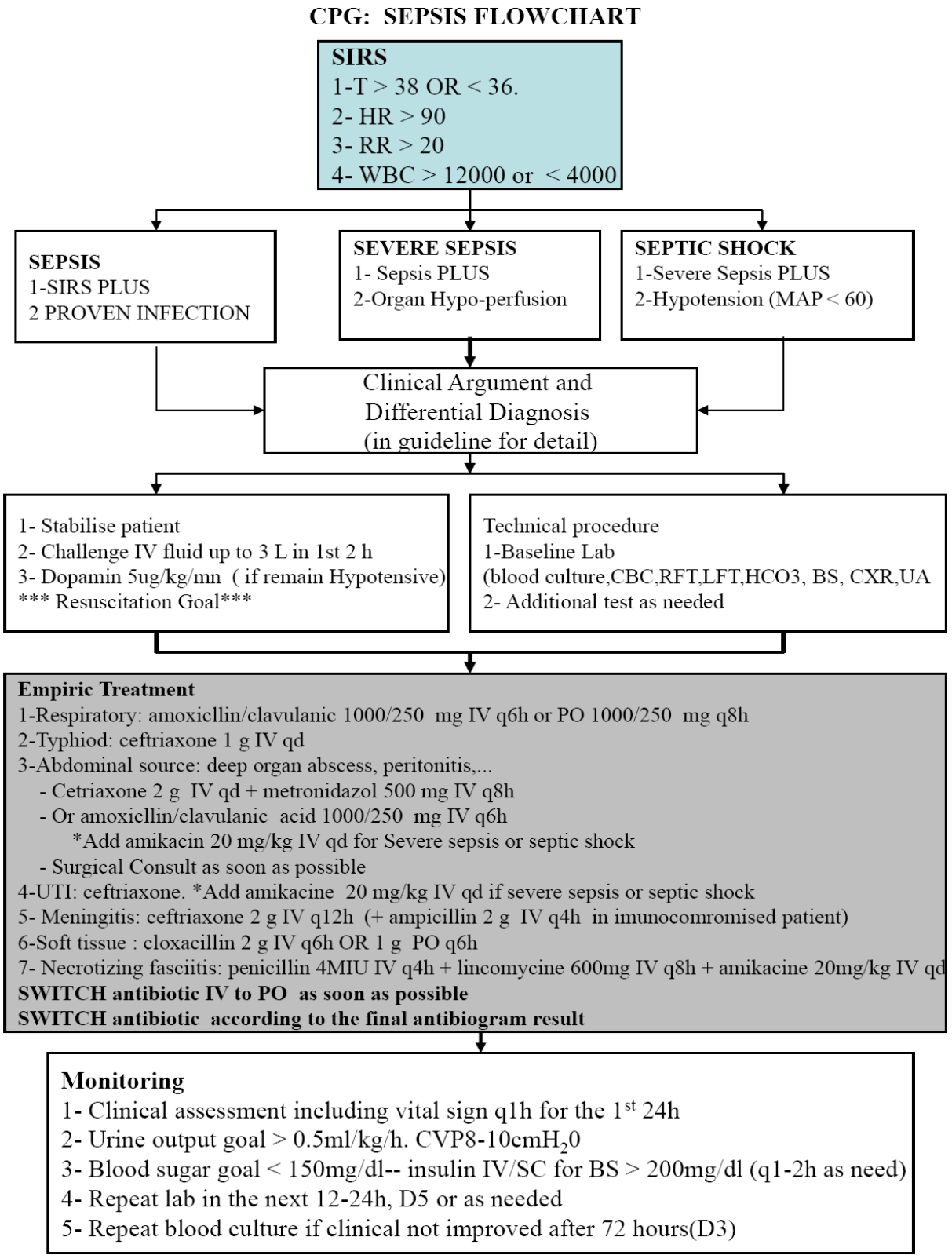
** Extract from: Sonja Kill Memorial Hospital, guideline Tetanus Prophylaxis*

References:

1- Sanford guide to antimicrobial therapy, 2014
2- WHO guidelines: Current recommendations for treatment of tetanus during humanitarian emergencies, January 2010.
3- Chaturaka Rodrigo, Deepika Fernando and Senaka Rajapakse. Pharmacological management of tetanus: an evidence-based review. Critical Care 2014, 18:217.

14. Annexes

Flowchart for management of sepsis



Procedure of blood sampling for culture

1. Prepare all materials needed for the procedure
2. Explain de patient about the procedure
3. Prepare 2 stickers with patient's name, hospital number, date and time of collection, and R for right arm or L for left arm. Put these stickers on the 2 aerobic blood culture bottles.
4. Clean hands with hand rub if available, if not: wash and dry hands
5. Put the tourniquet around the arm
6. Clean patient's skin with alcohol: use pre- pads, if not available use liquid alcohol and compress
7. Wipe with Betadine: start at the site you will puncture, move in circles around this site. After this do not touch the puncture site anymore
8. Allow the Betadine to act during 2 minutes. In the meantime: do 9, 10 and 11
9. Remove plastic flip-top from blood culture bottle
10. Wipe the rubber stopper of the blood cultures with Betadine. Let the Betadine act during 2 minutes
11. Put on examination gloves and prepare needle and syringe
12. Insert the needle into the vein and withdraw 10ml of blood in syringe Use a new needle if the first attempt is not successful
13. Insert the 10ml of blood in the culture each bottle, the culture bottle should be in a rack while doing this, to avoid needle stick accidents.

    *** <u>Note:</u>** there is no need to change the needle for this
14. Throw syringe with needle in sharps container
15. Mix the bottle by gentle movement
16. Cover the puncture site
17. Repeat the procedure for the other arm (5-8, 12-16): There is no need to change gloves but use a new syringe and needle
18. Clean hands with hand rub if available, if not: wash and dry hands
19. Transport the blood culture samples with request form immediately to the laboratory

    * Note: at laboratory closing hours, place bottles in incubator at ER 36oC – 37oC, bring the samples to the laboratory as soon as it opens.

*** In case of questions: please contact Mrs. Meak Kolenine/supervisor or**

Dr Lim Kruy/Dr Phe Thong/Mr Teav Syna

Procedure of urine sampling for culture (clean catch urine specimen)

ACTION	RATIONALE
1. Gather needed supplies: • gloves • sterile gauze pads • betadine • sterile specimen container • lab requisition form completed with the desired test, patient's name, age, sex, and hospital number • label with patient's name, age, sex, and hospital number, date and time of collection, and initials of nurse • plastic bag for transport to lab	Having needed supplies ready ensure performance of efficient procedure
2. Wash hands	Reduces transmission of microorganisms
3. Explain to patient what you will be doing and why	Patient cooperation is needed for specimen collection; explanation of procedure will promote greater understanding of what he or she needs to do
4. Place screens around bedside if specimen will be collected at bedside	Provides for patient privacy
5. If the patient is able, ask him or her to wash his/her perineal area with soap and water. The nurse must assist him/her if unable	Washing will decrease the amount of skin bacteria and decrease contamination of specimen
6. Assist the ambulatory patient to the bathroom or assist the patient on bedrest onto the bedpan. For the male patient assist with urinal; if needed	The female patient must be in a sitting or squatting position to obtain a non-contaminated specimen
7. Remove cap of specimen and place on flat surface being careful not to touch the inside of cup or cap	To prevent contamination and false result
8. Pour betadine over gauze and use to clean as follows: • <u>Female patient:</u> Clean the vulvar area from front to back while holding the labia apart • <u>Male patient:</u> Retract the foreskin and clean the tip of the penis from inside to outside in a circular motion	For disinfection of area around urinary meatus to decrease the contamination of sterile specimen

9. Patient should begin to void. After patient begins to void, place sterile container under stream of urine and collect 30 ml of urine	Initial stream of urine flushes out microorganisms that accumulate at meatus; begin collection at midstream to obtain an uncontaminated specimen
10. Remove the specimen cup before stream of urine stops	Prevents contamination of specimen with skin flora
11. Replace cap on specimen container	Maintains sterility of specimen. Prevents spillage of specimen
12. Cleanse urine from outside of container	Reduces transmission of microorganisms
13. Remove the bedpan and assist patient to a comfortable position as needed	Promotes patient's comfort
14. Place label on specimen container and place in specimen bag with lab requisition	Proper identification of specimen prevents error in diagnosis and treatment; specimen must be in plastic bag for transport to the lab to prevent contact with microorganisms
15. Remove gloves and wash hands	Reduces transmission of microorganisms
16. Bring specimen to lab immediately or place specimen in refrigerator if lab is closed	Bacteria grows in urine at room temperature, so if immediate processing is not available the specimen must be placed in refrigerator
17. Document specimen collection in progress notes	Communicates procedure to other members of health care team

Procedure of lumbar puncture

Definition: Lumbar puncture (LP) is an invasive medical act which has objective:

1. Take CSF for examination.
2. Measure opening pressure of CSF.
3. Inject some drugs (eg: anesthesia drug)

Indication of LP of CSF analysis:

- Meningeal syndrome
- Meningeal syndrome + focal neurologic signs

Contra-indications :

- Intracranial hypertension: fundoscopy before LP. If no material available, it is possible to assess based on clinical signs: intense headache (worsened by effort, variable localization), important vomiting, blurred vision and horizontal diplopy, consciousness alteration and psychologic problems.
- Infections near the puncture site
- Important disorder of coagulation function. LP should be postponed until the problem is corrected.
- Vertebral malformation

*** *Remark*** : The contra-indication should be kept in balance with the necessity of making the diagnosis. Nevertheless, the morbidity and mortality related to LP in a patient with lying-down position is much less than the risk of meningitis itself. **In cryptococcal meningitis, intracranial hypertension is not contra-indicated for LP**.

Possible complications:

- Meningitis due to inoculation of bacteria when performing LP
- Intense headache, back pain, paresthesia
- Accident of puncture of spinal medulla
- Accident of puncture of aorta or vena cava (severe bleeding)
- Cerebral herniation

Material :

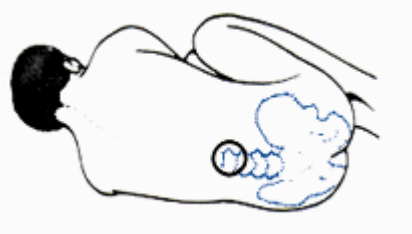
- 1 spinal needle N^{o} 20 or 22 gauge
- 3 sterile tubes
- Antiseptic solution
- Cotton, gauze, gloves, syringes

  Premedication: Lidocaine1-2% 5-10ml

Preparation of patient before doing LP:

1. Explain the indication of the procedure to be performed.
2. Ask the patient to sign consent form with a witness (done with patient's relative if patient confused or coma).
3. Inform the patient about the necessity to rest in bed for several hours after LP.
4. Provide confidence to the patient.

Procedure of LP:



- Place patient in the lateral decubitus position. The patient (helped by an assistant, if possible) should be in position with knees pulled up towards the stomach and head flexed onto chest.
- Keep universal precaution measures.
- Determine the location of the L4-L5 interspaces (L3-L4 if needed).
- Put on sterile glove and clean the area with povidone-iodine solution in a circular manner.
- Anaesthesia by lidocaine 2-3 ml over L4-L5 interspaces
- Insert spinal needle N^{o} 20 or 22 gauge into L4-L5 interspaces.
- Remove stylet to look for return of fluid, rotate the needle slightly if no fluid returns
- When fluid returns, attach IV line and measure the opening pressure (OP).
- Collect 0.5 to 2 ml CSF in serial of 3 tubes after measuring OP.
- Withdraw the needle and place a small adhesive bandage over the puncture site.
- Instruct the patient to lie prone for at least 2 hours following LP to avoid postural puncture headache and encourage increase water intake to prevent spinal headache.

Laboratory Sampling: (3 sterile plain tubes)

- **Tube 1 for bacteriology**: Gram stain, AFB, Chinese ink, culture (bacteriology, mycobacteriology, fungal).
- **Tube 2 for chemistry exam**: protein and glucose concentrations, VDRL, Cryptococcus Antigen.
- **Tube 3 for cell count**: blood cell count with differential

Procedure of paracenthesis

Indication

- To take ascites fluid for analysis to find cause of ascites
- To remove tension ascites

* Contraindication in patient with DIC/ platelet too low (<20 10x9/L)

Material

- Betadine, alcohol swap
- gauze, glove sterile,
- syringe 10cc and 5cc, one needle n° 24, 20, 18
- 2 to 3 red tubes, 1 violet tube, /aerobic blood culture bottle

Premedication: Lidocaine 1-2%: 5ml (optional)

Preparation of patient before doing paracentesis:

- Explain the indication of the procedure to be performed.
- Ask the patient to sign consent form with a witness (done with patient's relative if patient confused or coma).
- Provide confidence to the patient.

Procedure

- Place the patient on dorsal decubitus
- Determine the location for the paracenthesis
- Keep standard precaution measures
- Clean the area to be aseptic (first with alcohol, next with betadine) and perform local anesthesia on the puncture site.
- Insert the needle in Z ways and remove ascites fluid for sample collection into 1 blood culture bottle (5-10 cc) for culture and 3 tubes (see below).
- Attach IV line to remove the ascites fluid if indicated
- Withdraw the needle and place a small adhesive bandage over the puncture site.

Laboratory Sampling:

- 1 aerobic blood culture bottle (10 cc of ascites fluid): for ascites culture (preferred)
- **1 Sterile plain tube for bactoriology** : Gram stain, bacterial culture (if no ascites sample in blood culture bottle), and also AFB if indicated**.**
- **1 Sterile plain tube for chemistry exam**: protein and glucose concentrations.
- **1 EDTA tube (violet):** for blood cell count with differentiation

Procedure of arthrocenthesis

Indication

- Suspected septic arthritis, bursitis
- Suspected crystal-induced arthritis
- Differentiation between non-inflammatory and inflammatory arthritis

Material

- Betadine, alcohol swap,
- gauze, glove sterile,
- syringe 10cc and 5cc, one needle n° 24, 20, 18
- 2 to 3 red tubes, 1 violet tube, /aerobic blood culture bottle

Premedication: Lidocaine 1-2%: 5 – 10 ml

Patient preparation:

- Explain the indication of the procedure to be performed.
- Ask the patient to sign consent form with a witness (done with patient's relative if patient confused or coma).
- Provide confidence to the patient.

Procedure

- Clean the joint area to be aseptic and perform local anesthesia.
- Take the synovial out as much as possible

Laboratory sampling

- 1 aerobic blood culture bottle (10 cc): for synovial fluid culture (preferred)
- **1 Sterile plain tube for bactoriology** : Gram stain, bacterial culture (if no ascites sample in blood culture bottle), and also AFB if indicated**.**
- **1 Sterile plain tube for chemistry exam**: glucose concentrations.
- **1 EDTA tube (violet):** for blood cell count with differentiation

SOP for chest tube site care

ACTION	RATIONALE
1. Dressings over chest tube sites will be changed and the site cleaned once a day unless ordered specifically by the doctor	Dressing changes can help decrease the possibility of infection. It also provides an opportunity for assessment of the site and cleaning the area
2. Obtain necessary supplies: - non-sterile gloves - sterile gloves - alcohol swab-sticks - betadine swab-sticks - sterile scissors - sterile petroleum (Vaseline) gauze - sterile drain sponges (if available) - Sterile 4 x 4 gauze - Wide tape - Sterile drape for work area	Having all supplies ready and available allows the procedure to be completed in an efficient manner
3. Wash hands	Decreases transmission of microorganisms
4. Explain procedure to patient	Promotes cooperation with procedure and involves patient in care
5. Place screens around bedside	For patient privacy
6. Put on non-sterile gloves	To reduce exposure to blood or body fluid- borne bacteria
7. Help position patient in the bed so that the chest tube insertion site can be seen clearly	Site must be seen clearly and be in easy reach to complete dressing change
8. Carefully remove dressing from around chest tube while securing tube with one hand	Stabilize tube with one hand to prevent tube from coming out of place
9. Observe chest tube site for presence of drainage, pus, and bleeding; observe sutures and skin around tube site	Observation is a key part of assessment; presence of pus or redness may indicate infection at site
10. Open supplies while maintaining sterility and place sterile items on sterile work area	Chest tube site must be cared for and cleaned using sterile technique
11. Apply sterile gloves	Sterile items must be handled with sterile gloves to maintain sterility
12. Clean site around chest tube with the alcohol swabs and then with the betadine swabs in a circular motion, moving from inside to outside	Cleaning in a circular motion moves from area of least contamination to area of great contamination and prevents the nurse from recontaminating sterile area

13. Apply Petroleum gauze around site, being sure to place it under the tube	Petroleum gauze creates a seal around the tube site to prevent air leakage around the chest tube
14. Place 2 -3 sterile drain sponges over site, fitting it around the tube; if no drain sponges are available, cut sterile 4 x 4s to fit around tube (using sterile scissors)	Helps prevent microorganisms from entering site; drain sponges can be used to fit securely around tube and help anchor the tube in place
15. Place uncut 4 x 4s over site, making sure to cover an area of about 7 cm around tube	Creates barrier to microorganisms
16. Secure dressing with wide tape, covering dressing completely with tape	Keeps dressing clean and dry and secures it in place
17. Using tape, secure the tube to patient's skin below the dressing; DO NOT tape tube to bed or side rails	Helps to prevent tube from accidentally being pulled out; taping tube to bed can lead to tube accidentally being pulled out while patient is moving
18. Assess chest tube collection system for presence of air leaks and continued drainage; make sure tube is NOT clamped in any area unless specifically ordered by doctor for a pleural effusion or pleurodesis.	To make sure that the tube remains in place; presence of air leak could indicate dislodged tube; kinked tubing will prevent free-flowing drainage. **Chest tubes should not be clamped for any reason (not for transport, dressing changes, or changing collection system) because of high risk of a tension pneumothorax developing. Pleural effusions are often drained intermittently to prevent hypotension and pleurodesis requires clamping.**
19. Help patient return to comfortable position in bed and remove screens from around bedside	Promotes patient's comfort
20. Clean up supplies and remove gloves; wash hands	Reduces transmission of microorganisms
21. Report any signs of infection or air leaks to the doctor	Communication of any abnormal findings allows for prompt intervention by the medical team
22. Write date, time and initials of nurse performing dressing change on the dressing and document dressing change in the progress notes, noting signs of infection, presence of drainage at site, etc.	Documentation is a means of communication regarding patient status and response to treatment; documents care given

SOP for chest tube maintenance

ACTION	RATIONALE
1. Check patient's chart for orders regarding chest tube maintenance (ie. amount of suction, etc.)	Communication of orders between medical and nursing staff will prevent patient injury
2. Continue to monitor patient status; • V/S will be taken as doctor orders, • breath sounds, chest wall movement and SaO2 will be checked **at least** every shift, and changes documented and reported to doctor	Patient with a CT is at a greater risk for pneumothorax and other complications than other patients and therefore, it is important to have a baseline respiratory assessment in case of an emergency
3. Do not clamp except doctor's order	Do **NOT** clamp the chest tube unless the patient has a pleural effusion being drained intermittently **OR** the patient is having pleurodesis done and there is a specific doctor's order. Clamping a chest tube can cause a tension pneumothorax if left on too long.
4. Check the level of the water in the water seal and suction control chambers once a shift and add sterile water (or NSS if no sterile water available), if needed, to maintain the desired level of suction	Due to evaporation, the level of water decreases over time and therefore the suction will decrease also if the water level is not maintained
5. Observe for presence/absence of air bubbles (air leak) in the water seal chamber every shift and note every shift. Notify doctor with any changes in the assessment	The development of an air leak can mean a pneumothorax has formed or that the system needs to be checked for air leaks and re-taping connections may be indicated. And the lack of an air leak, when there was one previously could mean that there is a clot/kink in the tube, or the lung is fully expanded
6. Note amount of drainage throughout shift. Check for change in quality and/or sudden drop or increase in quantity	To monitor for changes in patient status and provide for prompt intervention as needed
7. Keep tubing as straight as possible and educate patient/family not to lie on it	To prevent system blockage and involve patient/family in care
8. Empty the connecting tube every hour. But, do not strip or milk the tubing to mobilize drainage; this should only be done under a doctor's order/supervision	The fluid in the tube, if not emptied frequently, especially with an empyema, may become blocked or clotted. Stripping creates a high degree of negative pressure, possibly pain and has potential of dislodging the chest tube
9. Secure the collection system in an upright position and do not elevate drainage system to the level of patient's chest	Prevent system from falling over and having to be changed. Elevating system may cause drainage to flow back into the lung
10. Teach patient coughing, deep breathing exercise or IS, to be done per hospital protocol	Prevent atelectasis and facilitate lung expansion
11. If chest tube becomes disconnected, quickly restore the connection or clamp tube and attach new drainage system as soon as possible. Remove clamp after restoring connection!	Leaving tube clamped for long period of time may cause tension pneumothorax

SOP for sterile wound dry dressing

ACTION	RATIONALE
1. Check physician's order	Confirms correct procedure
2. Gather equipment	Allows for an efficient and uninterrupted procedure
3. Identify the patient and explain procedure	Promotes patient's cooperation and involves patient in care
4. Assess patient's comfort level and give pain medication if needed	Removal of dressing can be painful; patient may require pain medication
5. Put screens around bed	Allows for privacy
6. Raise bed to comfortable working level and lower side rails	Provides easy access to wound area and prevents injury to nurse
7. Place receptacle for soiled dressings near wound site	Collects contaminated materials in a known contaminated area
8. Wash hands	Reduces transmission of microorganisms
9. Clean off over-bed table and place sterile supplies on over-bed table. May use dressing cart if available	Provides clean working space
10. Reposition patient to allow access to wound, and place absorbent pad under area	Allows access to wound and to prevent soiling linens
11. Put on clean gloves and apply face mask or other protective wear needed	Gloves are necessary for universal precautions but sterile gloves are not needed at this time
12. Remove tape on wound by slowly pulling tape toward the wound and parallel to the skin	Pulling toward the wound decreases the pain of tape removal by not putting pressure on edges of wound
13. Remove soiled dressings. Soak dressings stuck to wound with normal saline before removing. Observe character, amount of drainage in wound and on dressing and note size, color, odor, edges, and healing of wound, and dispose in receptacle	Soaking dressings loosens them for removal and prevents tissue damage and pain. Facilitate accurate assessment of wound status. Collects contaminated materials in a known contaminated area
14. Obtain wound culture if ordered after rinsing wound with sterile 0.9% normal saline	Wound culture should be obtained before wound is cleaned, but wound must be rinsed first to remove surface organisms
15. Remove gloves, discard, and wash hands	Gloves are now contaminated and need to be removed before cleaning wound
16. Open sterile packages and place on table. Arrange packages to ensure no crossing over sterile field when using dressings	Organizes supplies to protect sterile field. 2.5cm of each edge of opened package should be considered contaminated
17. Cut tape into appropriate strips, and place on table edge	Make tape available for use at end of procedure

18. Put on clean gloves	
19. Open cleansing solution, and pour over wound. Do not use high pressure to irrigate – catheter smaller than 16G is contraindicated. Place emesis basin next to skin surface to catch overflow	Provides gentle flow of solution to wet the wound and remove loose debris
20. Discard gloves and put on sterile gloves	Sterile gloves reduce the transmission of microorganisms to wound bed
21. Form a ball with gauze pads by tucking all four corners together. Use the center of gauze pads to cleanse the wound	This action prevents contamination of hands during cleaning
22. Cleanse the wound; - Start at the cleanest area and work away from that area - Never return to an area you have previously cleaned - Usually start at the middle of the wound and work toward periphery - Use a separate pad for each cleansing stroke - Use gentle pressure to avoid tissue trauma - Pat dry the wound	This reduces amount of microorganisms introduced into wound. Cleansing the wound in a rough manner can remove new epithelium, may cause bleeding and prolonged wound healing
23. Clean with a separate gauze pad under drain and around the site with gauze and cleaning solution if a drain is present	Drain sites can provide areas for bacteria to grow and be introduced into body
24. Place appropriate amount of gauze under drain	Absorbs drainage
25. Place sterile gauze over the wound. Cover with ABD pad if necessary: remove gloves and tape securely.	Absorbs wound exudate.
26. Remove the blue pad and assist the patient to a comfortable position	Allows for patient comfort
27. Lower bed and raise side rails	Provides for patient safety
28. Wash hands	Reduces transmission of microorganisms
29. Document dressing change. Note date, time, patient's response to treatment and condition of wound (include: size, color, drainage, odor, and any signs of infection)	Communicates progress of wound healing, patient's response to treatment to other members of health care team

Dose adjustment of commonly used antibiotics in adults with renal impairment

For patients with **acute renal insufficiency** (e.g. due to sepsis), use normal doses for the first 24-48 hours. Then, consider to adapt dosages according to the actual creatinine clearance and this table.

While the patient (and his renal function) recovers, revise daily the clearance and re-adjust the dosage accordingly.

For patients with **already known chronic renal insufficiency**, the first dose (loading dose) is a normal dose (in order to achieve quickly effective serum drug levels), the next doses need adaption.

Antibiotic	**Dosage based on estimate GFR [(1)]**			Supplement dose after hemodialysis or peritoneal dialysis
	≥ 50 ml/min	**50 – 10 ml/min**	**< 10 ml/min OR anuria**	
Amikacin	20 mg/kg IV qd	20 mg/kg IV q48-72h	20 mg/kg IV q96h	10 mg/kg IV
Amoxicillin-clavulanic acid	1000/250 mg PO q8h 1000/250 mg IV q4-6h	500/125 mg PO q8h 1000/250 mg IV q12h	500/125 mg PO q24h 1000/250 mg IV q24h	500/125 PO 1000/250 mg IV
Amoxicillin Ampicillin	1 g PO q6h 2 g IV q4-6h	1 g PO q6h 2 g IV q4-6h	1 g PO q8h 2 g IV q8h	1 g PO 2 g IV
Azithromycin	250-500 mg PO q24h	250-500 mg PO q24h	250-500 mg PO q24h	None
Cefazolin	1-2 g IV q6h	1-2 g IV q12h	1-2 g IV q24h	500 mg-1 g IV
Ceftazidime [(2)]	2 g IV q8h	2 g IV q24h	2 g IV q48h	2 g IV
Cefuroxime	750 mg -1.5 g IV q8h	750 mg -1.5 g IV q12h	750 mg -1.5 g IV q12h	750 mg -1500mg IV
Ciprofloxacin	500 mg PO q12h 400 mg IV q12h	500 mg PO q18h 400 mg IV q18h	500 mg PO q24h 400 mg IV q24h	None None
Clarithromycin	500 mg PO q12h	375 mg PO q12h	250 mg PO q24h	None
Clindamycin	600 mg PO q8h 600 mg IV q8h	600 mg PO q8h 600 mg IV q8h	600 mg PO q8 h 600 mg IV q8h	None
Cloxacillin	1 g PO q6h 2 g IV q6h	1 g PO q6h 2 g IV q6h	1 g PO q6h 2 g IV q6h	None
Cotrimoxazole[(2)]	160/800 mg PO q12h 160/800 mg IV q12h	80/400 mg PO q12h 80/400 mg IV q12h	Not recommended	None
Gentamicin	6 mg/kg IV qd	6 mg/kg IV q48h	6 mg/kg IV q72h	1 mg/kg IV
Lincomycin	500 mg PO q6h 600 mg IV q8h	500 mg PO q12h 600 mg IV q12h	250 mg PO q24h 300 mg IV q24h	None
Levofloxacin	500 mg PO q24h 500 mg IV q24h	250 mg PO q24h 250 mg IV q24h	250 mg PO q48h 250 mg IV q48h	None None
Meropenem [(2)]	1 g IV q8h	1 g IV q12h	500-1000 mg IV q24h	500 mg IV
Nitrofurantoin	100 mg PO q8h	Not recommended	Not recommended	Not recommended
Penicillin G	4 MIU IV q4h	3 MIU IV q4h	2 MIU IV q4h	2 MIU IV
Penicillin V	250-500 mg PO q6h	250-500 mg PO q6h	250-500 mg PO q6h	250-500 mg PO
Vancomycin	1 g IV q12h	1 g IV q24h	1 g IV q96h	None

** Adapted from "The Sanford Guide to antimicrobial therapy; 2008-2009, Belgian/Luxembourg ed."*

Note: [(1)]GFR : glomerular filtration rate, calculated by estimate creatinine clearance rate (eCrCl):

- eCrCl (ml/min) = [(140-age) x body weight in kg x 1.2]: serum creatinine in µmol/L OR
- eCrCl (ml/min) = [(140-age) x body weight in kg]: [72 x serum creatinine in mg/dL]

* For female: (time 0.85) = eCrCl x 0.85 ml/min

[(2)] Please see chapter 8 for dose adjustment of ceftazidim, cotrimoxazole and meropenem for treatment of melioidosis