UNIVERSITY OF NAIROBI

KENYATTA NATIONAL HOSPITAL
Guidelines for
Empiric Antimicrobial Therapy

2023 Edition

Foreword

Antimicrobial Stewardship Programs involve organizational or system-wide health care strategies to promote appropriate use of antimicrobials through the implementation of evidence-based interventions. The goals of antimicrobial stewardship are to optimize antimicrobial use, to improve patient outcomes, control costs and minimize adverse consequences associated with antimicrobial resistance.

The increasing rate of Antimicrobial Resistance (AMR) remains a major public health concern worldwide as it threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. Resistance leads to inappropriate empirical therapy, delays in starting effective therapy and the use of less effective more toxic and more expensive medicines. AMR is also associated with treatment failure, prolonged hospitalization, increased costs of care as well as morbidity and mortality. There is therefore an urgent need to control AMR by improving antimicrobial use within our hospital.

This empiric antimicrobial therapy guide has been developed under the leadership of the KNH Antimicrobial Stewardship Committee with engagement of key stakeholders. The committee operates within the hospital's Medicine and Therapeutics Committee and is focused on implementing strategies on appropriate antimicrobial use that are informed by quality susceptibility data generated from our state-of-the-art microbiology laboratory as well as antimicrobial consumption and use data from the pharmacy division.

It is noteworthy that diagnostic stewardship as well as infection prevention and control practices are key in preventing antimicrobial resistance and supporting antimicrobial stewardship strategies. This guide is to be used together with available guidelines on appropriate microbiology sample collection and handling, and adherence to infection prevention and control measures.

Antimicrobial stewardship is applicable at all levels of antimicrobial use including selection, procurement, prescribing, distribution, dispensing and administration. This guide seeks to promote appropriate and effective antimicrobial use to enhance quality of patient care and improve clinical outcomes. It is therefore the responsibility of all health care workers to adhere to these guidelines.

Signed

Dr. Evanson Kamuri, EBS
Chief Executive Officer

Editorial Note

This guideline has been developed by a multidisciplinary team of medical specialists including Infectious Disease specialists, microbiologists, clinical pharmacists, surgeons, obstetricians and gynaecologists, physicians, paediatricians, infection control and prevention specialists and nurses; and is an update of the previous guideline published in 2018.

The hospital antibiogram for the years 2021-2022 was used to identify the most common pathogens and their antibiotic susceptibility profiles and this informs the recommendations in this guideline.

The aim of this document is to provide guidance on the most appropriate empiric antibiotic choices for both community and hospital acquired infections at the KNH, to promote rational antibiotic use and ultimately to reduce the emergence and spread of drug resistant bacteria.

This document complements the following handbooks; the clinician's handbook on appropriate use of microbiologic diagnostic tests and the KNH guideline for antibiotics use for surgical prophylaxis which are available at the hospital.

Proper clinical work up of all patients is paramount and it is important to note that this guideline may not apply uniformly to all patients. Patient care must be individualised and the choice of antimicrobials may need to be modified in special groups such as pregnant and lactating mothers, in renal and hepatic dysfunction, in patients with history of severe antibiotic allergy and in the presence of significant drug interactions.

It is important that all health care workers implement this guideline and where there is need for significant variation in antimicrobial choice, then the Infectious Disease or antimicrobial stewardship team at the hospital should be consulted.

This guideline will be revised periodically as informed by any changes in the hospital antibiogram, availability of antibiotics and new evidence on antibiotic use.

Signed

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Chair- Antimicrobial Stewardship Committee

Signed

Dr. Philomena Owende
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List of Abbreviations

AVPU	Alert, Voice, Pain, Unresponsive
CONS	Coagulase Negative Staphylococcus
CNS	Central Nervous System
CRP	C-reactive Protein
CSF	Cerebral Spinal Fluid
CVS	Cardiovascular System
DFAT	Direct Fluorescent Antibody Testing
ESR	Erythrocyte Sedimentation Rate
EVD	External Ventricular Drain
GCS	Glasgow Coma Scale
HIV	Human Immuno-deficiency Virus
IDS	Infectious Disease Specialist
IPC	Infection Prevention and Control
IV	Intravenous
LP	Lumbar Puncture
MDRO	Multidrug-resistant Organism
MRI	Magnetic Resonance Imaging
MRSA	Methicillin Resistant Staphylococcus Aureus
PCT	Procalcitonin
PJP	Pneumocystis Jirovecii pneumonia
PO	Per Oral
RBS	Random Blood Sugar
RR	Respiratory Rate
RS	Respiratory System
Sp.	Species

Hand Hygiene Technique

INFECTION PREVENTION AND CONTROL UNIT-
HAND HYGIENE TECHNIQUE STEPS

Wet hands with water

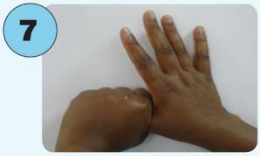
Apply enough soap to cover all hand surfaces

Rub hands palm to palm

Right palm over left dorsum and left palm dorsum

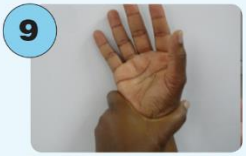
Palm to palm fingers interlaced

Backs of fingers to opposing palms with fingers interlocked



Rotational rubbing of right thumb clasped in left palm and vice versa

Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa



Rotational rubbing of the wrist right palm and vice versa

Rinse hands with water

Dry hands thoroughly with a single use towel

Adopted from WHO

MIKONO MISAFI
HUOKOA MAISHA

Table 1: Infection Prevention Measures For Invasive Procedures

Central line insertion	Peripheral cannula insertion	Urinary catheter insertion
• Perform hand hygiene	• Perform hand hygiene	• Perform hand hygiene
• Put on sterile Personal Protective Equipment	• Use aseptic technique	• Use aseptic technique
• Prepare skin with 4% chlorhexidine gluconate solution	• Prepare skin with 4% chlorhexidine gluconate solution	• Prepare skin with 4% chlorhexidine gluconate solution
• Insert the central line avoiding the femoral site	• Secure line with transparent dressing	• Insert catheter after applying sterile lubricating gel. Use the appropriate size catheter to minimize bladder neck and urethral trauma
• Secure line with sterile gauze or transparent dressing. Gauze should be changed after 48hrs and transparent dressing after 7 days or when visibly soiled.	• Change dressing when visibly soiled	• Secure catheter to prevent movement and urethral traction.
• Label date of insertion and document procedure.	• Use aseptic technique while flushing the line	• Maintain a closed drainage system.
• Use aseptic technique while flushing the line	• Remove when no longer required	• Drain the urine bags observing standard precautions always
• Remove central venous lines when no longer required and no longer than 2 weeks • Note that the femoral site should only be used in patients in whom accessing an alternative site would be dangerous and these should be replaced within 48-72 hours		• Clean the meatal surface during daily routine bathing - don't use antiseptic baths

Good Practice on Antimicrobial Use

1. Not all admitted patients require antibiotics, fever does not necessarily mean presence of a bacterial infection
2. Appropriate investigations are recommended for all infections. These are necessary for diagnosis, treatment and follow up
3. Microbiological specimens should be collected before initiating antimicrobial therapy
4. Prescribe antimicrobials contained in the hospital formulary
5. For community acquired infections in children under the age of five, use the updated Basic Paediatric Protocols from the Ministry of Health
6. Check for factors that will affect drug choice and dose such as age, renal and hepatic dysfunction, drug interactions, hypersensitivity reactions, pregnancy and lactation
7. Ensure that an appropriate dose is prescribed; if uncertain consult the clinical pharmacist or check in the hospital formulary
8. The need for antimicrobial therapy should be reviewed at 48 hours and regularly thereafter. If investigations do not suggest an infection, antibiotics should be stopped and other appropriate management instituted
9. For most infections 5 days of antimicrobial therapy is sufficient. Exceptions include: meningitis, deep seated abscesses, infective endocarditis, osteomyelitis, pyelonephritis, blood stream infections secondary to methicillin resistant staphylococcus aureus (MRSA) and Pseudomonas aeruginosa
10. Once culture and sensitivity reports are available, step down to the narrowest spectrum, most efficacious and most cost-effective option
11. Prescription of a carbapenem (meropenem or imipenem) in the general wards will require approval by the Infectious Disease (ID) team or clinical pharmacist
12. In case of multidrug resistant (MDR) infections, observe strict contact precautions (this will include gowns and gloves) notify the infection prevention and control unit (IPC) and consult the Infectious Disease Specialist

Good Practice on Microbiology Sample Collection

(Also refer to the Diagnostic Stewardship guidelines)

Collecting Specimens For Bacteriology:

1. Sterile technique should be observed. Appropriate sterile containers should be used
2. Samples should be collected at time of patient presentation/onset of illness and before administration of any antibiotics
3. Samples should be collected only when clinically indicated. Avoid routine screening cultures such as routine tracheal aspirates or routine urine cultures

Adequate Specimen Collection:

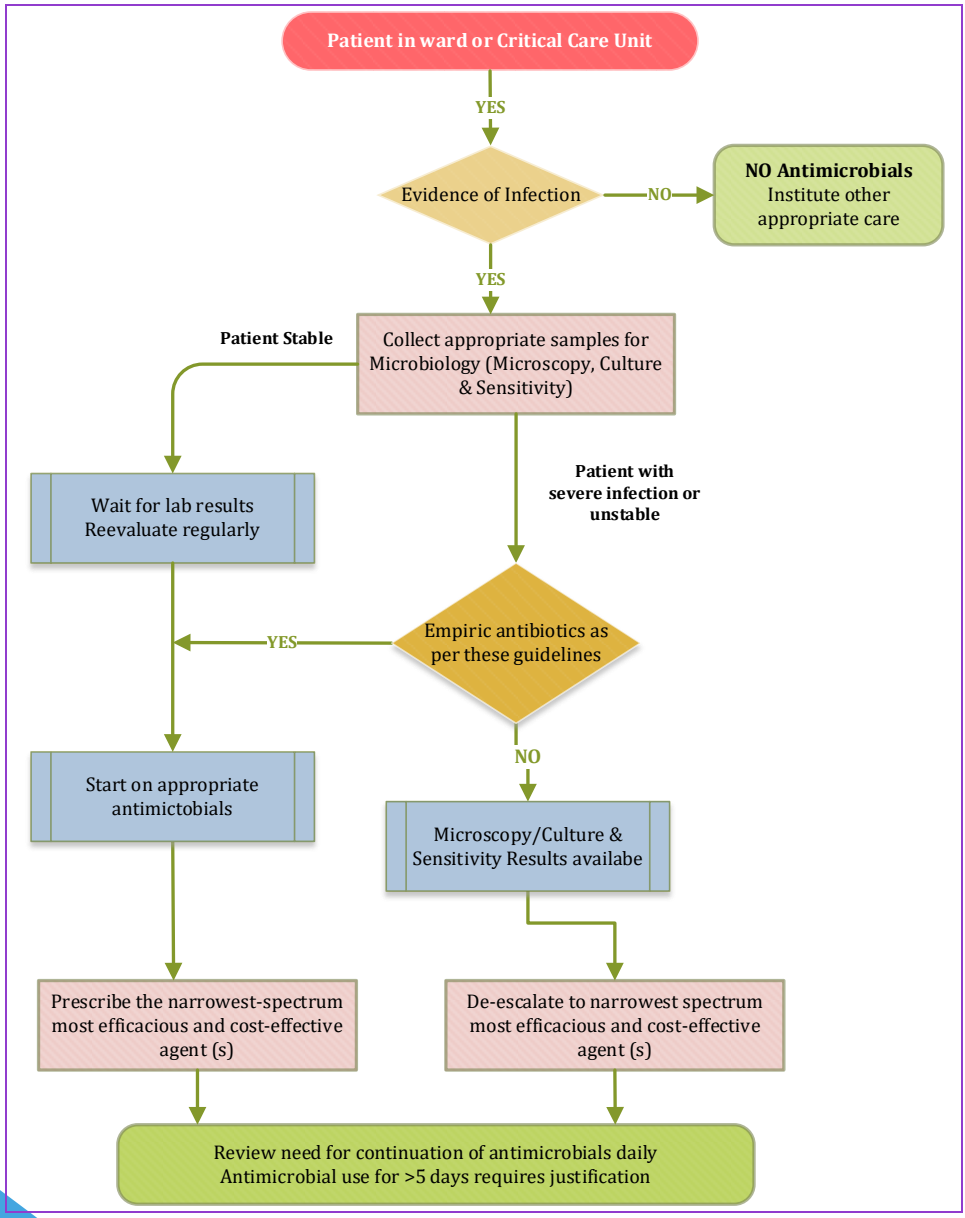
1. Blood - should be taken from 2 sites e.g., from a central line and a peripheral site or 2 peripheral sites. When taking a blood culture sample from a peripheral site, clean the site with an alcohol swab and allow 30seconds to dry before puncture, **do not** palpate the vessel before puncture unless sterile gloves are worn.
   Central venous catheter tip cultures must be accompanied by blood for culture.
   For adults draw 10-15mls of blood from each site, for children under 5 years, collect 1-5mls of blood for culture
2. Urine - should be a clean catch midstream sample, from a freshly inserted catheter or cleaned catheter hub where urine will be collected directly from the tubing. **Do not** collect urine from a urine bag or an indwelling catheter. Urine catheter tip cultures **should not** be sent for culture
3. Abdominal fluid - should be taken straight from the abdomen or from a newly placed drain. **Do not** collect specimens from existing drains
4. Wound swabs are often not useful due to contamination, to collect a swab, first clean the wound with normal saline and attempt to get a swab from the base or alternatively, get a tissue specimen for culture. **Do not** collect a superficial sample from the surface of a wound
5. A sterile procedure should always be used for collection of cerebrospinal fluid (CSF), a mask should be worn to avoid respiratory contamination
6. For abscesses, bullae, blisters, aspirate directly from the abscess with a sterile needle and syringe.

Interpreting Bacteriology Results

1. The clinical context must be taken into account when interpreting cultures as this will help in differentiating true infection from colonization or contamination
2. Coagulase negative staphylococci in blood will only be considered relevant if grown in more than 1 bottle in an appropriate clinical scenario (site of infection)
3. True infection is almost always present if the blood culture is positive for one of the following:
    - Aerobic and facultative gram-negative rods e.g., Escherichia coli, Klebsiella pneumoniae, Enterobacter, Pseudomonas
    - Anaerobic cocci e.g., peptococcus, peptostreptococcus
    - Anaerobic gram-negative rods e.g., Bacteroides, Prevotella, fusobacterium
    - Streptococci (non-viridans)
    - Yeast e.g., candida species.
4. Suspect contamination if only one of several cultures is positive, if detection of bacterial growth is delayed (≥5 d), or if multiple organisms are isolated from one culture
5. Tracheal aspirates should only be collected if clinically indicated, avoid taking routine tracheal aspirates for culture. Consider the organism cultured as the possible cause of infection if the chest radiograph shows infiltrates consistent with pneumonia

If you are unsure of how to interpret culture and sensitivity results, consult the Infectious Disease team (drop a consult in the ID unit or call the ID specialist in urgent cases)

Antibiotic Prescribing Algorithm



NOTE: Use of Carbepenems in general wards requires approval

Empiric Antibiotic Guidelines

Meningitis in Children > 2months

Definition: Acute syndrome characterized by signs of meningeal inflammation.

Diagnosis:

A. Clinical:

Symptoms: Fever, lethargy, irritability, altered level of consciousness, coma, nausea, vomiting inability to feed, convulsions – generalized or partial.

Older children: headache and photophobia. Can be preceded by symptoms of respiratory tract infection.

Signs: AVPU < A, stiff neck, bulging fontanelle, sutural diastasis, unequal pupils, focal neurologic signs, hypotonia or hypertonia, maculopapular / hemorrhagic/ purpuric rash

Consider tuberculous meningitis – subacute presentation

B. Laboratory Investigation:

CSF analysis is mandatory in the diagnosis of meningitis and should be done prior to antibiotic initiation

- CSF pleocytosis with a predominance of neutrophils appearance (consider meningitis only if the WBC count is >6WBC/MicroL with predominant neutrophils), elevated CSF protein, decreased CSF glucose, positive gram stain, culture and sensitivity, Gene Xpert
- Blood culture indicated for all patients with suspected meningitis
- Complete blood count
- ESR, CRP, malaria blood slide
- Electrolytes: calcium, potassium, magnesium, random blood sugar
- HIV test
- Coagulation studies

Contraindications of lumbar puncture:

1. Signs of raised ICP.
   - Reduced or fluctuating level of consciousness. (GCS <13/15, or a drop in GCS of 2 or more)
   - Relative Bradycardia or Hypertension
   - Focal neurological sings
   - Abnormal posture
   - Unequal pupils/ poorly responsive to light
   - Papilloedema
   - Abnormal dolls eye movement
2. Shock
3. Extensive or spreading purpura
4. Coagulation abnormalities
   - Coagulation profile outside the normal range
   - Platelets < 50 x 10^9
   - Receiving anticoagulant therapy

5. Localized superficial infection
6. Respiratory insufficiency

C. Imaging:

Brain CT scan or MRI, Cranial ultrasound for < 1 month age

Indications:

- Focal neurological signs,
- Signs of raised intracranial pressure
- Encephalitis
- Seizures > 72 hours after start of treatment/ prolonged seizure
- Increasing head circumference in young infants
- Prolonged obtundation – no improvement in GCS in 48 hours
- Evidence of continued infection

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	*Streptococcus pneumoniae, Haemophilus influenzae,* *Neisseria meningitidis*	Special population: Ventriculitis and meningitis in children with previous ventricular-peritoneal (VP) shunt, external ventricular drain (EVD), spina bifida, myelomeningocele, neonates: *Coagulase negative Staphylococcus aureus* *Staphylococcus aureus* *Gram negative organisms: Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*
EMPIRIC THERAPY	High dose **Ceftriaxone 100 mg/kg IV/day** in two divided doses	High dose **cefepime 50mg/kg IV** 8 hourly **PLUS** **Vancomycin 15mg/kg/dose IV** 6 hourly

COMMENTS	**Duration of therapy: 10 -14 days (average)** • *N. meningitidis* – 7 days • *H. influenzae* – 10 days • *S. pneumoniae* – 10 days • *S. aureus* - 14 days • Group B streptococcus – minimum 14 days • 21 days for Gram negative organisms and L. *monocytogenes* **Adjuvant treatment** 1. Corticosteroids to be used in patients > 3 months of age with a diagnosis of probable meningitis (frankly purulent CSF, CSF white cell count> 1000 cells/µl, raised CSF white cells with protein more than 1mg/dL, bacteria on Gram stain). • Dexamethasone – 0.15mg/ kg administered before the 1st dose of the antibiotics. To be given every 6 hours for the 1st 48 hours. 2. Fluids • Do not restrict fluids or overhydrate. Give maintenance fluids • Correct any electrolyte abnormalities. If there is high suspicion of HSV encephalitis, add acyclovir IV If there no improvement after 48 -72 hours, re-evaluate patient

Bacterial Meningitis in Adults

Definition: Meningitis is an inflammatory disease of the leptomeninges

Diagnosis:

1. **Clinical features:**
   Symptoms: Acute onset< 48hours. The patient should have at least 2 or more of the following: Severe headache, fever, change in mental status, convulsions, skin rash
   Signs: nuchal rigidity, positive Kernigs' and Brudzinski sign, cranial nerve palsies, papilledema
2. **Lab investigations:**
   Lumbar puncture and CSF Analysis is mandatory in the diagnosis of bacterial meningitis and should be done prior to antibiotic initiation

The following features on CSF analysis are characteristic of bacterial meningitis:

- Low CSF glucose (<2.22mmol/L with a SCF to serum glucose ratio of ≤0.4)
- Elevated protein >2000mg/L
- Elevated WBC >1000/microL

Other tests: Complete blood count, Serum electrolytes, Blood glucose, HIV test

3. **Imaging:**
   A head CT scan should be performed before Lumbar Puncture (LP) in adults with one or more of the following risk factors: history of central nervous system (CNS) disease (mass lesion, stroke, or focal infection), new onset seizure (within one week of presentation), papilledema, abnormal level of consciousness, Focal neurologic deficit

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	*Streptococcus pneumoniae, Neisseria meningitidis*	*Staphylococci and aerobic gram-negative bacilli*
EMPIRIC THERAPY	**Ceftriaxone 2g IV** 12hourly for 10 days	**Cefepime 2g IV** every 8hours for 21 days
COMMENTS	• Antibiotics should be initiated within an hour of presentation. • In case of allergy to beta lactams: Vancomycin and levofloxacin can be used. • For patients with a device e.g., ventriculoperitoneal (VP) shunt, lumbar puncture and cerebral spinal fluid analysis should be done prior to initiation of antibiotics, culture and sensitivity results should guide subsequent therapy. Where feasible, the device should be removed	

Pneumonia in Children > 60 Days

Definition: Inflammation of lung tissue due to bacterial or viral infection
Diagnosis:
1.Clinical features:
Symptoms: Cough, fever, difficulty breathing
Signs: Oxygen saturations <90%, increased work of breathing, tachypnoea (RR ≥ 50/min 2-11 months; RR ≥ 40/min 12-59 months) flaring alae nasi, lower chest wall indrawing, reduced breath sounds, crepitations

Grading severity:

- Severe pneumonia: one of: oxygen saturation <90%, central cyanosis, inability to drink/breastfeed, AVPU < A, grunting
- Non-severe pneumonia: one of: lower chest wall in-drawing or RR ≥ 50/min (age 2-11months) RR ≥ 40/min (age 12-59 months)
- None of above: no pneumonia: cough or cold

2. Lab investigations:

- Full blood count
- ESR, CRP or PCT
- Blood culture
- Nasopharyngeal swab for influenza, respiratory syncytial virus, rhinovirus during flu season
- Induced sputum for *Pneumocystis jiroveci pneumonia* Direct Fluorescent Antibody Testing (PJP DFAT)) if HIV positive or severely malnourished
- Sputum (induced sputum, gastric aspirate) for gene Xpert for recurrent pneumonia/ non response to treatment

3. Imaging:
Chest radiograph: Indication- Treatment failure, progression/worsening of pneumonia, non-response after 48hours, recurrent pneumonia
Upper GI studies: children with cerebral palsy, swallowing in-coordination, aspiration pneumonia

NOTE: Viral etiologies are the predominant causes of pneumonia in early childhood. Gradual onset, preceding upper respiratory tract symptoms, diffuse findings on auscultation and a non-toxic appearance suggest a viral pneumonia and **should not** be treated with antibiotics

KNH guidelines for Empiric Antibiotic Guidelines

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	*Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Pneumocystis jirovecii pneumonia Mycoplasma pneumonia, Mycobacterium tuberculosis*	*Streptococcus pneumoniae, Staphylococcus aureus, Pseudomonas, Klebsiella pneumonia, Escherichia coli*
EMPIRIC THERAPY	**Non-severe pneumonia:** **Oral high dose amoxicillin 40-45mg/kg q12h.** Counsel on danger signs, review after 48 hr **Severe pneumonia:** **1st line** **Benzylpenicillin 50,000 IU/kg/dose IV** 6 hourly **PLUS** **Gentamicin 7.5 mg/kg IV** once daily **OR** **If S. aureus suspected:** **Flucloxacillin 50mg/kg 8** hourly **plus Gentamicin 7.5 mg/kg iv** once daily **2nd line:** **Amoxicillin+ clavulanic acid** 45mg/kg 12 hourly **PLUS** **Erythromycin** **30-50mg/kg/day PO** in 3-4 divided doses **OR** **Azithromycin 10mg/kg PO** once daily	**Piperacillin+ tazobactam 200-300mg/kg/day IV** divided 6 hourly **PLUS** **Amikacin 15mg/kg IV** once daily

COMMENTS	Duration of therapy: 7 days For suspected Pneumocystis jirovecii pneumonia (PJP) add Co-trimoxazole at 30mg/kg/dose q8h for 21 days Tuberculosis can present as acute pneumonia. Investigate and manage as per the current basic pediatric protocol. High dose steroids e.g. oral prednisone at 2mg/kg/day for 4 weeks tapered over 2 weeks need to considered in TB disease with likely obstruction from lymphadenopathy; and PJP steroids started within 48 hours to reduce mortality. Complicated pneumonia specifically empyema will require drainage of the infected pleural fluid; and requires intrapleural antifibrinolytics such as alteplase and reteplase if not contraindicated, to avert further complications. The presence of lung abscesses may require addition coverage for of anaerobic organisms and *Staphylococcus aureus.* In this case, consider adding clindamycin

Bacterial Pneumonia in Adults

Definition: an acute infection of the lung parenchyma, associated with radiological pulmonary shadowing.

Community acquired pneumonia (CAP): infection acquired in the community

Hospital acquired pneumonia (HAP): pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission

Ventilator acquired pneumonia (VAP): A type of HAP that develops more than 48 hours after endotracheal intubation

Diagnosis:

1. **Clinical features:**
   Symptoms: Cough, pleuritic chest pain, fever, difficulty in breathing, sputum production, tachypnea
   Signs: respiratory distress, bronchial breath sounds, crackles, reduced oxygen saturation
2. **Lab Investigation:**
   Determine each patient CURB*-65 or CRB**-65 score and classify as follows:
   - Mild/low risk - CURB/CRB-65 score = 0-1
   - Moderate/intermediate risk - CURB/CRB-65 score = 2
   - Severe/high risk - CURB/CRB-65 score ≥ 3 or patient with a lower score but with significant co-morbidities

Mild pneumonia can be managed as Outpatient. Order a sputum culture and gene X-pert only if the patient has failed antibiotic therapy.

For those who require admission, the following are indicated:

- Blood culture
- Sputum for Pneumocystic jiroveci pneumonia direct fluorescent antibody testing (PJP DFAT) if HIV positive
- NP swab for influenza PCR if flu season
- NP swab for COVID test
- C reactive protein and procalcitonin if available to help guide treatment
- Sputum gram stain and culture

NB: Take specimens for culture prior to initiation of antibiotics.

3. Imaging:

Chest radiograph

KNH guidelines for empiric antibiotic therapy

	COMMUNITY ACQUIRED (CAP)	HOSPITAL ACQUIRED (HAP)	VENTILATOR ACQUIRED (VAP)
COMMON PATHOGEN	*Streptococcus pneumoniae, Staphylococci spp.*	*Escherichia coli, Klebsiella pneumoniae*	*Acinetobacter baumanii, Klebsiella pneumoniae, Pseudomonas sp.*
EMPIRIC THERAPY	For low severity illness, treated as out-patient: **Amoxicillin 1g PO** 8 hourly for 5 days For patients who require admission or with co-morbidities: **Amoxycillin 875mg+ clavulanic acid 125mg PO** 12hourly **OR 1.2g IV** 8 hourly for 5 days For severe pneumonia, add **Azithromycin 500mg PO** once a day for 3 days **OR** **Clarithromycin 500mg PO** 12 hourly for 5 days	**Piperacillin+** **Tazobactam 4.5g IV** 6 hourly	**Piperacillin+ Tazobactam 4.5g IV** 6 hourly **PLUS** **Amikacin 15mg/Kg/day IV** For patients with significant antibiotic exposure or know to be colonised with MDR organisms, consult Infectious Disease Where there is high risk of MRSA e.g., in patients known to be colonised with MRSA, the addition of linezolid 600mg IV BD or Vancomycin may be considered pending culture results

COMMENTS	• Duration of treatment is 5 days for community acquired pneumonia and 7 days for hospital acquired pneumonia • In case of penicillin allergy use Doxycycline 100mg twice a day for CAP • For patients not improving evaluate for complications e.g. empyema • Monitor patients closely and if not improving, consult Infectious Disease specialist
	*The CURB-65 scoring can be used to assess for severity of illness: C- Confusion (1 point), U- Urea >7mmol/l (1 point), R- Respiratory rate >30bpm (1 point), B-Blood pressure <90mmHg systolic or <60mmHg diastolic (1 point)65 - Age > 65 (1 point) **The CRB-65 score, which does not require laboratory values for its calculation, can also be used, the score value interpretation is the same as for CURB-65 **Clinical judgement should be used for all patients when determining appropriate site of care. Prediction scores such as CURB-65 or PSI are useful but should not be the only determinant of location of care of the patient**

Neonatal Sepsis in Infants < 60 Days

Definition: Acute life-threatening infection characterized by organ dysfunction in new born infants < 60 days.
Early onset neonatal sepsis (EONNS): < 72 hours
Late onset neonatal sepsis (LONNS): > 72 hour after birth.
Symptoms:
One of: fever, temperature instability (Temperature > 38.0 C or lower than 35.5 C), convulsions, apnoea, inability to feed, central cyanosis or SPO_2 <90%, bulging fontanelle, persistent vomiting, movement only when stimulated
Signs:
General: fever, jaundice pallor, petechiae, purpura, bleeding, mottling, sclerema,
Abdominal: Abdominal distention, hepatomegaly, splenomegaly
Respiratory: Apnoea, tachypnoea, retractions, grunting, cyanosis,
Cardiovascular: Tachycardia, bradycardia, hypotension
Central nervous system: tremors, seizures, hypotonia, abnormal reflexes, full fontanelle, high pitched cry

Categorisation:
Neonate at risk of sepsis: Risk factors include prolonged rupture of membranes (PROM) > 18 hours, maternal fever > 38°C, suspected or confirmed chorioamnionitis, mother treated for sepsis during labour or 24 hours before or after delivery
Neonatal sepsis: **One** of the following: Not feeding well on observation, temperature ≥ 38°C or ≤35.5°C, severe chest wall in-drawing, movement only when stimulated
Severe neonatal sepsis: **One** of the following: Unconscious, history of convulsions, unable to feed/poor feeding, apnoea, Unable to cry/high pitched cry, central cyanosis/SPO_2 < 90%, bulging fontanelle, persistent vomiting.

If neonate has none of the signs of neonatal sepsis: Systemic bacterial infection unlikely. Assess for other illness and treat appropriately. Give mother advice and arrange for review.

Lab investigations: Full blood count, CRP, procalcitonin, blood culture, LP for CSF studies, urine MCS

Imaging: Chest radiograph, Cranial ultrasound, Abdominal XRay as indicated based on presentation

KNH guidelines for Empiric Antibiotic Guidelines

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	**Early onset sepsis** *Group B Streptococcus, Gram negative enteric bacilli (Escherichia coli, Klebsiella pneumoniae)* **Late onset sepsis** *CONS, Staphylococcus aureus, Candida, Escherichia coli, Group B Streptococcus, Klebsiella pneumoniae, Pseudomonas aeruginosa*	*Klebsiella pneumoniae, Coagulase negative Staph, Enterococcus faecium, Enterococcus faecalis, Acinetobacter baumanii*
EMPIRIC THERAPY	***Neonate at risk of sepsis:*** Stop IV antibiotics after 48 hours if all signs of possible sepsis have resolved, neonate is feeding well, and LP if done is normal. **Early onset sepsis:** **1st line**: **Benzylpenicillin** Plus **Gentamicin** If Staphylococcus is suspected: **Flucloxacillin** plus **Gentamicin** **Late onset sepsis:** **1st line: Benzylpenicillin** Plus **Gentamicin** 2nd line/ deranged renal function: **Ceftazidime**	**1st line:** **Piperacillin/ tazobactam** Plus **Amikacin** **2nd line:** **Cefepime**

COMMENTS	**Adjust treatment based on culture results** Add metronidazole if there is necrotising enterocolitis **Duration of therapy:** ***Neonate at risk of sepsis:*** Well baby, breastfeeding well, no signs of sepsis: 48 hours of iv antibiotics Reassess at 48-72 hours: clinical and lab results If well and lab parameters are normal/negative - discharge without antibiotics. Follow-up at 48 hours at nearest facility ***Neonatal sepsis: 48 hours of iv antibiotics*** Reassess at 48-72 hours: clinical and lab results If breastfeeding well and clinically stable, discharge on oral treatment – **dispersible** high dose amoxicillin 45mg/kg 12 hourly to complete 5 days of antibiotic treatment. ***Severe neonatal sepsis: Complete 7 days of iv antibiotics*** Reassess at 48-72 hours: clinical and lab results Improving: complete antibiotics and discharge ***Confirmed sepsis: Complete 7-10 days of iv antibiotics*** Reassess at 48-72 hours: clinical and lab results Meningitis: IV treatment for 14 days 21 days for gram negative organisms **Treatment failure**: Administer antibiotics for at least 48-72 hours. If baby is not improving, or deteriorating during treatment, do complete clinical re-evaluation, repeat hemogram, blood culture, CRP and appropriate investigations before switching antibiotics

Note: Refer to basic paediatric protocol for doses of penicillin, gentamicin

Neonatal Drug Doses

Amikacin:

Post Menstrual Age (Corrected Gestational Age)	Postnatal age	Dose	Frequency
< 30 weeks	≤ 14 days	15mg/kg/dose	48 hourly
	≥ 15 days	15mg/kg/dose	24 hourly
30-34 weeks	All	15mg/kg/dose	24 hourly
≥ 35 weeks	≤ 7 days	15mg/kg/dose	24 hourly
	> 7 days	17.5 mg/kg/dose	24 hourly

Cefipime

Postnatal age	Dose
≤ 28 days	40mg/kg/dose q8h
> 28 days	50mg/kg/dose q8h

Piperacillin-tazobactam (dose expressed as piperacillin component)

Post Menstrual Age (Corrected Gestational Age)	Postnatal age	Dose
< 30 weeks	≤ 28 days	100mg/kg/dose q12h
	> 28 days	100 mg/kg/dose q8h
30-36 weeks	≤ 14 days	100 mg/kg/dose q12h
	> 14 days	100 mg/kg/dose q8h
> 36 weeks	≤ 7 days	100mg/kg/dose q12h
	> 7 days	100 mg/kg/dose q8h

Neutropenic Fever

Definition: This is fever in neutropenic patients e.g., as occurs in patients with neoplastic diseases receiving cytotoxic myelosuppressive chemotherapy.

- Fever: Body temperature >38.0°C
- Neutropenia: Temporary reduction of the absolute neutrophil count (ANC) <1000 cells/uL (<1.0 x10^9/L)

Diagnosis:

1.Clinical features:

- Fever: Body temperature >38.0°

2.Lab investigations

- Complete blood count, bilirubin, creatinine, electrolytes, blood gas analysis, whole blood lactate, C-reactive protein and/or procalcitonin

3.Imaging:

Imaging will be guided by clinical presentation and are targeted to identify the likely source of infection.

- Chest radiograph and abdominal ultrasound

CT scans of the abdomen and chest - as additional imaging to expand diagnostic work-up or to exclude a complicated infection if no clinical improvement after a few days of treatment

KNH guidelines for Empiric Antibiotic Guidelines

	COMMUNITY ACQUIRED	**HOSPITAL ACQUIRED** (neutropenic sepsis, stable)	**HOSPITAL ACQUIRED** (neutropenic sepsis in shock)
COMMON PATHOGENS	*Escherichia coli, Klebsiella*	*Escherichia coli, Klebsiella*	*Escherichia coli, Klebsiella and Pseudomonas aeruginosa; Methicillin Resistant Staphylococcus aureus (MRSA)*
EMPIRIC THERAPY	**Amoxicillin+ clavulanate acid 500mg+125mg PO** 8 hourly	**Piperacillin+ tazobactam 4gm+500mg IV** 6 hourly	Suspected MDR organisms **Piperacillin+ tazobactam 4gm+500mg IV** 6 hourly PLUS **Amikacin 15mg/Kg/day IV** **Alternative:** **Meropenem 1g IV** 8 hourly If Methicillin Resistant Staphylococcus aureus (MRSA) suspected, add **Vancomycin 15-20mg/kg IV** 12hourly
COMMENTS	If fever persists and there is no clinical improvement after 48-72 hours, reevaluate to look for other non-bacterial causes (such as fungal and viral causes) or complications such as deep abscesses or resistant organisms		

Blood Stream Infections

Definition: bacterial invasion of the blood stream resulting in fever and other features of infection

Diagnosis:

1. **Clinical features:**
   Fever, rigors, altered mental status, hypotension, chills, malaise, nausea, vomiting, diarrhoea, confusion

2. **Lab investigations:**
   Blood cultures: take 1 set of cultures through the central line and another set of cultures from a peripheral site or 2 sets of cultures from a peripheral site.

	COMMUNITY ACQUIRED BSI	HOSPITAL ACQUIRED BSI	CENTRAL LINE ACQUIRED BSI
COMMON PATHOGENS	*Staphylococcus aureus,* *Escherichia coli*	*Enterobacteriaceae*	*Staphylococcus aureus, Escherichia coli, Klebsiella, Methicillin Resistant Staphylococcus aureus (MRSA), Coagulase negative Staphylococci*
EMPIRIC THERAPY	**Amoxicillin-Clavulanic Acid 1.2g IV** 8 hourly **OR** **Levofloxacin 750mg IV** once a day **OR** **Ciprofloxacin 400mg IV** 12 hourly for penicillin allergy	**Piperacillin+ tazobactam 4.5g IV** 6 hourly	**Piperacillin+ tazobactam 4.5g IV** 6 hourly **PLUS** **Vancomycin 1g IV** 12hourly. Where there is no improvement consult **Infectious disease specialist.**

COMMENTS	**Duration of treatment:** • **No catheter or catheter removed**: Treat for 7 days. For Staphylococcus aureus if catheter removed treat for 14 days from first negative blood culture • **Catheter retained**: Treat for 14 days. If Staphylococcus aureus is isolated, treat for 28 days after the last negative culture. For patients with Staphylococcal bacteremia screen for complications of hematogenous spread such as infective endocarditis (ideally by transesophageal echocardiogram), vertebral osteomyelitis and septic arthritis. For Staphylococcal bacteremia repeat blood cultures after 72hours. If the culture is still positive consult ID team. THE CVC SHOULD BE REMOVED if the following organisms are cultured: Staphylococcus aureus, Pseudomonas aeruginosa, drug resistant gram-negative bacilli, Candida species. If catheter removal is not possible then antibiotic lock therapy should be given in addition to systemic antimicrobials. The same antibiotics used for systemic therapy are used as lock therapy. Consult the ID team. **When to repeat cultures:** This will depend on the organism isolated. For Staphylococcal bacteremia repeat blood cultures after 72hours. If the culture is still positive consult ID team. A repeat blood culture is not required from gram negative bacteraemia if the patient is improving. Once culture and antibiotic susceptibility results are available, antibiotics should be de-escalated to the narrowest spectrum, most appropriate antibiotic to which the organism is susceptible.

Urinary Tract Infections

Definition: An infection of any part of the urinary tract including the bladder, ureters or kidneys.

Classification:

Lower urinary tract infection - evidence of urinary tract infection with symptoms suggestive of cystitis (dysuria or frequency without fever, chills, or back pain).

Upper urinary tract infection - evidence of urinary tract infection with symptoms suggestive of pyelonephritis (loin pain, flank tenderness, fever, rigors, or other evidence of systemic inflammatory response).

Uncomplicated UTI – infection in a structurally/functionally normal urinary tract.

Complicated UTI – infection in patients with a structural or functional abnormality of the urinary tract.

Asymptomatic bacteriuria - presence of bacteriuria in urine revealed by quantitative culture or microscopy in a sample taken from a patient without any typical symptoms of lower or upper urinary tract infection. In contrast with symptomatic bacteriuria, the presence of asymptomatic bacteriuria should be confirmed by two consecutive urine samples.

Pyuria - occurrence of ≥10 white blood cells per high power field in a freshly voided specimen of urine. Higher numbers of WBC are often found in healthy asymptomatic women. Pyuria is present in 96% of symptomatic patients with bacteriuria of >105 colony forming units (cfu)/ml, but only in <1% of asymptomatic, abacteriuric patients. Pyuria in the absence of bacteriuria may be caused by the presence of a foreign body, for example, a urinary catheter, urinary stones or neoplasms, lower genital tract infection or, rarely, renal tuberculosis.

Short term catheter - indwelling urethral catheter for <7 days.

Medium term catheter - indwelling urethral catheter for 7-28 days.

Long term catheter - indwelling urethral catheter for >28 days

Diagnosis:

1. **Clinical features:**

Dysuria, frequency of urination, suprapubic tenderness, urgency, polyuria, hematuria

2. **Lab investigations:**
    - Urinalysis and urine culture
    - Consider pelvic examination for women with symptoms of vaginal itch or discharge.
    - Dipstick tests

Imaging: Kidney Ureter Bladder ultrasound (KUB) for males after 1st episode UTI or with suspected anatomic abnormality.

Criteria for diagnosis of Urinary Tract Infection

	No indwelling catheter	Indwelling catheter (If catheter in place >2 weeks, change catheter before obtaining sample for culture)
Microbiologic criteria	Positive urinalysis (WBC≥10/HPF) And Positive urine culture (≥10^5 cfu/ml in voided specimen)	Positive urinalysis (WBC≥10/HPF) And Positive urine culture (≥10^3 cfu/ml)
Symptom criteria	Acute dysuria ----------OR---------- If Fever* present, at least 1 of the following; if no fever present, at least 2 of the following (new or worsening): ✓ Urinary urgency ✓ Urinary incontinence ✓ Frequency ✓ Gross haematuria ✓ Suprapubic pain ✓ Costovertebral angle tenderness	At least one of the following (new or worsening): • Fever* ✓ Rigors ✓ Delirium ✓ Flank pain ✓ Pelvic discomfort ✓ Acute haematuria ✓ Malaise/ lethargy with no other cause

Note: A new onset of delirium is NOT a symptomatic criterion of a UTI for patients without an indwelling catheter.

*Fever- >37.9°C or 1.5°C increase above baseline temperature.

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	*Escherichia coli, Klebsiella pneumoniae, Proteus species*	*Escherichia coli, Klebsiella pneumoniae, Pseudomonas spp.*
EMPIRIC THERAPY	Uncomplicated cystitis: **Nitrofurantoin 100mg** 12 hourly for 5 days in females and 7 days in males **OR** **Amoxicillin+ clavulanic acid** 625 mg 12 hourly for 3 days in females and 7 days in males Complicated UTI or upper UTI: **Amoxicillin + clavulanic acid 1g 12 PO** hourly or **1.2 g IV** 8 hourly for 10-14 days **OR** **Amikacin 15-30mg/Kg** once a day IV for 7 days in females and 14 days in males if unable to take orally	Lower UTI: **Nitrofurantoin 100mg** 12 hourly for 5-7 days **Amikacin 15-30mg/Kg** once a day if unable to take orally for 3 days in females and 7 days in males Upper UTI: **Amikacin 15-30mg/Kg** IV once a day for 10-14 days Alternative: **Piperacillin/tazobactam 4.5g** every 6 hours IV for 10-14 days
COMMENTS	• With recurrent infections, previous culture results could guide empiric therapy pending urine culture and sensitivity results. • Antibiotic therapy should be tailored once urine culture and sensitivity results are available at which point, the narrowest spectrum, most efficacious and appropriate antibiotic should be prescribed • For cystitis caused by MDR E.coli, **fosfomycin** may be an oral option give as **3g sachet stat**	

Intra-Abdominal Infections

Definition: Intra-abdominal infections are usually classified into uncomplicated and complicated.

Uncomplicated infection involves a single organ and does not proceed to peritoneum. Patients with such infections can be managed with either surgical source control or with antibiotics alone.

Complicated infection extends beyond a single organ and causes either localized peritonitis or diffuse peritonitis.

Low risk - mild to moderate community acquired intra-abdominal infections with not risk factors for antibiotic resistance or treatment failure

High risk - severe intra-abdominal infections or in patients at high risk for adverse outcomes or resistance e.g. patients known to be colonized with MDR organisms

Diagnosis:

1. **Clinical features:**
   Values of blood pressure-hypotension or low MAPs, PR 100bpm, RR>22 bpm, urine output <30ml/kg/hour, altered mentation
2. **Lab investigations:**
   White cell count>120000, Lactate >2, deranged BGA, elevated CRP/Procalcitonin.
3. **Imaging:**
   X-ray/Ultrasound/CT scan abdomen

	COMMUNITY ACQUIRED	HOSPITAL ACQUIRED
COMMON PATHOGENS	*Escherichia coli, Bacteroides, Klebsiella spp., Proteus, Enterobacter spp*	*Enterococcus, Pseudomonas spp., resistant Enterobacteriaceae, streptococci and anaerobes*
EMPIRIC THERAPY	**Low risk:** **Amoxicillin+ clavulanate 1.2 g IV** 8 hourly **OR** **Amikacin 15mg/kg/day** **PLUS** **Metronidazole 500mg IV 8 hourly** **High risk:** **Piperacillin+ tazobactam 4.5 g IV** 6 hourly **OR** **Amikacin 15mg/kg/day** **PLUS** **Metronidazole 500mg IV** 8 hourly	**Cefepime 2g IV** 8 hourly **PLUS** **Metronidazole 500mg IV** 8 hourly Where there is suspicion for MDR organisms, add **Amikacin 15mg/kg/day** **Consult ID** if patient not improving

COMMENTS	• Source control is key in management of complicated intra-abdominal infections • Duration of treatment is 5 days after adequate source control • With multiple abdominal surgeries consider candida infections and take appropriate samples for fungal cultures. **Consult ID** • Carbapenems and piperacillin/tazobactam provide adequate anaerobic cover, do not add metronidazole or clindamycin when using these agents • Ensure adequate patient monitoring and fluid management

Skin And Soft Tissue Infections

Definition: encompass a variety of pathological conditions that involve the skin and underlying subcutaneous tissue, fascia, or muscle, ranging from simple superficial infections to severe necrotizing infections.

Diagnosis:

1. **Clinical features:** skin erythema, edema, and warmth, extremity swelling, pain, fever-38°C, hypotension, sustained tachycardia, purulent drainage or exudate, crepitus
2. **Lab investigations:** leukocytosis with neutrophia, CRP/Procalcitonin. Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score based on laboratory indicators including white cell count, hemoglobin, sodium, glucose, creatinine, and CRP.
3. **Imaging:** Ultrasound, CT scan

COMMON PATHOGENS	*Staphylococcus aureus, Streptococcus spp.* *Necrotizing fasciitis consider-Pseudomonas, Enterobacteriaceae as its polymicrobial infection.*	
Condition	**Description**	**Empiric therapy**
Abscesses & Carbuncles **Cellulitis** If there is a concern for necrotizing fasciitis, admit the patient to hospital	Simple abscesses/carbuncles <5cm Antibiotics are required if any of the following are present: • Severe, extensive, rapidly progressive cellulitis • Abscess >5cm • Signs or symptoms of systemic illness • Elderly, immunosuppressed, malignancy or DM • Circumstances where an abscess is difficult to drain • Associated septic phlebitis	Incision and Drainage is the mainstay of treatment In addition to I&D; **Flucloxacillin 500mg-1000mg PO** 6 hourly/**2g IV** 6 hourly **OR** **Clindamycin 600mg IV** 6 hourly **OR** **Doxycycline 100mg PO** 12 hourly

	• Inadequate response to incision and drainage alone	
Necrotizing Fasciitis including Fourniere's gangrene& Meleney's gangrene.	Early and aggressive surgical exploration and debridement is critical Emergent surgical consultation is recommended	**Piperacillin- Tazobactam 4.5 g IV** 8 hourly **PLUS** **Clindamycin 600mg IV** 6 hourly For penicillin allergy use: **Amikacin 15mg/kg/day** **PLUS** **Clindamycin 600mg IV** 6 hourly
Diabetic foot infections **Decubitus or sacral wound infection without osteomyelitis**	Most do not require antibiotic therapy Start empiric antibiotic treatment only if there are local features of inflammation (surrounding cellulitis or abscess) and systemic features Obtain a **tissue culture** for infected wounds. Avoid pus swabs.	Surgical debridement is an important component in management **Amoxicillin+ clavulanic acid 1.2 g** IV 8 hourly **OR** **Doxycycline 100mg PO 12 hourly** **PLUS** C**lindamycin 600mg IV** 6 hourly
Traumatic Wound Infections of Extremity Usually, polymicrobial from environmental contamination	Traumatic wounds without evidence of local infection or systemic signs of infection typically do not need antimicrobial therapy beyond appropriate surgical prophylaxis In the presence of systemic features of infection	Debridement of devitalized tissues and source control is critical to successful healing **Amoxicillin+ Clavulanic acid 1.2 g IV** 8 hourly **OR** **Clindamycin 600mg IV** 6 hourly

Surgical Site Infections	Infections involving the subcutaneous tissue within 30 days of operation Presence of more than ONE local and systemic features e.g. erythema and induration extending >5 cm from wound edge, fever >38.5°C, HR >110 beats/minute, WBC >12,000 Infections involving the deep fascia, muscle and organ space involvement within 30 days of operation.	Adjunctive systemic antimicrobial therapy is not routinely recommended unless there is systemic response. Suture removal plus incision and drainage should be performed. **Piperacillin+ Tazobactam 4.5 g IV** 8 hourly **PLUS** **Clindamycin 600mg IV** 6 hourly
COMMENTS	• Incision & drainage and debridement remain the cornerstone of management; avoid using antibiotics for chronic wounds except where there are features of cellulitis, systemic response or positive blood cultures. • Incision and drainage without antibiotics are adequate for small abscesses (<5cm) • For necrotising infections, aggressive debridement of necrotic tissue until healthy, viable (bleeding) tissue is reached. Inspection and debridement in the operating room should be continued every one to two days until necrotic tissue is no longer present. For severe necrotizing infection involving the extremities, amputation may be needed to control the infection e.g., wet gangrene of a diabetic foot. • Duration of treatment should be **7-10 days.** Antibiotics should be continued until no further debridement is needed and the patient is hemodynamically stable in the setting of septic shock. • Tigecycline is not to be used for diabetic foot ulcers	

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