Ministry of Health Malaysia

NATIONAL ANTIMICROBIAL GUIDELINE 2019

Officially launched on 26th September 2019

THIRD EDITION
FULL WEB VERSION CAN BE DOWNLOADED FROM :
www.pharmacy.gov.my
www.moh.gov.my
SEPTEMBER 2019

This guideline is constantly being reviewed and will be updated periodically via website

ISBN 978-967-5570-78-0

Publisher and Distributor :
PHARMACEUTICAL SERVICES PROGRAMME
MINISTRY OF HEALTH MALAYSIA
LOT 36, JALAN UNIVERSITI
46350 PETALING JAYA
SELANGOR , MALAYSIA

Tel : 603-78413200
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MESSAGE FROM THE DIRECTOR GENERAL OF HEALTH MALAYSIA

The NATIONAL ANTIMICROBIAL GUIDELINE is one of the most exciting initiatives that Ministry of Health (MOH) is proud of since its first launch in 2008. The threat brought on by antimicrobial resistance is a key factor driving this reference update, which the secretariat to this day has made every effort to ensure is in accordance with the latest scientific evidence.

The third edition of NATIONAL ANTIMICROBIAL GUIDELINE was produced through series of discussions held between the Editorial Board and the team of each discipline. It involved a structured and intensive discussion process to ensure that the content was carefully reviewed and coordinated for consistency. Some new topics have been introduced in this issue, such as `clinical pathways for primary care physicians', 'approach to antimicrobial allergies', while some were revised, such as 'surgical prophylaxis'.

I also which to express my sincerest congratulations and heartfelt gratitude to all those involved in the preparation of this latest edition, led by Datuk Dr. Christopher K.C. Lee, for their commitment during the preparation process. Well done and congratulations.

This NATIONAL ANTIMICROBIAL GUIDELINE is undoubtedly one of the essential documents which will benefit all MOH employees irrespective of their expertise and workplace as infections can occur to their patients at anytime and anywhere. I am sure many will look forward to having this updated edition.

To all MOH health care workers, let us make this NATIONAL ANTIMICROBIAL GUIDELINE as one of our primary reference in our daily practice.

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ABLC : Amphotericin B lipid complex
ABU: Asymptomatic Bacteriuria
ABW : Actual Body Weight
ACT : Artemisinin-based Combination Therapy
AFB: Acid-fast Bacilli
AMS : Antimicrobial Stewardship
ANC : Absolute Neutrophil Count
APACHE : Acute Physiology and Chronic Health Evaluation
ART : Antiretroviral Therapy
ARV: Antiretroviral Agents
ASA : Aspirin
ASMQ : Artesunate and Mefloquine
ASP : Antimicrobial Stewardship Program
AUC : Area Under The Curve
AVF : Arteriovenous Fistula
BI : Bacteriological Index
BMI : Body Mass Index
C&S : culture & sensitivity
C&S: Culture and Sensitivity
CAP : Community-Acquired Pneumonia
CAPD : Continuous Ambulatory Peritoneal Dialysis
CDC : Centers for Disease Control and Prevention
CF : Cystic fibrosis
CFU: Colony Forming Unit
ClCr : Creatinine Clearance
cm : centimetre
CMC : Chloramphenicol
CMV : *Cytomegalovirus*
CNS : Central Nervous System
COAD : Chronic Obstructive Airways Disease
CoNS: Coagulase-Negative Staphylococci
COPD : Chronic Obstructive Pulmonary Disease
CRBSI: Catheter Related Blood Stream Infection
CrCl : Creatinine Clearance
CRE : Carbapenem Resistant Enterobactericae
CRP : C-reactive Protein
CSF : Cerebrospinal Fluid
CT SCAN : Computed Tomography Scan
CVVH : Continuous Veno-Venous Hemofiltration
CVVHD : Continuous venovenous hemodialysis
CVVHDF : Continuous VenoVenous HemoDiaFiltration
CXR : Chest X-ray
DG : Director General of Health
E: Ethambutol
EIA : Enzyme Immunoassay
EID : Extended- Interval Therapy
ENT : Ear, Nose, Throat
EPTB : Extrapulmonary tuberculosis
ERCP : Endoscopic Retrograde Cholangiopancreatogram
ESBL : Extended-spectrum β-lactamases
ESC : European Society of Cardiology
ESRD : End-stage Kidney Disease
ESRF : End-Stage Renal Failure
EVAR : Endovascular Aneurysm Repair
FBC : Full Blood Count
FEME : Full Examination, Microscopic Examination
FEV1 : Forced Expiratory Volume in 1 second
FFA: Fundus Fluorescein Angiography

G6PD : Glucose-6-phosphate Dehydrogenase
GBS : Group B Streptococcal
GFR : Glomerular Filtration Rate
GIT : Gastrointestinal Tract
gm : gram
GNB : gram negative bacilli
H: Isoniazid
HAART : Highly Active Antiretroviral Therapy
HAP : Hospital-Acquired Pneumonia
HCAP : Health-care Associated Pneumonia
HCL : Hydrochloride
HD : Hemodialysis
HIV : *Human Immunodeficiency Virus*
HIV-TB : H*uman Immunodeficiency Virus*- Tuberculosis
HLR: High Level Resistance
HSV : Herpes Simplex Virus
IBW : Ideal Body Weight
ICU : Intensive Care Unit
IDSA : Infectious Diseases Society of America
IE : Infective Endocarditis
IFA : Indirect Fluorescent Antibody
IM : Intramuscular Administration
IPD : Intermitted peritoneal dialysis
IV : Intravenous Administration
IVDU : Intravenous Drug User
kg : kilogram
KOH prep : Potassium hydroxide preparation
LD : Loading dose
LP : Lumbar Punctures
LRTI : Lower Respiratory Tract Infections
MCUG : Micturating Cystourethogram
MD : Maintenance dose
MDR : Multidrug-resistant
MDR-TB : Multidrug-resistant Tuberculosis
MIC : Minimum Inhibitory Concentration
MOH : Ministry of Health
MRSA : Methicillin-resistant Staphylococcus aureus
MSSA : Methicillin-sensitive Staphylococcus aureus
MU : Mega Units
NAAT : Nucleic Acid Amplification Test
NSAID : Non-Steroidal Anti-Inflammatory Drugs
NSU : Non-Specific Urethritis
NVE : Native Valve Endocarditis
ORL : Othorhinolaryngology
ORS : Oral Rehydration Salts
PAE : Post-antibiotic Effect
PAS stain : Periodic acid–Schiff stain
PCNL : Percutaneous Nephrolithotomy
PCR : Polymerase Chain Reaction
PD : Peritoneal Dialysis
PEP: Post-Exposure Prophylaxis**PI** : Protease inhibitors
PID: Pelvic Inflammatory Disease
PO : (*per os*) oral administration
PPI : Proton Pump Inhibitors
PPROM: Preterm Premature Rupture of Membranes
PROM: Premature Rupture Of Membranes
PSD : Pharmaceutical Services Division
PTB : Pulmonary Tuberculosis

PUD : Peptic Ulcer Disease
PVE : Prosthetic Valve Endocarditis
q12h : every 12 hours
q24h : every 24 hours
q6h : every 6 hours
q8h : every 8 hours
R: Rifampicin
RCMM : Robertson's Cook Meat Medium
RIRS : Retrograde Intrarenal Surgery
S: Streptomycin
SBE : Subacute Bacterial Endocarditis
SDD : Single Daily Dosing
SGC : Soft Gel Capsule
SIRS : Systemic Inflammatory Response Syndrome
sp. : species
spp. : species
SSG : Split skin grafting
STD : Sexually Transmitted Diseases
TAHBSO : Total Abdominal Hysterectomy Bilateral Saphingo-Oophorectomy
TB : Tuberculosis
TDM : Therapeutic Drug Monitoring
TEVAR: Thoracic Endovascular Aneurysm Repair
TIG : Tetanus Immune Globulin
TMJ: Temporomandibular joint
TMP-SMX : Trimethoprim/ sulfamethoxazole
TURP : Trans-Urethral Resection of the Prostate
URS : Uretero-Renoscopy
UTI : Urinary Tract Infection
VAP : Ventilator-associated pneumonia
VAS : Visual Analogue Score
VDRL : Venereal Disease Research Laboratory
VRE : Vancomycin Resistant Enterococus
WBC : White blood cell
WCC : White call count
WHO : World Health Organization
yr : year
Z: Pyrazinamide

INTRODUCTION TO THE GUIDELINE

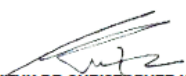
The appropriate use of antibiotics has become a worldwide priority. In the year 2000, it was estimated 54 billion standard units of antibiotics have been consumed globally, and this increased by 36% in the subsequent 10 years, creating the preconditions of a global public health crisis. Inappropriate prescribing and high consumption contributed to an increase in bacterial selection pressure. Time trend analyses have reported an increase in antimicrobial resistance (AMR) including extended spectrum beta-lactamase (ESBL), Gram-negative bacteria resistant to carbapenems (CRE) or plasmid-mediated colistin resistance. Such resistance patterns have been associated with significant negative impact on clinical and public health burden, including deaths, attributable to AMR.

There is now an urgent need for emphasis to modify prescribers' understanding and behaviours. Antimicrobial guidelines emerge as an ever important intervention to support clinical decision-making through a consensual process based on evidence and a collective action to tackle relevant disease problems. The adoption of guidelines targeting antibiotic prescribing, a medical behaviour characterised by inadequate diligence in the past, has been associated with significant benefits, encompassing improvements in morbidity, mortality, healthcare utilization, costs as in some cases even in resistance rates. Conscious-scientific societies can contribute to control AMR by producing necessary, appropriate and specific recommendations to optimise the use of antibiotics and inviting health professionals to adhere to them.

It has been 5 years since the last edition of the National Antimicrobial Guidelines. Significant changes have taken place in the local AMR situation; with some areas of positive progress but unfortunately there has been areas with continued deterioration. Hence, the Ministry of Health deems it timely for a revision of the national guidelines to keep pace with the new clinical realities. These guidelines have been formulated by a large core team of stakeholders including infectious disease physicians, clinical microbiologists and pharmacists. To ensure acceptance and ownership of these guidelines, they have worked with all clinical disciplines over a period of more than a year. These guidelines have been formulated with some guiding principles; that our recommendations will not just only be evidence-based but also that it has to be pertinent to the local situation and realities. We do remind all our clinical colleagues that while we focus on the treatment of the individual patient we must always be cognizant of the collateral damage of AMR.

I would like to acknowledge and thank the core editorial team and all the heads of clinical services for their support and patience in this long review process. A word of thanks also go to our team of external reviewers for their time and constructive input. I would particularly like to convey my gratitude to the Pharmacy Division and their team of dedicated pharmacists, for playing a critical role in the production of this document.

Practice guidelines, of any kind, would only be effective if they are adhered to. We hope as we grapple with the continued global threat of AMR, we would all play our own roles in preserving the "Miracle of Antimicrobials" for ourselves and our future generations.



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PRINCIPLES OF ANTIBIOTIC THERAPY AND RATIONAL ANTIBIOTIC PRESCRIBING

Infections remain a common cause of presentation to the outpatient department and inpatient admissions to the hospital. Antibiotics are widely being prescribed to treat infections, both in the community and hospital setting. Selection of appropriate anti-infective therapy can be challenging to the clinician. Consequently, understanding the basic principles of anti-infective therapy is important to ensure optimal outcome and to reduce selective pressure on antibiotics, which may be associated with the development of antibiotic resistance. The overuse and misuse of antibiotics have contributed to increased bacterial resistance to antibiotics, among other contributory factors. Antibiotics are frequently prescribed for indications in which their use is not warranted; at other times, an inappropriate or suboptimal antibiotic is prescribed. The available evidence suggests that when antibiotic use is warranted, choosing the narrowest spectrum antibiotic most likely to achieve clinical cure and treating for the shortest effective length of time will result in a lower incidence of complications and lower antibiotic resistance.

A thorough clinical assessment of the patient is imperative to ascertain the underlying disease process, and if it is an infection, to predict the likely pathogens associated with the infection and select an antibiotic that will target the likely organisms. Where appropriate and clinically indicated, the initial assessment should be supported by relevant laboratory investigations to establish a definitive microbiological diagnosis and to determine the susceptibility of the organism to various antibiotics. The routine use of antibiotics to treat fever is inappropriate, as not all fever is caused by infection and antibiotics are only indicated for bacterial infections. Antibiotics should not be prescribed when bacterial infections are unlikely, such as for the common cold, coughs and bronchitis, as irrational antibiotic prescribing is one of the main factors that drive the emergence of antibiotic-resistant pathogens.

When choosing an antibiotic for empirical treatment, the following factors are important to assist and guide the decision-making process:

Determining and documenting if there is an indication for an antimicrobial agent?

Indications for an antibiotic include the unambiguous demonstration or the strong suspicion that the etiologic agent is bacterial. This should be based on the signs and symptoms of the infection, as well as on other factors, including the age of the patient, the patient's medical history, and the presence or absence of comorbidities.

What are the most common organisms causing the infection and the local antibiotic susceptibility pattern?

Knowledge of the likely organisms causing an infection and the local susceptibility profile are useful to select the antibiotic. For example, erysipelas is caused primarily by *Streptococcus pyogenes* which is usually sensitive to penicillins and macrolides, while impetigo may be caused by Streptococcus pyogenes or *Staphylococcus aureus, both usually sensitive to penicillase-resistant penicillins such as cloxacillin.* This guideline lists the common etiological bacterial that are well known to cause the infection and it is found in the first column of the tables.

What is the antibiotic spectrum of the chosen empirical agent?

The antibiotic spectrum refers to the range of microorganisms an antibiotic is usually effective against and is an important consideration for empiric therapy. Decision on choice of antibiotic based on the spectrum of coverage should be made based on severity of illness, pathogen probabilities (eg. whether gram-positive or gram-negative bacteria), local resistance patterns, comorbid conditions and recent antibiotic exposure. The definitive choice of antibiotics should subsequently be made after release of culture and susceptibility results and therapy should be tailored accordingly. The antibiotics suggested in these guidelines are mainly for empirical use prior to the release of culture results.

What are the known pharmacokinetics and pharmacodynamics that are associated with a particular antibiotic?

Knowledge of the pharmacokinetic and pharmacodynamic principles assist the clinician in predicting the clinical and microbiologic success of antibiotic treatment. Concentration-dependent bacterial killing is a feature of antibiotics such as aminoglycosides and fluoroquinolones, higher concentrations resulting in more rapid killing. Time-dependent bacterial killing is associated with beta-lactam antibiotics, greater degree of bacterial killing occurring when the time of exposure is above the minimal inhibitory concentration of the pathogen. These guidelines attempt to give guidance for antibiotic dosing, route of administration (including a chapter on early intravenous to oral switch for certain

infections), pertinent drug-drug interactions that affect common antimicrobials and the optimal method of administration.

What host factors might affect antibiotic selection and dosing?

Host factors, such as patient age and underlying disease, are important considerations in selecting appropriate antibiotic therapy for suspected bacterial infections. Host factors influence the types of bacteria likely to be pathogenic and organ failures may impact on dosing regimens and predispose to adverse drug reactions.

What is the cost-effectiveness of the antibiotic selection?

Choosing inappropriate therapy is associated with increased costs, including the cost of the antibiotic and increases in overall costs of medical care because of treatment failures and adverse events. Using an optimal course of antibiotics can have economic as well as clinical advantages, including a faster return to normal daily routine and earlier return to full health. Wherever there is a choice between two antibiotics which share the same efficacy and side effect profile, this guideline has put the preferred agent as the antibiotic that is more widely available to most hospitals and clinics

What are the antibiotic adverse reactions?

Antibiotic prescribing may be associated with potential side effects that may affect the relative risks and benefits of therapy. All antibiotics have potential side effects, and it is important for the clinician to be aware of how these might affect the patient. It would not be possible for this guideline to give an exhaustive list of side effects for each antimicrobial agent, however where there are prominent or common adverse effects, these are listed.

What is the optimal duration of treatment?

There are few infections for which the duration of treatment has been precisely defined. This reflects the fact that the endpoints for assessing treatment are largely clinical rather than microbiological. However, an increasing number of infections have now evidence-based trials that have compared effective durations of treatment to fall back on. These recommendations are mentioned in these guidelines. As never data emerges, we can expect changes in recommendations in some of these infections in the future.

What is de-escalation therapy and when is it warranted?

De-escalation of antibiotic therapy refers to an initial short-term, broad-spectrum antibiotic coverage in severely ill patients followed by changes to more narrow-focused regimens that are driven by culture and other laboratory results once there are signs of clinical stability. This strategy balances the mortality and morbidity risks of serious infections with limiting the risks of potential adverse effects of long-term broad-spectrum antibiotic use, which are primarily the emergence of resistant organisms or new infections. This approach is particularly pertinent when dealing with life-threatening conditions especially infections in the critical care patients, immunocompromised patients and patients with risk factors for hospital acquired infections; where delay in initiating the appropriate antibiotic therapy may result in mortality. Broad-spectrum initial therapy, if used in the short term, limits the risk of emergence of antibiotic resistance. The choice of the initial antibiotic regimen should be based on the local microbiological surveillance data. The antibiotics suggested in these guidelines are ideally customized to each respective hospital.

In conclusion, antibiotic prescribing should be made after careful consideration of the underlying infective process, the likely etiologic agents, local susceptibility pattern, known spectrum of a chosen antibiotic, host factors and comorbidities. Rational antibiotic prescribing improves patient outcomes, minimizes duration of hospitalization, minimizes antibiotic side effects and the development of antibiotic resistance and reduces the cost of healthcare.

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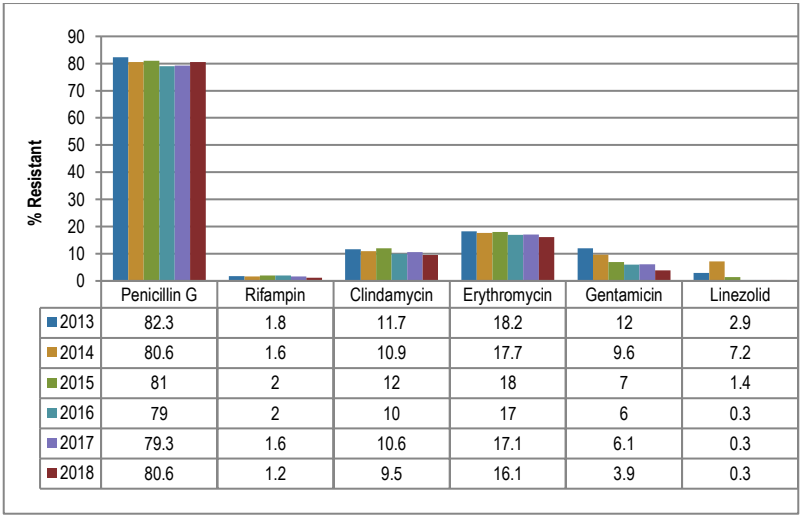
PERCENTAGE OF ANTIBIOTIC RESISTANCE AMONG GRAM POSITIVE BACTERIA

GRAM POSITIVE ORGANISMS

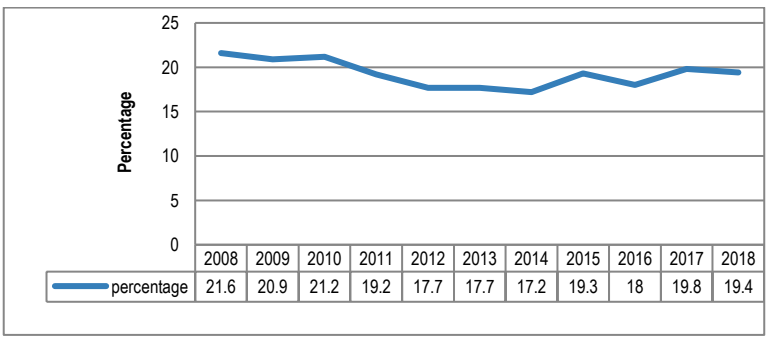
A. Staphylococcus aureus



	Penicillin G	Rifampin	Clindamycin	Erythromycin	Gentamicin	Linezolid
2013	82.3	1.8	11.7	18.2	12	2.9
2014	80.6	1.6	10.9	17.7	9.6	7.2
2015	81	2	12	18	7	1.4
2016	79	2	10	17	6	0.3
2017	79.3	1.6	10.6	17.1	6.1	0.3
2018	80.6	1.2	9.5	16.1	3.9	0.3

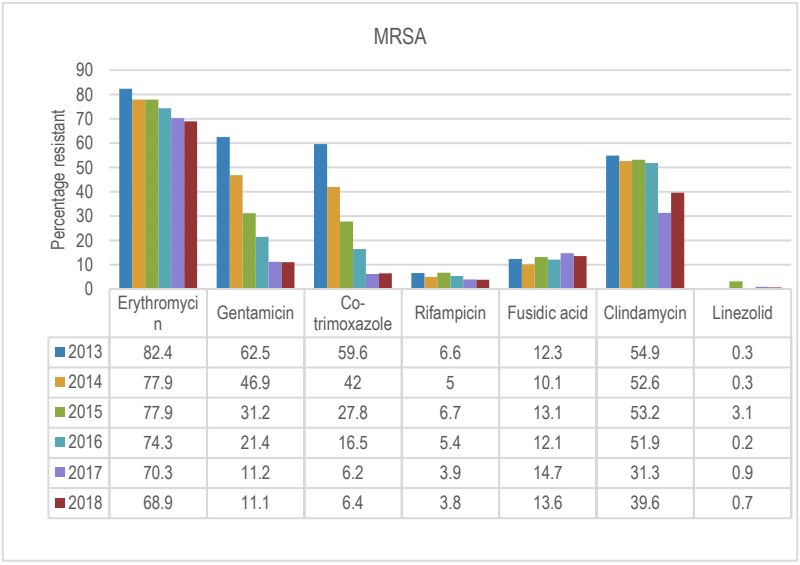
Chart 1: 6 year trend of antimicrobial resistance for *Staphylococcus aureus* from all samples, against selective antibiotics. (Linezolid - using EUCAST breakpoint.)

MRSA



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
percentage	21.6	20.9	21.2	19.2	17.7	17.7	17.2	19.3	18	19.8	19.4

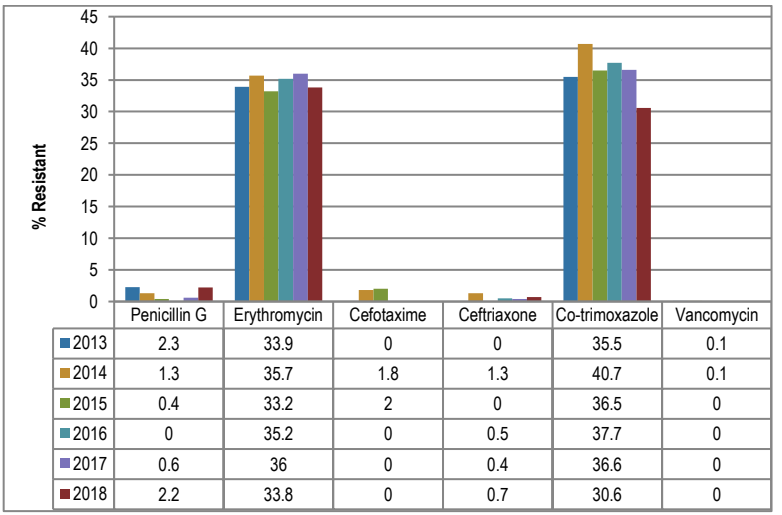
Chart 2: Trend of MRSA rates 2008 – 2018, from all samples.



	Erythromycin	Gentamicin	Co-trimoxazole	Rifampicin	Fusidic acid	Clindamycin	Linezolid
2013	82.4	62.5	59.6	6.6	12.3	54.9	0.3
2014	77.9	46.9	42	5	10.1	52.6	0.3
2015	77.9	31.2	27.8	6.7	13.1	53.2	3.1
2016	74.3	21.4	16.5	5.4	12.1	51.9	0.2
2017	70.3	11.2	6.2	3.9	14.7	31.3	0.9
2018	68.9	11.1	6.4	3.8	13.6	39.6	0.7

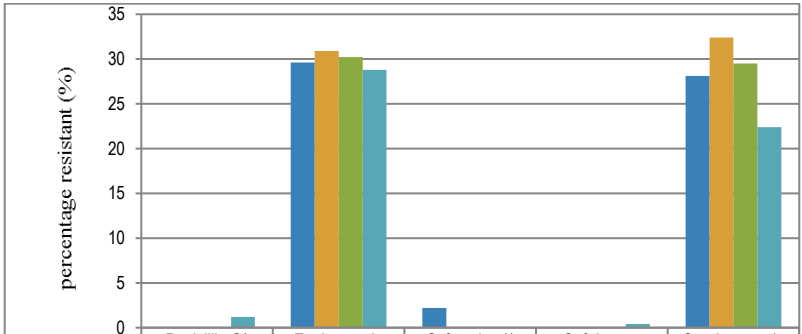
Chart 3: Antibiotic resistance trend for MRSA isolated from all samples 2013-2018.

B. Streptococcus pneumoniae



	Penicillin G	Erythromycin	Cefotaxime	Ceftriaxone	Co-trimoxazole	Vancomycin
2013	2.3	33.9	0	0	35.5	0.1
2014	1.3	35.7	1.8	1.3	40.7	0.1
2015	0.4	33.2	2	0	36.5	0
2016	0	35.2	0	0.5	37.7	0
2017	0.6	36	0	0.4	36.6	0
2018	2.2	33.8	0	0.7	30.6	0

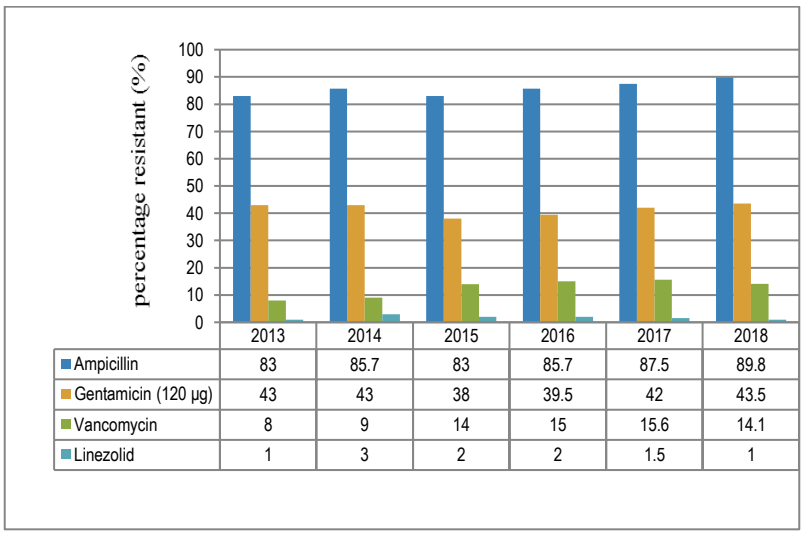
Chart 4: Antibiotic resistance trend for *Streptococcus pneumoniae* isolated from all samples, 2013-2018.



	Penicillin G*	Erythromycin	Cefotaxime**	Ceftriaxone	Co-trimoxazole
2015	0	29.6	2.2	0	28.1
2016	0	30.9	0	0	32.4
2017	0	30.2	0	0	29.5
2018	1.2	28.8	0	0.4	22.4

Chart 5: Antibiotic resistance for *Streptococcus pneumoniae* isolated from blood. *using non-meningitis breakpoints. **not verified at reference laboratory

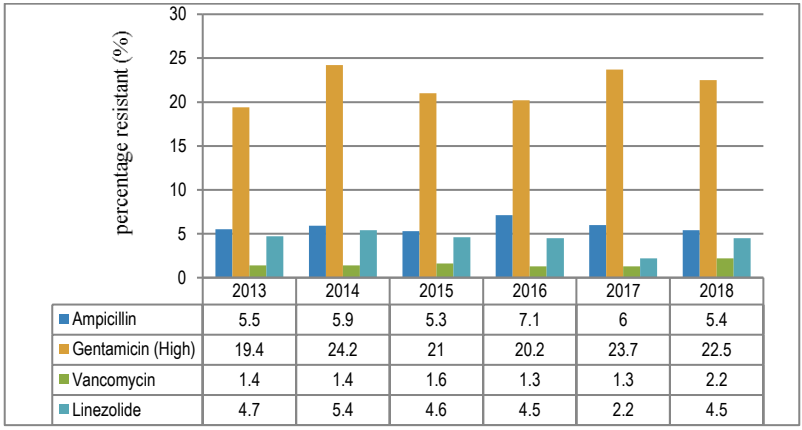
C. *Enterococcus faecium*.



	2013	2014	2015	2016	2017	2018
Ampicillin	83	85.7	83	85.7	87.5	89.8
Gentamicin (120 µg)	43	43	38	39.5	42	43.5
Vancomycin	8	9	14	15	15.6	14.1
Linezolid	1	3	2	2	1.5	1

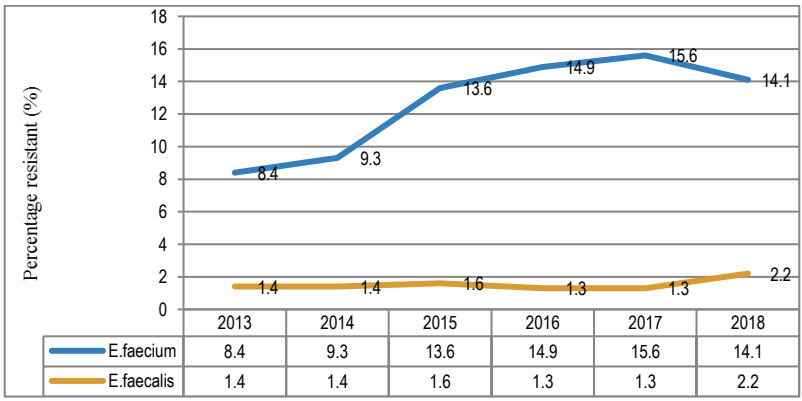
Chart 6: 6 year trend of antimicrobial resistance for *Enterococcus faecium* against selective antibiotics (2013 - 2018)

***D. Enterococcus faecalis*.**



	2013	2014	2015	2016	2017	2018
Ampicillin	5.5	5.9	5.3	7.1	6	5.4
Gentamicin (High)	19.4	24.2	21	20.2	23.7	22.5
Vancomycin	1.4	1.4	1.6	1.3	1.3	2.2
Linezolide	4.7	5.4	4.6	4.5	2.2	4.5

Chart 7: 6 year trend of antimicrobial resistance for *Enterococcus faecalis* against selective antibiotics (2013-2018)

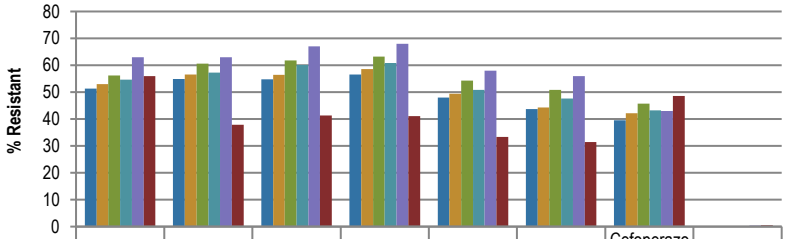


	2013	2014	2015	2016	2017	2018
E.faecium	8.4	9.3	13.6	14.9	15.6	14.1
E.faecalis	1.4	1.4	1.6	1.3	1.3	2.2

Chart 8: Trend of vancomycin resistance in *Enterococcus faecium* and *Enterococcus faecalis* from all clinical samples, 2013-2018.

GRAM-NEGATIVE ORGANISMS

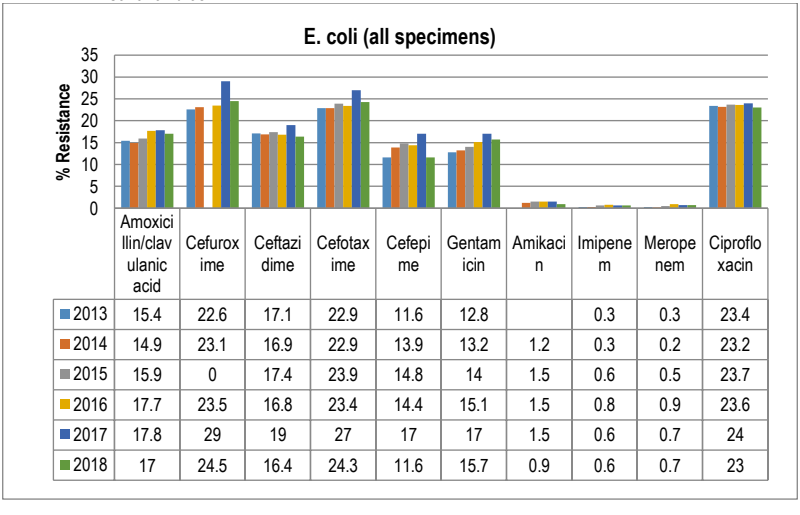
A. *Acinetobacter baumanii*



	Ampicillin/sulbactam	Ceftazidime	Imipenem	Meropenem	Gentamicin	Amikacin	Cefoperazone/sulbactam	Polymixin B
2013	51.3	54.9	54.8	56.5	48	43.7	39.5	0
2014	53	56.6	56.4	58.6	49.4	44.3	42.2	0
2015	56.2	60.6	61.8	63.2	54.3	50.9	45.7	0
2016	54.6	57.3	60.1	60.8	50.8	47.6	43.2	0
2017	63	63	67	68	58	56	43	0.4
2018	56	37.9	41.3	41.1	33.3	31.5	48.6	0.5

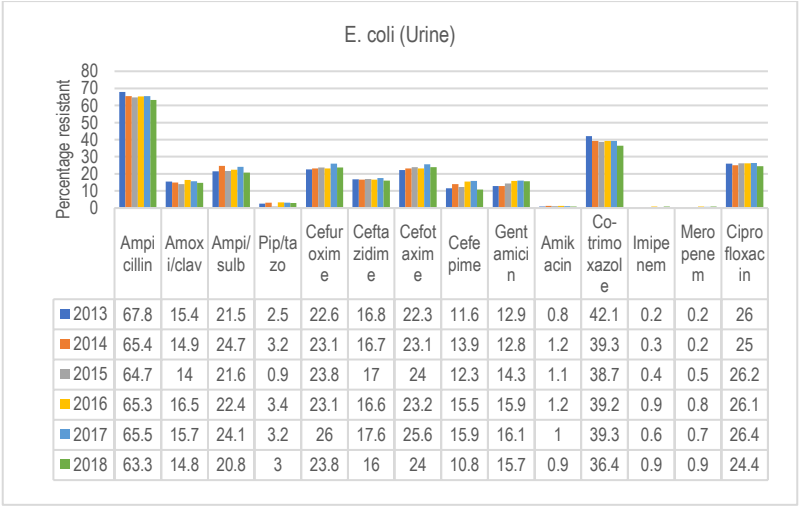
Chart 9: 6 year trend of antimicrobial resistance for *Acinetobacter baumanii*. against selective antibiotics 2013-2018), from all samples

B. *Escherichia coli*



	Amoxicillin/clavulanic acid	Cefuroxime	Ceftazidime	Cefotaxime	Cefepime	Gentamicin	Amikacin	Imipenem	Meropenem	Ciprofloxacin
2013	15.4	22.6	17.1	22.9	11.6	12.8		0.3	0.3	23.4
2014	14.9	23.1	16.9	22.9	13.9	13.2	1.2	0.3	0.2	23.2
2015	15.9	0	17.4	23.9	14.8	14	1.5	0.6	0.5	23.7
2016	17.7	23.5	16.8	23.4	14.4	15.1	1.5	0.8	0.9	23.6
2017	17.8	29	19	27	17	17	1.5	0.6	0.7	24
2018	17	24.5	16.4	24.3	11.6	15.7	0.9	0.6	0.7	23

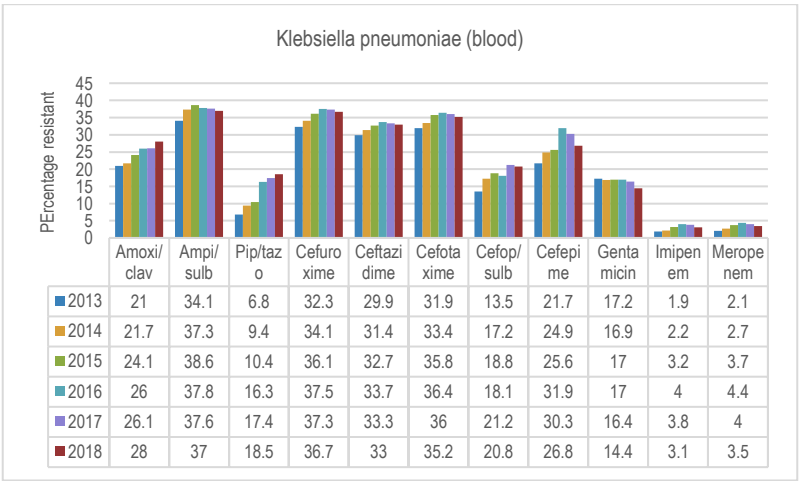
Chart10: 6 year trend of antimicrobial resistance for *E.coli.* against selective antibiotics (2013-2018)



	Ampicillin	Amoxi/clav	Ampi/sulb	Pip/tazo	Cefuroxime	Ceftazidime	Cefotaxime	Cefepime	Gentamicin	Amikacin	Co-trimoxazole	Imipenem	Meropenem	Ciprofloxacin
2013	67.8	15.4	21.5	2.5	22.6	16.8	22.3	11.6	12.9	0.8	42.1	0.2	0.2	26
2014	65.4	14.9	24.7	3.2	23.1	16.7	23.1	13.9	12.8	1.2	39.3	0.3	0.2	25
2015	64.7	14	21.6	0.9	23.8	17	24	12.3	14.3	1.1	38.7	0.4	0.5	26.2
2016	65.3	16.5	22.4	3.4	23.1	16.6	23.2	15.5	15.9	1.2	39.2	0.9	0.8	26.1
2017	65.5	15.7	24.1	3.2	26	17.6	25.6	15.9	16.1	1	39.3	0.6	0.7	26.4
2018	63.3	14.8	20.8	3	23.8	16	24	10.8	15.7	0.9	36.4	0.9	0.9	24.4

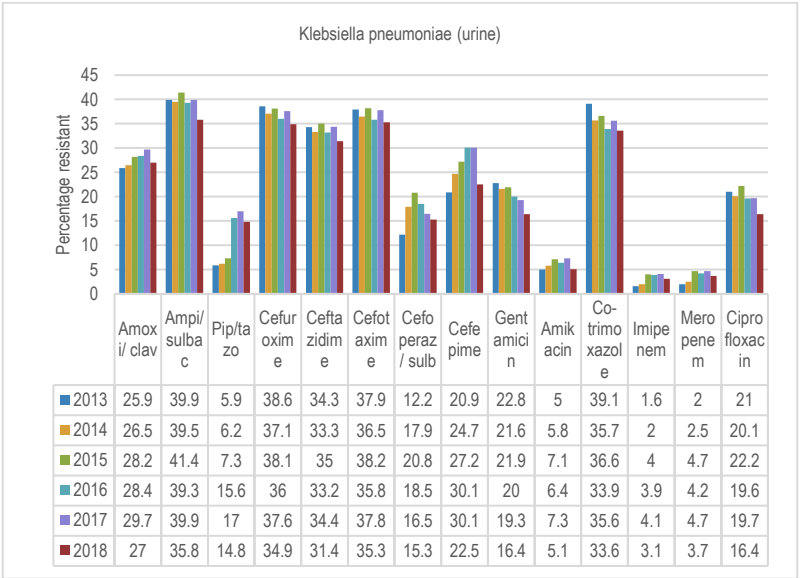
Chart 10: Antibiotic resistant trend for *E. coli* isolated from urine, 2013-2018.

C. Klebsiella pneumoniae



	Amoxi/clav	Ampi/sulb	Pip/tazo	Cefuroxime	Ceftazidime	Cefotaxime	Cefop/sulb	Cefepime	Gentamicin	Imipenem	Meropenem
2013	21	34.1	6.8	32.3	29.9	31.9	13.5	21.7	17.2	1.9	2.1
2014	21.7	37.3	9.4	34.1	31.4	33.4	17.2	24.9	16.9	2.2	2.7
2015	24.1	38.6	10.4	36.1	32.7	35.8	18.8	25.6	17	3.2	3.7
2016	26	37.8	16.3	37.5	33.7	36.4	18.1	31.9	17	4	4.4
2017	26.1	37.6	17.4	37.3	33.3	36	21.2	30.3	16.4	3.8	4
2018	28	37	18.5	36.7	33	35.2	20.8	26.8	14.4	3.1	3.5

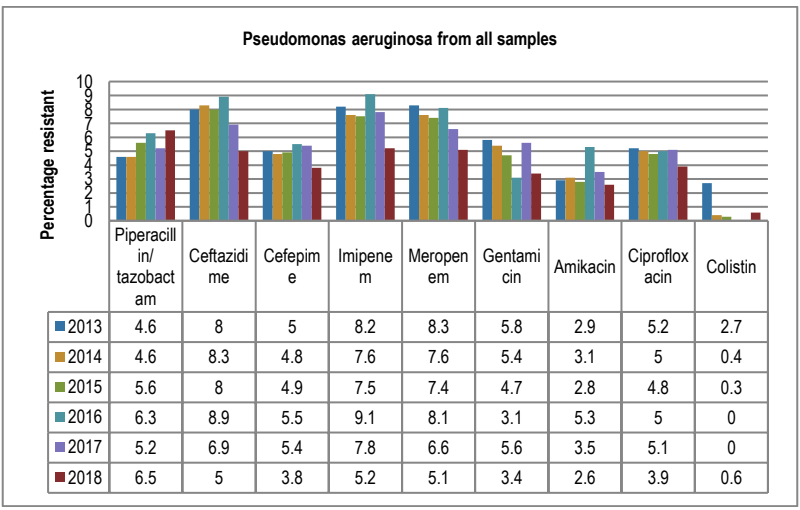
Chart 11: 6 year trend of antimicrobial resistant for *Klebsiella pneumoniae* against selective antibiotics (2013-2018), from blood.



	Amoxi/ clav	Ampi/ sulbac	Pip/tazo	Cefuroxime	Ceftazidime	Cefotaxime	Cefoperaz / sulb	Cefepime	Gentamicin	Amikacin	Co-trimoxazole	Imipenem	Meropenem	Ciprofloxacin
2013	25.9	39.9	5.9	38.6	34.3	37.9	12.2	20.9	22.8	5	39.1	1.6	2	21
2014	26.5	39.5	6.2	37.1	33.3	36.5	17.9	24.7	21.6	5.8	35.7	2	2.5	20.1
2015	28.2	41.4	7.3	38.1	35	38.2	20.8	27.2	21.9	7.1	36.6	4	4.7	22.2
2016	28.4	39.3	15.6	36	33.2	35.8	18.5	30.1	20	6.4	33.9	3.9	4.2	19.6
2017	29.7	39.9	17	37.6	34.4	37.8	16.5	30.1	19.3	7.3	35.6	4.1	4.7	19.7
2018	27	35.8	14.8	34.9	31.4	35.3	15.3	22.5	16.4	5.1	33.6	3.1	3.7	16.4

Chart 12: Antibiotic resistant trend for *Klebsiella pneumoniae* isolated from urine, 2013-2018.

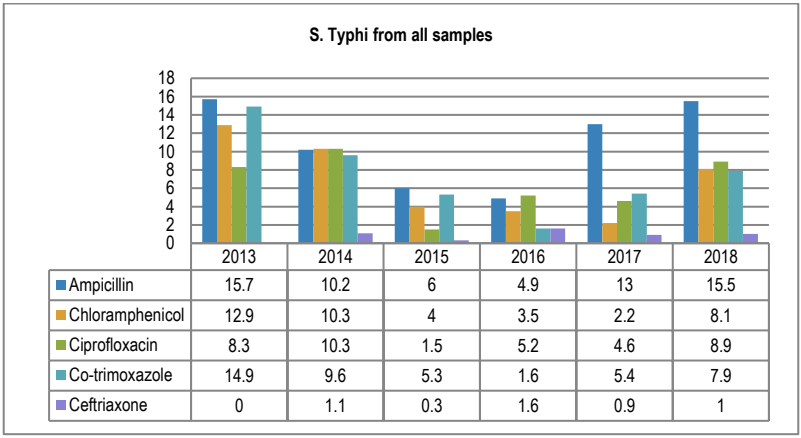
D. ***Pseudomonas aeruginosa***



	Piperacillin/ tazobactam	Ceftazidime	Cefepime	Imipenem	Meropenem	Gentamicin	Amikacin	Ciprofloxacin	Colistin
2013	4.6	8	5	8.2	8.3	5.8	2.9	5.2	2.7
2014	4.6	8.3	4.8	7.6	7.6	5.4	3.1	5	0.4
2015	5.6	8	4.9	7.5	7.4	4.7	2.8	4.8	0.3
2016	6.3	8.9	5.5	9.1	8.1	3.1	5.3	5	0
2017	5.2	6.9	5.4	7.8	6.6	5.6	3.5	5.1	0
2018	6.5	5	3.8	5.2	5.1	3.4	2.6	3.9	0.6

Chart 13: Antibiotic resistant trend for *Pseudomonas aeruginosa* isolated from all samples, 2013-2017

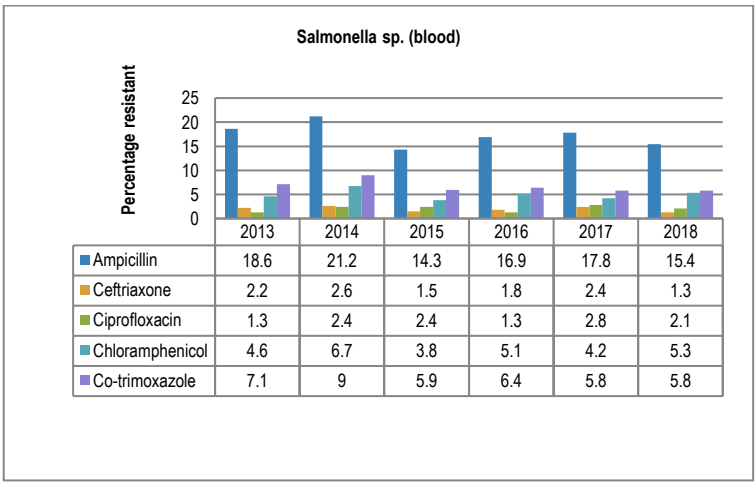
E. Salmonella Typhi



	2013	2014	2015	2016	2017	2018
Ampicillin	15.7	10.2	6	4.9	13	15.5
Chloramphenicol	12.9	10.3	4	3.5	2.2	8.1
Ciprofloxacin	8.3	10.3	1.5	5.2	4.6	8.9
Co-trimoxazole	14.9	9.6	5.3	1.6	5.4	7.9
Ceftriaxone	0	1.1	0.3	1.6	0.9	1

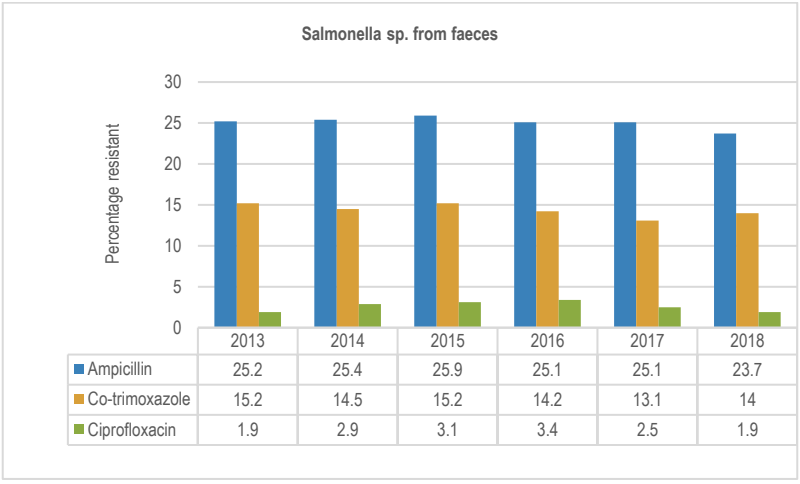
Chart 14: Antibiotic resistant trend for Salmonella Typhi isolated from all samples, 2013-2018.

F. Salmonella spp.



	2013	2014	2015	2016	2017	2018
Ampicillin	18.6	21.2	14.3	16.9	17.8	15.4
Ceftriaxone	2.2	2.6	1.5	1.8	2.4	1.3
Ciprofloxacin	1.3	2.4	2.4	1.3	2.8	2.1
Chloramphenicol	4.6	6.7	3.8	5.1	4.2	5.3
Co-trimoxazole	7.1	9	5.9	6.4	5.8	5.8

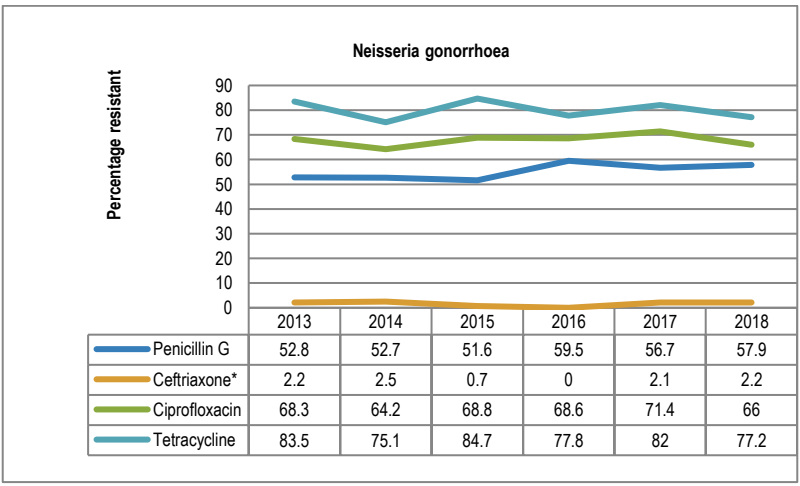
Chart 15: Percentage antibiotic resistance for *Salmonella* sp isolated from blood samples.



	2013	2014	2015	2016	2017	2018
Ampicillin	25.2	25.4	25.9	25.1	25.1	23.7
Co-trimoxazole	15.2	14.5	15.2	14.2	13.1	14
Ciprofloxacin	1.9	2.9	3.1	3.4	2.5	1.9

Chart 16: Percentage of Salmonella sp. Resistant to antibiotics, 2013-2018

G. *Neisseria gonorrhoea*



	2013	2014	2015	2016	2017	2018
Penicillin G	52.8	52.7	51.6	59.5	56.7	57.9
Ceftriaxone*	2.2	2.5	0.7	0	2.1	2.2
Ciprofloxacin	68.3	64.2	68.8	68.6	71.4	66
Tetracycline	83.5	75.1	84.7	77.8	82	77.2

*Not verified by coordinating laboratory

Chart 17: Antibiotic resistant trend for *Neisseria gonorrhoea*, 2013-2018

ANTIBIOTIC UTILISATION

Based on DDD/1000 patient-days

Total antibiotic utilisation: All Wards*

Currently, there are 18 antibiotics from six antibiotic groups being monitored under the National Surveillance on Antibiotic Utilisation. For All Wards*, the total antibiotic utilisation showed 7.3% increment in 2018 as compared to 2017. Four antibiotic groups have increased utilisation as compared to 2017: penicillin/ β-lactamase inhibitor combination (21.2%), glycopeptide (20.7%), cephalosporins (8.0%) and fluoroquinolones (1.6%).

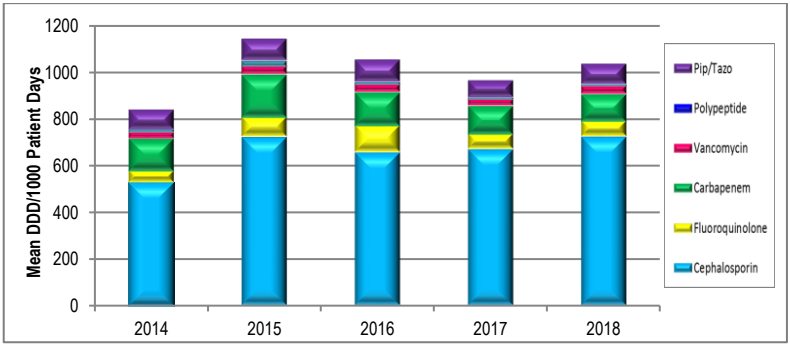


Figure 1: Antibiotic utilisation over five years at MOH, university, military and private hospitals (All Wards*)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

Total antibiotic utilisation: ICU-only

In ICUs, the total antibiotic utilisation in 2018 have increased only slightly (0.47%) as compared to the utilisation in 2017. Four antibiotic groups have increased utilisation as compared to 2017: penicillin/β-lactamase inhibitor combination (89.8%), glycopeptide (88.5%), fluoroquinolones (17.4%) and cephalosporins (3.4%).

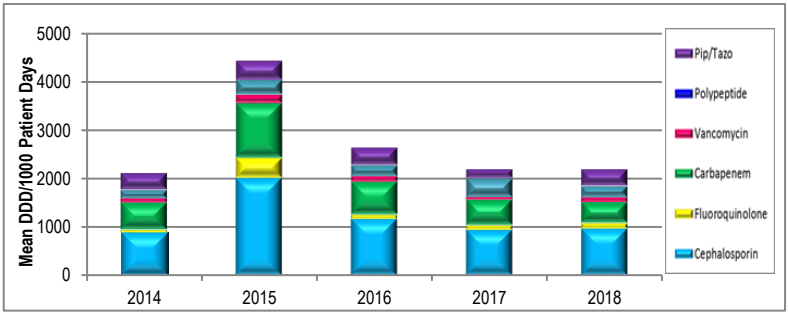


Figure 2: Antibiotic utilisation over five years at MOH, university, military and private hospitals (ICU-only)
Cephalosporins

Ceftriaxone contributed the highest proportion of cephalosporin use every year from 2014-2018, in All Wards* and ICU. Increase in utilisation in All Wards* and ICU (2018 versus 2017) is seen with cefuroxime (All Wards*: 7.4%, ICU-only: 179.2%), ceftriaxone (All Wards*: 19.9%, ICU-only: 1.4%), cefoperazone (All Wards*: 1.6%, ICU-only: 6.7%) and cefoperazone/sulbactam (All Wards*: 53.4%, ICU-only: 24.1%). Increase in cefotaxime use was only seen in ICU (155.9%) but not All Wards*.

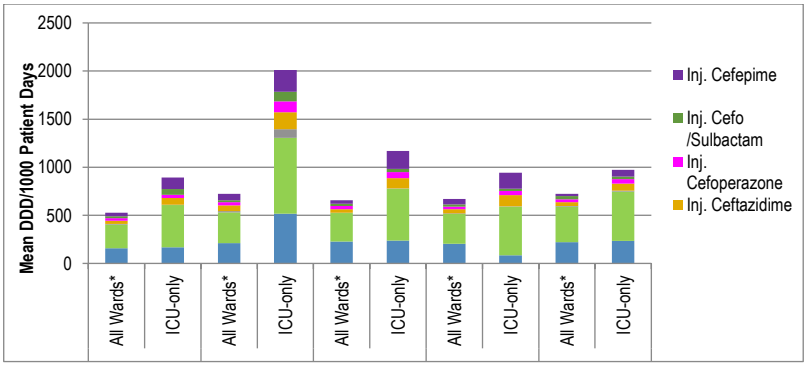


Figure 3: Utilisation of cephalosporin injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

Carbapenems

Carbapenem utilisation was contributed most by meropenem. For All Wards*, all carbapenems showed decreased utilisation in 2018 as compared to 2017 except ertapenem. For ICU, there was decreased utilisation of all carbapenems except ertapenem.

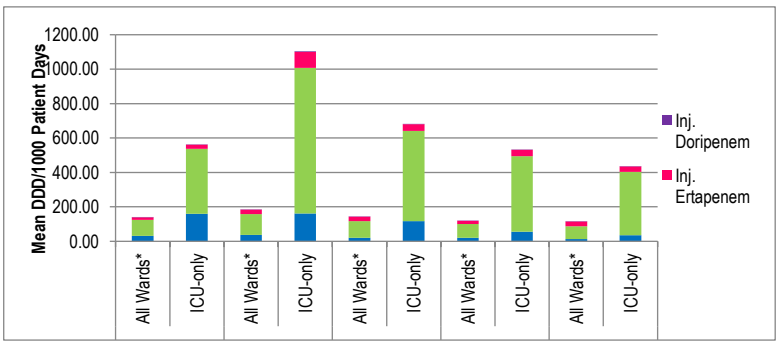


Figure 4: Utilisation of carbapenem injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

Polymyxins

From 2014 to 2016, colistin has been used more than polymyxin B in All Wards* and ICU. In 2017, polymyxin B started to show higher utilisation (85.4% of total polymyxins) than colistin (14.6% of total polymyxins) in ICU. In 2018, polymyxin B was used more than colistin in All Wards* (68.2% of total polymyxins) and ICU (67.6% of total polymyxins).

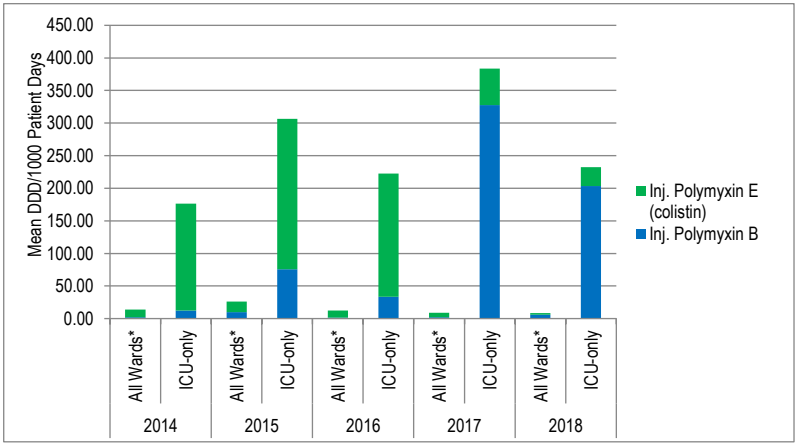


Figure 5: Utilisation of polymyxin injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

Penicillin/β-lactamase inhibitor combination

Piperacillin/tazobactam is the only penicillin/β-lactamase inhibitor combination being monitored currently. The utilisation of piperacillin/tazobactam has increased in 2018 as compared to 2017, for All Wards* (21.2%) and ICU (89.8%).

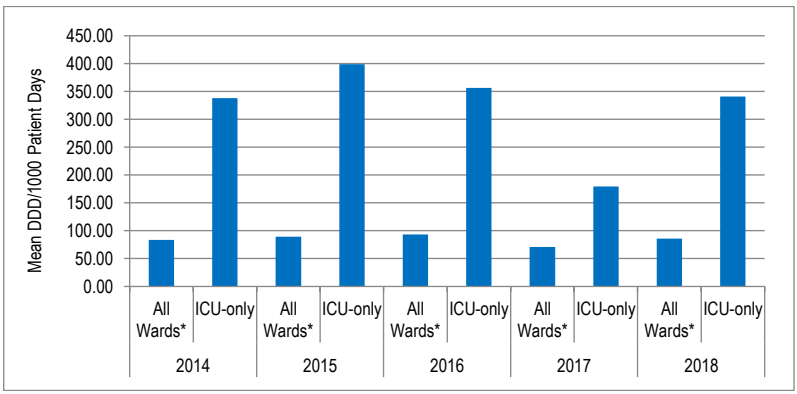


Figure 6: Utilisation of piperacillin/tazobactam injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**
Fluoroquinolones

Fluoroquinolone utilisation was contributed most by ciprofloxacin. From 2016 to 2018, the utilisation of ciprofloxacin demonstrated a decreasing trend in All Wards* but there was an increasing trend in the ICU.

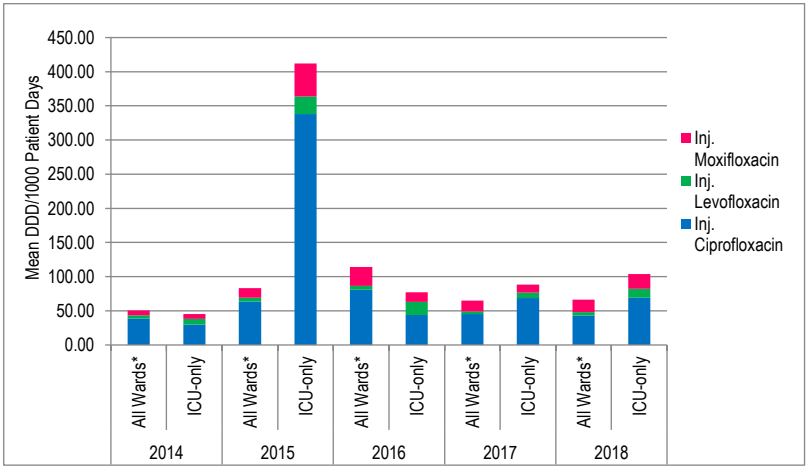


Figure 7: Utilisation of fluoroquinolone injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

Glycopeptide

Vancomycin is the only glycopeptide being monitored currently. Vancomycin utilisation has increased in 2018 as compared to 2017, in All Wards* (20.7%) and ICU (88.5%).

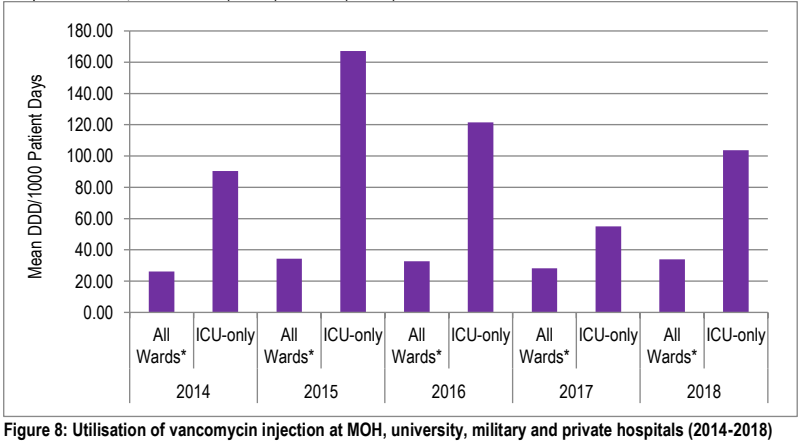


Figure 8: Utilisation of vancomycin injection at MOH, university, military and private hospitals (2014-2018)
*** 2016 & 2017: 63 hospitals excluded ICU data; 2018: 66 hospitals excluded ICU data**

SECTION A
ADULT

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
A. INFECTIVE ENDOCARDITIS			
Empirical Treatment (native valve)			
	Benzylpenicillin 18MU/day IV q4-6h **OR** Ampicillin 12gm/day IV q4-6h **PLUS** Gentamicin 3mg/kg/day IV q24h **PLUS/MINUS** **Cloxacillin 12gm/day IV q4-6h	**Penicillin Allergy:** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose **PLUS** Gentamicin 3mg/kg IV q24h	*Vancomycin loading dose refer to Appendix 1. **Cloxacillin: For patients with suspected *Staphylococcus aureus* infections (such as IVDU or patients with prosthesis) and acute presentation. Penicillin allergy refer to Appendix 8
Empirical Treatment (prosthetic valve)			
Prosthetic valve (early, <1 y)	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose **PLUS** Gentamicin 3mg/kg IV q24h **PLUS/MINUS** **Rifampicin 300-450mg PO/IV q12h **PLUS/MINUS** ***Cefepime 2gm IV q8h		*Vancomycin loading dose refer to Appendix 1. **Rifampicin is only recommended for PVE and it should be started 3-5 days later than vancomycin and gentamicin ***Cefepime is indicated if local Epidemiology suggests for non-HACEK Gram- negative rod infections (such as Pseudomonas)
Prosthetic valve (late, ≥ 1 y)	Ampicillin 12gm/day IV q4-6h **PLUS** Gentamicin 3mg/kg IV q24h	**Penicillin Allergy** : *Vancomycin 15-20 mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose	*Vancomycin loading dose refer to Appendix 1. **Cloxacillin: For patients with suspected *Staphylococcus aureus* infections (such

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	PLUS/MINUS **Cloxacillin 12gm/day IV in 4-6 equally divided doses	**PLUS** Gentamicin 3mg/kg IV q24h	as IVDU or patients with prosthesis) and acute presentation.
Viridans Streptococci & *Streptococcus bovis* It is recommended MIC estimation is done for these isolates to facilitate management			
Native and Prosthetic Valves MIC: < 0.125µg/mL Penicillin-Susceptible Viridans Streptococci *& Streptococcus bovis*	Benzylpenicillin 3MU IV q4-6h for 4 weeks (native valves) or 6 weeks (prosthetic valves)	Ampicillin 2gm IV q4h for 4 weeks (native valves) or 6 weeks (prosthetic valves) **OR** Ceftriaxone 2gm IV q24h for 4 weeks (native valves) or 6 weeks (prosthetic valves) **<u>Penicillin Allergy:</u>** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for 4 weeks (native valves) or 6 weeks (prosthetic valves)	Penicillin-susceptible viridans streptococci, monotherapy with benzylpenicilin, ampicillin or ceftriaxone is adequate. 4 weeks for NVE and 6 weeks for PVE. *Vancomycin: For loading dose refer to Appendix 1. Penicillin allergy refer to Appendix 8
Native and prosthetic Valves MIC: > 0.125µg/mL- 2µg/mL Penicillin-Relatively Resistant Viridans Streptococci *& Streptococcus bovis*	Benzylpenicillin 4MU IV q4h (total 24 MU/24h) or 24 MU IV continuously for 4 weeks (native valves) or 6 weeks (prosthetic valves) **PLUS** *Gentamicin 3mg/kg IV q24h for 2 weeks (native valves) or 6 weeks (prosthetic valves)	Ceftriaxone 2gm IV q24h for 4 weeks (native valves) or 6 weeks (prosthetic valves) **PLUS** *Gentamicin 3mg/kg IV q24h for 2 weeks (native valves) or 6 weeks (prosthetic valves) **<u>If unable to tolerate Penicillin/Ceftriaxone:</u>** **Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for 4 weeks (native valves) or 6 weeks (prosthetic valves) **PLUS**	Penicillin-relatively resistant streptococcus viridans, gentamicin has to be added to the regime. 2 weeks for NVE and 6 weeks for PVE. *Gentamicin: aim for pre-dose (trough) serum level of < 1mg/l **Vancomycin loading dose refer to Appendix 1. Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		*Gentamicin 3mg/kg IV q24h for 2 weeks (native valves) or 6 weeks (prosthetic valves)	
Native and Prosthetic Valves MIC > 2µg/mL Penicillin-resistant Viridans Streptococci *& Streptococcus bovis*	Treat as resistant enterococcal endocarditis - see below **		
Nutritionally variant streptococci; NVS (*Abiotrophia defective* and *Granulicatella* species, both formerly known as NVS)	Ampicillin 2gm IV q4h for 6 weeks **OR** Benzylpenicillin (Crystalline penicillin) 4MU IV q4h or 24MU/day as a continuous infusion) for 6 weeks **PLUS** Gentamicin 1mg/kg IV q8h for 2 weeks	Ceftriaxone 2gm IV q24h for 6 weeks **PLUS** Gentamicin 1mg/kg IV q8h for 2 weeks **OR** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2 gm/dose, for 6 weeks	*Vancomycin loading dose refer to Appendix 1.
**** Enterococcus (It is recommended that all these isolates are tested for high level resistance (HLR) to Gentamicin)**			
Native and Prosthetic Valves Enterococcal Endocarditis (sensitive to Gentamicin)	Ampicillin 2gm IV q4h for 4 or 6 weeks **PLUS** *Gentamicin 1mg/kg IV q8h for 4 or 6 weeks		Duration of Therapy: • Symptoms < 3 months: 4 weeks therapy (4 weeks ampicillin, 2 weeks gentamicin) • Symptoms > 3 months or prosthetic valves: 6 weeks therapy (6 weeks ampicillin and gentamicin) *Gentamicin: In order to maximise synergistic effect, administer Gentamicin at the same time or temporally close to Ampicillin/Penicillin

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			For Enterococcal Endocarditis with high level resistance to Gentamicin, consult Infectious Disease Specialist
Enterococcus (sensitive to Gentamicin) (renal impairment and elderly patients)	Ampicillin 2gm IV q4h for 6 weeks **PLUS** Ceftriaxone 2gm IV q12h for 6 weeks		
Enterococcus (resistance to gentamicin) (MIC > 500mg/l) Sensitive to penicillin and vancomycin	Ampicillin 2gm IV q4h for 6 weeks **PLUS** Ceftriaxone 2gm IV q12h for 6 weeks		Ceftriaxone should not be used alone for enterococcus infection, as they are intrinsically resistant. This combination is not active against *Enterococcus faecium*.
Enterococcus (resistance to penicillin and susceptible to aminoglycosides and vancomycin)	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2 gm/dose, for 6 weeks **PLUS** **Gentamicin 1 mg/kg IV q8h for 6 weeks		*Vancomycin loading dose refer to Appendix 1. **Gentamicin: aim for pre-dose (trough) serum level of < 1mg/l.
Staphylococcus aureus			
Native Valves Methicillin-Susceptible Staphylococci (MSSA)	**Left sided endocarditis or complicated right sided endocarditis:** Cloxacillin 2gm IV q4h for 4 to 6 weeks	**β-lactam Allergy:** **<u>Immediate type hypersensitivity to penicillin (anaphylaxis)</u>:** **Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for 4 to 6 weeks **<u>For non-immediate type hypersensitivity</u>:** Cefazolin 2gm IV q8h for 4 to 6 weeks	*2 weeks' regime is sufficient provided the patient fulfils all the following criteria (uncomplicated IE): • MSSA • Absence of associated prosthetic valve or left sided valve infection • Good response to treatment • Absence of metastatic sites of infection or empyema • Absence of cardiac and extracardiac complications
	Right sided endocarditis (tricuspid valve) in uncomplicated endocarditis (see comments*): Cloxacillin 2gm IV in q4h for 2 to 4 weeks		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			• Vegetation < 10 mm • Absence of severe immuno-suppression (<200 CD4 cells/ml) with or without Acquired Immune Deficiency Syndrome (AIDS) **Vancomycin loading dose refer to Appendix 1.
Prosthetic Valves Methicillin-Susceptible Staphylococci (MSSA)	Cloxacillin 2gm IV in q4h for ≥ 6 weeks **PLUS** Gentamicin 1mg/kg IM/IV q8h for 2 weeks **PLUS** *Rifampicin 300-450mg PO q12h for ≥ 6 weeks	**Regimen for β-lactam allergic patients, replace Cloxacillin with the following:** **<u>Immediate type hypersensitivity to penicillin (anaphylaxis)</u>:** **Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for 4 to 6 weeks **OR** **<u>For non-immediate type hypersensitivity</u>:** Cefazolin 2gm IV q8h for 4 to 6 weeks	*Rifampicin: To avoid the development of resistance, it should be started after 3-5 days of effective initial cloxacillin therapy and/or once the bacteraemia has been cleared. **Vancomycin loading dose refer to Appendix 1.
Native Valves Methicillin-Resistant Staphylococci (MRSA)	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for 4 to 6 weeks	**Daptomycin 10mg/kg IV q24h for 4 to 6 weeks	*Vancomycin loading dose refer to Appendix 1. **Daptomycin: DG Item. Requires DG's approval. Daptomycin is superior to vancomycin for MRSA bacteraemia with vancomycin MIC > 1 mg/l.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Prosthetic Valves Methicillin-Resistant Staphylococci (MRSA)	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose, for ≥ 6 weeks **PLUS** Gentamicin 1mg/kg IV q8h for 2 weeks **PLUS** **Rifampicin 300-450mg PO q12h for ≥ 6 weeks*		*Vancomycin loading dose refer to Appendix 1. **Rifampicin: To avoid the development of resistance, it should be started after 3-5 days of effective initial vancomycin therapy and/or once the bacteraemia has been cleared
HACEK Microorganisms *(Haemophilus parainfluenzae, Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella kingae)*			
Native and Prosthetic valves	Ceftriaxone 2gm IV q24h for 4 weeks (native valve) or 6 weeks (prosthetic valve)	Ampicillin/sulbactam 3gm IV q6h for 4 weeks (native valve) or 6 weeks (prosthetic valve) **OR** Ciprofloxacin 400mg IV or 500mg PO q12h for 4 weeks (native valve) or 6 weeks (prosthetic valve)	
Therapy for Culture-Negative Endocarditis - Consultation with an infectious disease specialist needed			
Brucella spp.	Doxycycline 100mg PO q12h **PLUS** Rifampicin 300-600mg PO q24h **PLUS** Streptomycin 15mg/kg IM q24h (For first 2-4 weeks only) **OR** Gentamicin 5mg/kg IV q24h (For first 2-4 weeks only)		Duration of treatment 3-6 months depends on clinical response

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
***Coxiella burnetii* (agent of Q fever)**	Doxycycline 100mg PO q12h **PLUS** Hydroxychloroquine 600mg PO q24h or 200mg PO q8h		For 18-24 months based on clinical and serological response
***Bartonella* spp.**	Doxycycline 100mg PO q12h for 6 weeks **PLUS** Gentamicin 3mg/kg IV q24h for 2 weeks		
Therapy for *Candida* Endocarditis (Native and Prosthetic valve)			
***Candida* Endocarditis (native and prosthetic valve)**	**Initial therapy:** Amphotericin B deoxycholate 0.6 -1mg/kg IV q24h for at least 6 weeks after surgery **OR** Lipid formulation Amphotericin B 3-5mg/kg IV q24h for at least 6 weeks after surgery **PLUS/MINUS** *Flucytosine 25 mg/kg PO q6h for at least 6 weeks after surgery	**Initial therapy:** High dose of echinocandins are recommended.	Valve replacement surgery is mandatory. Continue therapy for 6 weeks after surgical replacement or longer in patient with perivalvular abscess If prosthetic valve cannot be replaced, lifelong suppressive therapy with Fluconazole 400mg (6mg/kg) daily is recommended The duration of therapy will depend on patient response and surgical intervention Patients with *Candida* IE should be referred to ID physician *Flucytosine: For synergistic effect. Causes dose related marrow toxicity. Avoid using in patients with renal failure.
	Step down therapy: Fluconazole 400-800mg (6-12mg/kg) PO q24h for susceptible microorganism in stable patients with negative blood cultures (clearance of Candida from blood stream)		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Footnotes for antibiotic treatment of endocarditis: • Vancomycin: aim for serum trough level of 15 – 20mg/L (10 – 14 µmol/L) for both adults and paediatrics. Vancomycin dose should be adjusted in patients with renal impairment. For dosing adult patients with renal impairment, obese patients and monitoring recommendations refer to Appendix 2 (Antibiotic Dosage in Adult with Impaired Renal Function). • Gentamicin: for obese patients use ideal body weight. Monitor gentamicin levels weekly. Aim for gentamicin peak level (one hour after injection) of 6 – 10 µmol/L (3 – 5 mcg/mL) and trough level of <2 µmol/L (<1mcg/mL) when 2 – 3 divided doses are used. Refer to Appendix 1 (Clinical Pharmacokinetic Guidelines (Aminoglycosides & Vancomycin)). • There should be a high tendency for stopping Gentamicin in patients with deteriorating renal function or other signs of toxicity. • If there is high level gentamicin resistance (i.e. MIC >128 mg/L) Ampicillin/Sulbactam or Vancomycin will need to be continued for ≥6 weeks. Referral to an ID physician is recommended if high level Gentamicin resistance is present. • Rifampicin should always be used in combination with another effective antistaphylococcal drug (ideally two active agents, ie. Cloxacillin) to minimize risk of resistance. Rifampicin increases hepatic clearance of warfarin and other drugs.			
B. CATHETER RELATED INFECTIONS			
Non- tunneled central venous catheter (subclavian, internal jugular) **Peripherally inserted central catheter** Common organisms: *Staphylococcus aureus* *Streptococcus epidermidis*	Cloxacillin 1-2gm IV q6h **OR** Cefazolin 1-2gm IV q8h	**If patient has risk factor for MRSA:** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose **If local epidemiology shows high ESBL prevalence AND if patient severely ill (eg: Hypotension, multiorgan failure):** Meropenem 2gm IV q8h **OR** Imipenem 1gm IV q8h	Peripheral blood C&S is mandatory when suspecting CRBSI. If blood C&S negative, consider alternative diagnosis. Antibiotic of choice depends on local epidemiology of CRBSI and guided by antibiogram results. Need to remove catheter as very low cure rates. *Vancomycin loading dose refer to Appendix 1.
Tunnel type indwelling venous catheters and ports (Broviac, Hickman) **Haemodialysis catheter** Common organisms:	Cloxacillin 2gm IV q4-6h **OR** Cefazolin 2gm IV q8h **PLUS** Ceftazidime 2gm IV q8h	**If patient has risk factor for MRSA:** *Vancomycin 15-20 mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose **PLUS**	Adjust dose according to renal function. *Vancomycin loading dose refer to Appendix 1.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
CoNS, *Streptococcus epidermidis, Staphylococcus aureus,* Gram negative rods		Ceftazidime 2gm IV q8h	
C. TREATMENT OF PACEMAKER INFECTIONS			
Pacemaker Infection	Refer to Ministry of Health Malaysia's Clinical Practice Guidelines for the Prevention, Diagnosis & Management of Infective Endocarditis 2017		
Empirical therapy for superficial post-surgical Sternal Wounds	Cloxacillin 2gm IV q6h **OR** Cefazolin 1-2gm IV q8h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose	Duration of treatment: 7-10 days To discuss with Cardiothoracic unit that operated on the patient if uncertain whether deep sternal wound infection is present. *Vancomycin loading dose refer to Appendix 1. Aim for serum trough level of 15–20 mg/L.

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Meningitis (acute)			
Empirical treatment on admission: Common organisms: *Streptococcus pneumoniae* *Neisseria meningitidis* *Haemophilus influenzae* Other organisms: Gram-negative rods	Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q6h	Chloramphenicol 1gm IV q6h **Alternative ONLY for immunocompromised host:** Meropenem 2gm IV q8h	Antibiotic should not be delayed if lumbar puncture is delayed by radiological investigation. If no organism is isolated from CSF C&S but LP is suggestive of bacterial meningitis and patient is responding, continue antibiotics for 14 days. Dexamethasone 10mg IV q6h is recommended 15 to 20 minutes before or at the time of first dose of antibiotics. Continue for 4 days if the Gram stain and/or cultures consistent with S. pneumoniae. Discontinue if not *Streptococcus pneumonia* or if bacterial meningitis is subsequently thought not to be present. Incidence of listeriosis increases in people > 60 years of age, immunosuppressed & pregnancy. Consider empirical cover for this organism especially if the course of disease is indolent or there is epidemiological risk (refer section on treatment of listeriosis). Duration: 10-14 days

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Causative organism isolated:			
Haemophilus influenzae (Gram-negative bacilli)	Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q6h	Cefepime 2gm IV q8H **If organism is susceptible and patient is allergic to cephalosporins:** Chloramphenicol 50-100mg/kg/day IV q6h **OR** Ciprofloxacin 400mg IV q8h	Duration: 7-10 days
Streptococcus pneumoniae (Gram-positive cocci)	**Penicillin-sensitive strains (MIC to Penicillin < 0.12 mcg/ml)** Benzylpenicillin 4MU IV q4h		All attempts should be made to ascertain the MIC of isolated pneumococcus. Ceftriaxone or cefotaxime should be de-escalated to benzylpenicillin once the MIC result has been confirmed. Duration: 10-14 days *Vancomycin loading dose refer to Appendix 1.
	Penicillin resistant strains (MIC to Penicillin ≥0.12 mcg/ml) Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q6h	**Penicillin resistant strain (MIC to Penicillin ≥0.12 mcg/ml)** Cefepime 2gm IV q8h **OR** Meropenem 2gm IV q8h	
	Cephalosporin resistant strains (MIC to Cephalosporin ≥2 mcg/ml): *Vancomycin 25-30mg/kg loading dose then 15-20mg/kg IV q8-12h; not to exceed 2gm per dose **OR** Rifampicin 600mg IV/PO q12h **PLUS** Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q6h		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Neisseria meningitidis (Gram-negative diplococci)	Benzylpenicillin 4MU IV q4h (if MIC to Penicillin < 0.1 mcg/ml) **If MIC to penicillin is > 0.1 mcg/ml use:** Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q6h	**If organism is susceptible and patient is allergic to cephalosporins:** Chloramphenicol 50-100mg/kg/day IV q6h	Duration: 5-7 days
Prophylaxis for household and close contacts of meningococcal meningitis cases	**Age > 15 years:** Ciprofloxacin 500mg PO as single dose **OR** Rifampicin 600mg PO q12h for 2 days (4 doses) [not recommended in pregnant women]	Ceftriaxone 250mg IM as single dose (especially in pregnancy and lactating mothers) **OR** Azithromycin 500mg PO as single dose	Close contacts are defined as those individuals who have had contact for > 8 hours and within 1 metre of the index case. Individuals who were in contact with oropharyngeal secretions of the index case in the last 7 days before onset of symptoms up to 24 hours after appropriate antibiotics should also receive chemoprophylaxis. For index case who received only benzylpenicillin as therapy, chemoprophylaxis should also be given upon discharge to eliminate nasopharyngeal carriage.
	Children/Adolescent < 15 years: Refer to Paediatric Non-Surgical Chemoprophylaxis (Meningococcal Exposure) Section		
Listeriosis	Ampicillin 2gm IV q4h **OR** Benzylpenicillin 4MU IV q4h **PLUS/MINUS** Gentamicin 5mg/kg/day IV in 3 divided doses	Trimethoprim/sulfamethoxazole 10 to 20mg/kg/day [based on the TMP component] IV q6-12h **OR** Meropenem 2gm IV q8h	Duration of treatment is 3 weeks depending on clinical response. May be longer in immunocompromised host. Gentamicin is given until symptoms improve (minimum of 1 week).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Brain abscess/subdural empyema Common organisms: Streptococci Staphylococcus Gram-negative bacilli Anaerobes	**1. Brain abscess/subdural empyema suspected arising from an oral source:** Benzylpenicillin 4MU IV q4-6h **PLUS** Metronidazole 500mg IV q8h **2. Brain abscess/subdural empyema suspected arising from sinus or otogenic source:** Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q4-6h **PLUS** Metronidazole 500mg IV q8h **3. Brain abscess/subdural empyema arising from hematogenous spread or penetrating trauma (community acquired):** Ceftriaxone 2gm IV q12h **OR** Cefotaxime 2gm IV q4-6h **PLUS** Cloxacillin 2gm IV q4h **PLUS** Metronidazole 500mg IV q8h **4. Brain abscess arising from hematogenous spread (hospital acquired) or post- neurosurgical operation:** *Vancomycin 25-30mg/kg loading dose then 15-20mg/kg IV q8-12h; not to exceed 2gm per dose **PLUS** Ceftazidime 2gm IV q8h **OR** Cefepime 2gm IV q8h **OR** Meropenem 2 g IV q8h		Duration to be determined by clinical response (usually 4-8 weeks with IV therapy for 2 weeks minimum depending on whether surgical drainage done, clinical and radiological response). Third generation cephalosporins are recommended if the source is from the sinus or otogenic source. Benzylpenicillin is recommended if the source is from oral cavity. Add cloxacillin if suspected hematogenous spread, post-neurosurgeries or post penetrating injuries. If post neurosurgery or trauma, consider cover for pseudomonas.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Spinal Epidural abscess Common organism: *Streptococci* *Staphylococcus* Gram-negative bacilli	Cloxacillin 2gm IV q4h **OR** *Vancomycin 25-30mg/kg loading dose then 15mg/kg IV q8-12h; not to exceed 2gm per dose **PLUS** Gentamicin 4-7mg/kg/day IV in 3 divided doses **OR** **Ceftriaxone 2gm IV q12h **OR** **Cefotaxime 2gm IV q4-6h		Source control is strongly recommended. Duration to be determined by clinical response (usually 2-6 weeks with IV therapy for 2 weeks minimum, followed by oral depending on whether surgical drainage done, clinical and radiological response). *Vancomycin loading dose refer to Appendix 1. Vancomycin is indicated when suspecting MRSA or allergy to Cloxacillin. **3rd Generation Cephalosporin indicated when Gentamicin is contraindicated.
Viral encephalitis Common organisms: *Herpes simplex* *Varicella zoster*	*Acyclovir 10mg/kg IV q8h		*Consider using Ideal Body weight in obese patients. Duration: 14-21 days
Meningitis (Chronic)			
Tuberculous meningitis *Mycobacterium tuberculosis*	Intensive 2 months S/EHRZ **and** 10 months HR Isoniazid (H) 5(4-6)mg/kg/day PO (max: 300mg/day) **PLUS** Rifampicin (R) 10(8-12)mg/kg/day PO (max: 600mg/day) **PLUS** Pyrazinamide (Z)	Infection in HIV patients: Recommendations for the treatment of TB in HIV-infected adults are **identical** to those for HIV-uninfected adults when the disease is caused by organisms that are **known or presumed to be susceptible to the first-line drugs**. Daily dosing is recommended rather than intermittent dosing.	Add dexamethasone 12-16mg daily in divided doses for 6 weeks in tapering doses (intravenously initially, then switch to oral when safe to do so). Alternatively, prednisolone 30-40mg/day PO in tapering doses for 6 weeks. Treatment is continued for 12 months.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
	25 (20-30)mg/kg/day PO (max: 2000mg/day) **PLUS** Streptomycin (S) 15 (12-18)mg/kg/day IM (max: 1000mg/day) **OR** Ethambutol (E) 15 (15-20)mg/kg/day PO (max: 1600mg/day) Pyridoxine 10-50mg PO q24h needs to be prescribed together with Isoniazid	Rifampicin is not recommended in combination with all protease inhibitors (PIs) and rifabutin should be used with PI-based HAART for HIV-TB co-infected adults.	Refer to Clinical Practice Guidelines on Management of Tuberculosis (3rd edition) MOH/P/PAK/258.12(GU).
Cryptococcalmeningitis *Cryptococcus neoformans* (non-HIV, non-transplant pt)	**Induction Therapy**: Amphotericin B 0.7-1.0mg/kg/day IV q24h **PLUS** 5-Flucytosine 100-150mg/kg/day PO q6h **OR** Fluconazole 800-1200mg PO q24h	**Induction Therapy**: Fluconazole 1200mg PO q24h **PLUS** 5-flucytosine 100-150mg/kg/day PO q6h	Lipid formulations of amphotericin may be used in cases of severe nephrotoxicity. Duration of induction therapy: 4-6 weeks
	Consolidation Therapy: Fluconazole 400-800mg PO q24h		Duration of consolidation therapy: 8 weeks
	Maintenance Therapy: Fluconazole 200mg PO q24h		Duration of maintenance therapy: up to 12 months
Healthcare-associated ventriculitis and meningitis	Empirical treatment should be decided by the primary team based on local antibiogram and CSF gram stain result.		De-escalate antibiotics to targeted therapy when the culture results are available.
	If C&S is not available: Ceftazidime 2gm IV q8h	Meropenem 2gm IV q8h	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	PLUS/MINUS *Vancomycin 25-30mg/kg loading dose then 15-20mg/kg IV q8-12h; not to exceed 2gm per dose	**PLUS/MINUS** *Vancomycin 25-30mg/kg loading dose then 15-20mg/kg IV q8-12h; not to exceed 2gm per dose	*Vancomycin trough level should be 10-14µmol/L or 15-20mcg/L *Vancomycin loading dose refer to Appendix 1.
Cranial Trauma **Open fracture &** **Penetrating injuries**	Amoxicillin/clavulanate 1.2gm IV q8h	Cefuroxime 1.5gm IV q8H **PLUS** Metronidazole 500mg IV q8H	Duration: 5-7 days
Penetrating craniocerebral injuries	Ceftriaxone 2gm IV q12h **PLUS** Metronidazole 400mg PO q8h for 2 weeks initially and then review with microbiology		
Neurosyphilis	Refer to section (Sexually Transmitted Infections) Treatment is the same for neurosyphillis in patients with HIV infection		
HIV related CNS infection	Refer to section (Infections in Immunocompromised Patients - Human Immunodeficiency Virus)		

References:

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2. Pasquale Pagliano et al. Listeria monocytogenes meningitis in the elderly: epidemiological, clinical and therapeutic findings. Le Infezioni in Medicina, n. 2, 105-111, 2016
3. van de Beek, D. et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clinical Microbiology and Infection, Volume 22 , S37 - S62
4. McGill, F. et al. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults.Journal of Infection, Volume 7, Issue 4 , 405 – 438.
5. Solomon, T. et al. Management of suspected viral encephalitis in adults – Association of Brithish Neurologist and Brithish Infection Association National Guidelines. Journal of Infection, Volume 64, Issue 4 , 347 – 373.
6. Allan R. Tunkel et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis, Clinical Infectious Diseases, Volume 64, Issue 6, 15 March 2017,
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8. The Sanford Guide to Antimicrobial Therapy 2018.
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11. Chaudhuri A. et al. EFNS guideline on the management of community-acquired bacterial meningitis: report of an EFNS Task Force on acute bacterial meningitis in older children and adults. European Journal of Neurology 2008, 15: 649–659
12. Allan R. Tunkel et al. Practice Guidelines for the Management of Bacterial Meningitis Clinical Infectious Diseases 2004; 39:1267–84

A3. CHEMOPROPHYLAXIS

A3.i SURGICAL

The goal of antimicrobial prophylaxis is to prevent surgical site infection by reducing the burden of microorganisms at the surgical site during the operative procedure.

Single-dose prophylaxis is usually sufficient. If antimicrobial prophylaxis is continued post-operatively, duration should be less than 24 hours (up to 48 hours for cardiac surgery), regardless of the presence of intravascular catheters or indwelling drains.

If presence of pre-existing infections (known or suspected), use appropriate treatment regimen instead of prophylactic regimen for procedure. However, re-dosing is required just prior to skin incision.

The optimal time for administration of pre-operative antibiotics is 60 minutes prior to surgical incision. Some agents, such as fluoroquinolones and vancomycin, require administration over one to two hours; therefore, the administration of these agents should begin within 120 minutes before surgical incision.

An additional dose of prophylactic antibiotic during operation is indicated if:

- Excessive blood loss (>1500 ml)
- Procedures exceed two half-life of the drug
- if there are other factors that may shorten the half-life of the prophylactic agent (e.g. extensive burns)

Antimicrobial	Recommended Redosing Interval in Adults with Normal Renal Function (From Initiation of Preoperative Dose), (hr)
Cefazolin	4
Cefuroxime	4
Ampicillin/Sulbactam	2
Metronidazole	NA
Clindamycin	6
Vancomycin	NA
Gentamicin	NA
Amoxicillin/Clavulanate	3
Benzylpenicillin	2

For patients with penicillin allergy, vancomycin or clindamycin is recommended unless stated otherwise. The dose of Vancomycin is according to patient's body weight, as follows:

- <75 kg: 1 gm infused over 60 minutes
- ≥75 kg: 1.5 gm infused over 90 minutes

Administration of cefazolin in obese patients:

- 2 gm if body weight <120 kg
- 3 gm if body weight ≥120 kg

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
1. OBSTETRICS & GYNAECOLOGY SURGERY			
Cesarean Section a. Elective b. Emergency	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Ampicillin/sulbactam 3gm IV	
Elective surgery: TAHBSO Hysterectomy (vaginal or abdominal) Laparascopy (vagina and/or uterus entered)	Cefazolin 2gm IV (3 gm IV for patients weighing ≥120 kg) **OR** Cefuroxime 750mg IV **PLUS** Metronidazole 500mg IV	Ampicillin/sulbactam 3gm IV	Consider second or additional dose for prolonged procedures.
Laparoscopic surgery (vagina and/or uterus not entered)	Antibiotic not recommended	Antibiotic not recommended	
Repair of perineal tear e.g. third or fourth degree tears	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg) **PLUS** Metronidazole 500mg IV	Ampicillin/sulbactam 3gm IV	Duration: 5- 7days
Surgical termination of pregnancy	Doxycycline 400mg PO as a single dose (1 hour prior to procedure) **OR** Azithromycin 1gm PO (1 hour prior to procedure)		No evidence outcomes are improved by including Metronidazole in prophylactic regimens.[2]
Emergency laparotomy	As per elective surgery		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
References: 1. Bratzler DW, Dellinger EP, Olsen KM et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*.2013; 70:195-283 2. Antibiotic Expert Groups. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines Limited; 2014. 3. Van Eyk N, van Schalkwyk J, Infectious Diseases Committee. J ObstetGynaecol Can. 2012 Apr; 34(4):382-391. 4. Van Schalkwyk J, Van Eyk N et al. No 247 – Antibiotic Prophylaxis in Obstetric Procedures. 5. Journal of Obstetrics and Gynaecology Canada, Volume 39, Issue 9, September 2017, Pages e300-e308.			
2. OTORHINOLARYNGOLOGY SURGERY			
HEAD AND NECK			
Clean	Antibiotic not required	Antibiotic not required	
Clean with placement of prosthesis (excludes tympanostomy tubes)	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)		
Clean-contaminated cancer surgery Other clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg) **PLUS** Metronidazole 500mg IV	Cefuroxime 1.5gm IV **PLUS** Metronidazole 500mg IV **OR** Ampicillin/sulbactam 3gm IV	
References: 1. Simo R, French G. The use of prophylactic antibiotics in head and neck oncological surgery. *CurrOpinOtolaryngolHead Neck Surg.* 2006; 14:55-61 88			
3. ORAL / DENTAL SURGERY			
Clean Surgery (Class 1) ● Submandibular gland surgery ● TMJ surgery ● Excision of benign tumours /cysts Minor Clean-contaminated surgery (Class 2) ● Soft tissue surgery ● Dentoalveolar surgery*	Not indicated for most surgeries May be indicated i. if the duration of the surgery is expected to be very long ii. for open reduction and internal fixation of facial bone fractures		Prophylaxis is recommended for all patients with an increased risk of surgical wound infection - i.e. in immunocompromised patients. *In patients with cardiac conditions with increased risk of Infective Endocarditis,

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
• Periodontal surgery			chemoprophylaxis is indicated. Please refer to Chemoprophylaxis Non-Surgical section.
Minor Clean-contaminated surgery (Class 2) • Insertion of dental implants and use of graft material • High degree of difficulty / long duration	Amoxicillin 1gm PO **OR** Clindamycin 600-900mg PO/IV **OR** Benzylpenicillin 2MU IV	Amoxicillin/clavulanate 1.25gm PO or 1.2gm IV **OR** Cefuroxime 500mg PO or 1.5gm IV	
Major Clean-contaminated surgery (Class 3) • Orthognathic surgery • Excision / enucleation of large benign tumours / cysts • All oral cancer surgery • Open reduction and internal fixation of facial bone fractures	Benzylpenicillin 2MU IV **OR** Clindamycin 600-900mg IV	Amoxicillin/clavulanate 1.2gm IV **OR** Cefuroxime 1.5gm IV	For oral & maxillofacial fractures, antibiotics is recommended for the immediate post trauma period and should be discontinued once open reduction and internal fixation is completed.
Reference: 1. Oral Health Division Ministry of Health Malaysia. Antibiotic Prophylaxis in Oral Surgery for Prevention of Surgical Site Infection. Putrajaya: Dental Technology Section Oral Health Division (OHD) Ministry of Health Malaysia; 2015.			
4. PLASTIC SURGERY			
Not indicated: for the majority of clean procedures*, unless the patient has risk factors for postoperative infection (e.g. implantation of prosthetic material, prior skin irradiation). The continuation of antibiotics while waiting for non-infected skin grafts or flaps to epithelialize is not evidence-based.			
For clean–contaminated procedures	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Amoxicillin/clavulanate 1.2gm IV	
Reference: 1. Antibiotic Expert Groups. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines Limited; 2014.			
5. VASCULAR SURGERY			
Amputation of ischemic limb	Ampicillin/sulbactam 3gm IV	Amoxicillin/clavulanate 1.2gm IV	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Suspected organism: Staphylococcus spp. & anaerobic organism			
Open and endovascular repair of abdominal aneurysm	Amoxicillin/clavulanate 1.2gm IV	**Penicillin Allergy:** Vancomycin 1gm IV (1.5gm IV for patients weighing ≥75 kg)	Penicillin allergy refer to Appendix 8
Bypass surgery	Amoxicillin/clavulanate 1.2gm IV	**Penicillin Allergy:** Vancomycin 1gm IV (1.5gm IV for patients weighing ≥75 kg)	Penicillin allergy refer to Appendix 8
Arteriovenous graft	Amoxicillin/clavulanate 1.2gm IV **<u>If High Risk For MRSA:</u>** Vancomycin 1gm IV (1.5gm IV for patients weighing ≥75 kg)		MRSA risk (defined as history of MRSA colonisation or infection, **OR** inpatient of high risk hospital or unit (where MRSA is endemic).
Reference: 1. Bratzler DW, Dellinger EP, Olsen KM et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*.2013; 70:195-283			
6. GENERAL SURGERY			
Procedures involving entry into lumen of gastroinstestinal tract (bariatric, pancreaticoduodenectomy)	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV	
Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high risk patients	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Appendectomy for uncomplicated appendicitis Colorectal	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg) **PLUS** Metronidazole 500mg IV **OR** Ampicillin/sulbactam 3gm IV	Cefuroxime 1.5gm IV **PLUS** Metronidazole 500mg IV **Penicillin Allergy:** Clindamycin 600-900mg IV **PLUS** Gentamicin 5mg/kg IV	Penicillin allergy refer to Appendix 8
Small intestine	**Non-obstructed:** Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV **Penicillin Allergy** Clindamycin 600-900mg IV **PLUS** Gentamicin 5mg/kg IV	Penicillin allergy refer to Appendix 8
	Obstructed: Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg) **PLUS** Metronidazole 500mg IV	Cefuroxime 1.5gm IV **PLUS** Metronidazole 500mg IV **Penicillin Allergy:** Clindamycin 600-900mg IV **PLUS** Gentamicin 5mg/kg	
Hernia repair with mesh	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Amoxicillin/clavulanate 1.2gm IV **OR** Ampicillin/sulbactam 3gm IV	Includes laparoscopic repair Single / stat dose only.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Breast cancer surgery	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Amoxicillin/clavulanate 1.2gm IV **OR** Ampicillin/sulbactam 3gm IV	The benefits of routine postoperative antibiotic doses in reconstruction surgery are uncertain; there may be a benefit in obese patients or those treated with radiation therapy. The need for postoperative doses should be considered on an individual patient basis; if used, postoperative prophylaxis should not exceed 24 hours.[2]
Breast reshaping procedures	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Amoxicillin/clavulanate 1.2gm IV **OR** Ampicillin/sulbactam 3gm IV	
Breast surgery with implant (reconstructive or aesthetic)	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Amoxicillin/clavulanate 1.2gm IV **OR** Ampicillin/sulbactam 3gm IV	

References:
1. Bratzler DW, Dellinger EP, Olsen KM et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*.2013; 70:195-283
2. Antibiotic Expert Groups. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines Limited; 2014.

7. ORTHOPAEDIC SURGERY			
Clean operations involving hand, knee, or foot and not involving implantation of foreign materials	None	None	
Internal fixation of all closed fracture/ Total Joint Replacement/ Spine surgery (with and without instrumentation)/ Arthroscopy	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV **<u>Penicillin/Cephalosporin Allergy:</u>** Clindamycin 600-900mg IV	The benefits of routine postoperative antibiotic are uncertain. If used, postoperative prophylaxis should not exceed 24 hours. Penicillin allergy refer to Appendix 8

References:
1. Bratzler DW, Dellinger EP, Olsen KM et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm*.2013; 70:195-283
2. T.P Ruedi ,R.GBuckley,C.GMarani,AO principle of fracture management. A.H.R.W Simpson, BMJ 2015

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
8. UROLOGICAL SURGERY			
A. Diagnostic Procedures			
Transrectal ultrasound and prostate biopsy Common organisms: *Escherichia coli*, Klebsiella, Proteus, Enterococcus, Pseudomonas	Ciprofloxacin 500mg PO q12h for 3 days (start 24 hours before procedure) **PLUS/MINUS** Gentamicin 80mg IV single dose given 30-60 minutes before procedure	Targeted antibiotic therapy based on pre-operative rectal swab result.	Consider Povidone-iodine bowel preparation to further decrease infection risk.
Cystoscopy/ Urodynamics study	Antibiotic not recommended	Antibiotic not recommended	Prophylaxis only for high risk cases (immunocompromised patients, e.g. debilitated patients on long term catheters, patient with prosthesis/heart valves, diabetics, transplant recipients): Cefuroxime 250mg PO stat. If heart valve: Follow recommendation for SBE prophylaxis.
Retrograde pyelogram/Ureteric stenting	Cefuroxime 250mg PO stat		
B. Endourology			
Endourological surgery *e.g.* PCNL, URS, RIRS, TURP Common organisms: *Escherichia coli*, Klebsiella, Proteus, Enterococcus, Pseudomonas	Amoxicillin/clavulanate 1.2gm IV **OR** Ampicillin/sulbactam 3gm IV	Cefuroxime 1.5gm IV **OR** Ceftazidime 2gm IV (if urine grew *Pseudomonas*)	Antibiotic selection to be determined based on patient's latest urine culture result.
C. Open Surgery			

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Clean operations e.g. orchidectomy, orchidopexy, varicocelectomy, deroofing renal cysts	Antibiotic not required	Antibiotic not required	
Clean-contaminated (with opening of urinary tract) e.g. nephrectomy, prostatectomy, open stone surgery. Common organisms: *Escherichia coli*, Klebsiella, Proteus, Enterococcus, Pseudomonas	Amoxicillin/clavulanate 1.2gm IV q8h for 1 day **OR** Ampicillin/sulbactam 3gm IV q8h for 1 day	Cefoperazone 1gm IV q12h for 1 day **OR** Ceftazidime 2gm q8h IV for 1 day (if urine grew *Pseudomonas*)	
Clean-contaminated (with use of bowel segments) e.g. Cystectomy with urinary diversion, cystoplasty. Common organisms: *Escherichia coli*, Klebsiella, Proteus, Enterococcus, Pseudomonas, anaerobes	Cefoperazone 1gm IV q12h **PLUS** Metronidazole 500mg IV q8h	Gentamicin 1.5mg/kg IV q8h **PLUS** Metronidazole 500mg IV q8h	For duration of catheter presence.
Implant of prosthetic devices e.g. Insertion of penile prosthesis or artificial urinary sphincter, artificial slings Common Organism: *Staphylococcus aureus*	Cefuroxime 1.5gm IV q8h for 1 week	Amoxicillin/clavulanate 1.2gm IV q8h for 1 week **OR** Ampicillin/sulbactam 3gm IV q8h for 1 week	
Laparoscopic surgery	As for open surgery	As for open surgery	Depending on type of procedure performed whether clean or clean– contaminated.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Reference: 1. Pickard R., Bartoletti R., Bjerklund-Johansen TE., Bonkat G., Bruyere F., Cek M. et al. members of the EAU – ESTRO – ESUR –SIOG Urological Infections Guidelines Panel. EAU – ESTRO – ESUR – SIOG Guidelines on Urological Infections. Edn. presented at the EAU Annual Congress London 2017. 978-90-79754-91-5. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands.			
9. NEUROLOGICAL SURGERY			
Clean wounds (Uninfected operative wounds in which no inflammation is encountered and no viscus is entered during the procedures) Elective craniotomy or spinal procedures.	Cefuroxime 1.5gm IV (Given as a single IV dose at induction or within 60 minutes before incision. For prolonged procedures, additional intraoperative doses are given at every 4 hours interval during surgery in patients with normal renal function)	Vancomycin 15-20mg/kg IV (max 2g) (Infusion is started within 60-120 min before incision. Additional redose interval is at every 12 hours during surgery in patients with normal renal function) **OR** Telcoplanin 400mg IV (Given as a single IV dose at induction)	Situation where the use of vancomycin is appropriate: - • In hospitals in which MRSA or S.epidermidis are frequent causes of postoperative wound infection, • In patients previously colonized with MRSA, or • Those who are allergic to penicillins or cephalosporins. Rapid IV administration of Vancomycin may cause hypotension.
Clean wounds with Foreign Body or Instrumentation. CSF shunting procedures, implantation of cranial or spinal implants.	Cefuroxime 1.5gm IV **PLUS** Metronidazole 500mg IV (Given as a single IV dose at induction or within 60 minutes before incision. Additional redose interval is at every 4 hours during surgery in patients with normal renal function)	Vancomycin 15-20mg/kg IV (max 2g) **OR** Telcoplanin 400mg IV **PLUS** Gentamicin 5mg/kg IV (Given as a single IV dose at induction or within 60 minutes before incision in patients with normal renal function) **PLUS** Metronidazole 500mg IV (Given as a single IV dose at induction or within 60 minutes before incision. Additional redose interval is at 4 hours	Addition of another drug such as metronidazole and aminoglycoside is appropriate for procedures in which anaerobic and enteric gram negative bacilli or anaerobic are common pathogens.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		during surgery in patients with normal renal function)	
Clean-contaminated wounds (Operative wounds in which a viscus is entered and without unusual contaminations) Procedures that breach air cells or nasal or oral cavity.	Cefuroxime 1.5gm IV **PLUS** Metronidazole 500mg IV	Vancomycin 15-20mg/kg IV (max 2g) **OR** Telcoplanin 400mg IV **PLUS** Gentamicin 5mg/kg IV **PLUS** Metronidazole 500mg IV	
Contaminated wounds (Open, fresh accidental wounds, operation with major breaks in sterile technique, or gross spillage from a viscus)	Ceftriaxone 2gm IV (Given as a single IV dose at induction or within 60 minutes before incision. Additional redose interval is at every 12 hours during surgery in patients with normal renal function) **PLUS** Metronidazole 500mg IV	Vancomycin 15-20mg/kg IV (max 2g) **OR** Telcoplanin 400mg IV **PLUS** Gentamicin 5mg/kg IV **PLUS** Metronidazole 500mg IV	
Dirty wounds (Infected CSF shunt, Old traumatic wounds with retained devitalized tissue, foreign bodies or wounds that involve existing clinical infection or perforated viscus)	Ceftriaxone 2gm IV **PLUS** Metronidazole 500mg IV	Vancomycin 15-20 mg/kg IV (max 2g) **OR** Telcoplanin 400mg IV **PLUS** Gentamicin 5mg/kg IV **PLUS** Metronidazole 500mg IV	Settings where intraventricular antibiotics (vancomycin 10mg or gentamycin 5 mg) may be useful: • Failure to sterilize the CSF with IV therapy • Poor respond to IV systemic antibiotics • Presence of highly resistant organisms susceptible to only antibiotics with poor CSF penetration

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			• Circumstances in which shunt devices cannot be removed (including infected Ommaya reservoirs)
References: 1. Salford Royal, NHS. Antibiotic Prophylaxis in Cranial Neurosurgery Antibiotic Guidelines, Unique ID: 144TD(C)25(F4) Issue number: 6, 2018 2. SIGN 104 Antibiotic prophylaxis in surgery. July 2008, updated April 2014 3. Surgical Antimicrobial Prophylaxis Clinical Guideline v2.0. Department for Health and Ageing, Government of South Australia . October 2017			
10. CARDIAC SURGERY			
Coronary artery bypass	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV	
Cardiac device insertion procedures (eg. Pacemaker implantation)	Cefazolin 2gm IV (3gm IV for patients weighing ≥120 kg)	Cefuroxime 1.5gm IV	
Reference: 1. Bratzler DW, Dellinger EP, Olsen KM et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health-Syst Pharm.2013; 70:195-283			
11. OPHTHALMOLOGY SURGERY			
The use of povidone iodine 10% to the periorbital skin and 5% to the conjunctival sac as an antiseptic agent for preoperative surgical site preparations are recommended.			
Intracameral injection of 1mg Cefuroxime in 0.1ml at the end of cataract surgery is recommended. Careful dilution should be undertaken to prevent potential toxicity.			
Topical antibiotics at end of surgery.			
Reference: 1. Prophylaxis for intraocular surgery-CPG for Management of Post-Operative Endophthalmitis, Ministry of Health Malaysia, August 2006			
12. HEPATOBILIARY SURGERY			
Laparoscopic procedures Low risk	Cefazolin 2 gm (3 gm IV for patients weighing ≥120 kg)		1. Optimum antibiotic timing is to complete intravenous infusion ≤60min (optimal window 15 to 45 min) prior to skin incision ; to ensure adequate time to reach bactericidal serum and tissue concentration before skin is incised. 2. Repeat intraoperative dosing is recommended in : • Prolonged surgery > 4 hours
Laparoscopic procedures High risk : Stent insertion Biliary obstruction (High direct bilirubin)	Cefazolin 2 gm IV (3 gm IV for patients weighing ≥120 kg) **PLUS** Gentamicin 5mg/kg IV (2mg/kg IV single dose if CrCl< 20)		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Open surgery Low risk	Cefazolin 2gm IV (3 gm IV for patients weighing ≥120 kg)		• Massive blood loss> 1.5 L Aminoglycosides should not be re-dosed
Open surgery High Risk Multiple ERCP (≥ 2) done with stenting Biliary obstruction Biliary infection or surgery within < 30 days	Cefazolin 2 gm IV (3 gm IV for patients weighing ≥120 kg) **PLUS** Gentamicin 5mg/kg IV (2mg/kg IV single dose if CrCl< 20) If high risk ESBL/Multi-resistant organisms, eg ESBL in the last 3/12 but treated Piperacillin/tazobactam 4.5gm IV **PLUS** Gentamicin 5mg/kg IV (2mg/kg IV single dose if CrCl< 20)		
Pre-exiting infection before surgery, GB empyema, ascending cholangitis	Initiate antibiotic according to culture results, or refer to treatment guidelines If patient is at risk of infection with Multi-drug resistant organism , to discuss with consultant surgeons/ ID physicians		

A3.ii NON-SURGICAL

Table 1: Patients with cardiac conditions are considered as being at increased risk of developing IE and are indicated for antimicrobial prophylaxis prior to certain procedures.

TABLE 1	
1.	Prosthetic cardiac valves or prosthetic material used for cardiac valve repair
2.	Established rheumatic heart disease
3.	Previous history of infective endocarditis
4.	Unrepaired cyanotic congenital heart disease (CHD), including palliative shunts and conduits
5.	Completely repaired CHD with prosthetic material or device, for first 6 months after the procedure
6.	Repaired CHD with residual defects at the site or adjacent to the site of the prosthetic device (which inhibit endothelisation)
7.	Cardiac transplantation recipients who develop cardiac valvulopathy

Dental Procedures
For patients considered as high risk (table 1), antimicrobial prophylaxis is recommended for invasive dental procedures involve manipulation of gingival tissue or the periapical region of teeth or perforation of gingival mucosa.

Even with high cardiac risk of infective endocarditis, antibiotic prophylaxis is not recommended for

- local anaesthetic injections in non-infected tissues
- treatment of superficial caries
- removal of sutures
- dental X-rays
- placement or adjustment of removable prosthodontic or orthodontic appliances or braces
- following the shedding of deciduous teeth
- trauma to the lips and oral mucosa

Respiratory Tract Procedures:
Antimicrobial prophylaxis is recommended for patients with increased risk of IE (table 1) who undergo an invasive respiratory tract procedure that involve incision or biopsy of the respiratory mucosa. Patients who undergo an invasive respiratory tract procedure to treat an established infection, e.g. biopsy drainage of an abscess, should receive an antibiotic prophylaxis which contains an anti-staphylococcal agent.

Gastrointestinal or genitourinary procedures:
Routine pre-procedural antimicrobial prophylaxis is no longer recommended for patients undergoing genitourinary or gastrointestinal tract procedures. However, for high risk cardiac patients (table 1) who have an established gastrointestinal or genitourinary infection, or for those who receive antimicrobial therapy for surgical reasons, the antimicrobial regimen should include an agent active against enterococci, such as ampicillin or vancomycin.

Dermatological or musculoskeletal procedures:
For patients described in table 1 undergoing surgical procedures involving infected skin (including local abscesses), skin structure or musculoskeletal tissue, it is reasonable that the therapeutic regimen contains an agent active against staphylococci and beta-hemolytic streptococci. Vancomycin or clindamycin may be used in patients unable to tolerate a β-lactam antibiotic. If the infection is known or suspected to be caused by MRSA, vancomycin or another suitable agent should be administered.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
PROPHYLACTIC REGIMENS FOR HIGH-RISK DENTAL PROCEDURES IN HIGH-RISK PATIENTS			
Prophylactic Regimes	Amoxicillin 2gm PO single dose 30 to 60 minutes before procedure **OR** Ampicillin 2gm IV single dose 30 to 60 minutes before procedure	**Penicillin Allergy** : Clindamycin 600mg PO or IV single dose 30 to 60 minutes before procedure **Alternative**: Cefazolin 1gm IV single dose 30 to 60 minutes before procedure	See above for antibiotic prophylaxis in patients undergoing invasive surgical procedure to treat an established infection. Penicillin allergy refer to Appendix 8
SECONDARY PREVENTION OF RHEUMATIC FEVER			
Secondary Prevention of Rheumatic Fever	**Parenteral prophylaxis:** Benzathine Penicillin 1.2MU IM every 3 to 4 weeks **Oral prophylaxis:** Phenoxymethylpenicillin (Penicillin V) 250mg PO q12h	**Penicillin Allergy:** Erythromycin Ethylsuccinate 800mg PO q12h	Penicillin allergy refer to Appendix 8

TYPE OF INFECTION	DURATION OF TREATMENT
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	10 years or until 40 years of age, whichever is longer; sometimes lifelong prophylaxis
Rheumatic fever with carditis but no residual heart disease (no valvular disease)	10 years or until 21 years of age, whichever is longer
Rheumatic fever without carditis	5 years or until 21 years of age, whichever is longer

References:
1. Ministry of Health Malaysia's Clinical Practice Guidelines For The Prevention, Diagnosis & Management Of Infective Endocarditis 2017
2. ESC Guidelines on Prevention of Infective Endocarditis 2015
3. The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
HELICOBACTER PYLORI INFECTION			
Helicobacter Pylori Infection	**First line Treatment** Triple Therapy: Proton Pump Inhibitors PO q12h **PLUS** Amoxicillin 1gm PO q12h **PLUS** Clarithromycin 500mg PO q12h **OR** Metronidazole 400mg PO q12h	**<u>Penicillin Allergy</u>** Proton Pump Inhibitors PO q12h **PLUS** Clarithromycin 500mg PO q12h **PLUS** Metronidazole 400mg PO q12h	Dosages of Proton Pump Inhibitors: Omeprazole 20 mg PO q12h Pantoprazole 40 mg PO q12h Lansoprazole 30 mg PO q12h Esomeprazole 20 mg PO q12h Rabeprazole 20 mg PO q12h First line therapy recommended in areas with <15-20% Clarithromycin resistance. Consider 2nd line if Clarithromycin resistance exceed more than 15%[1] Duration of therapy = 14 days Meta-analysis of RCTs found 14 days duration of therapy showed greater eradication rate[2, 3]. Penicillin allergy refer to Appendix 8
	Second Line Treatment[1] <u>Bismuth Quadruple regimen:</u> Proton Pump Inhibitors PO q12h **PLUS** Bismuth subsalicylate 300mg **OR** Bismuth subcitrate 120-300mg PO q6h **PLUS** Tetracycline hydrochloride 500mg PO q6h **PLUS** Metronidazole 400mg PO q8h <u>Fluroquinolone triple therapy:</u>		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Proton Pump Inhibitors PO q12h **PLUS** Levofloxacin 500mg PO q24h **PLUS** Amoxicillin 1gm PO q12h **OR** Metronidazole 400mg PO q12h		

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1. Malfertheiner P et al.Management of *Helicobacter pylori* infection--the Maastricht IV/ Florence Consensus Report .Gut 2012;61: 646 – 64.
2. V. Mahachaiet al., "H. Pylori management in ASEAN: the Bangkok consensus report," Journal of Gastroenterology and Hepatology, vol. 33, no. 1, pp. 37–56, 2017
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OROPHARYNGEAL CANDIDIASIS	
Refer to section (Infections in Immunocompromised Patients - HIV)	
ESOPHAGITIS	
Candida	Refer to section (Infections in Immunocompromised Patients - HIV)
Herpes simplex virus	Refer to section (Sexually Transmitted Infections)

INFECTIOUS DIARRHOEA

Most community-acquired diarrhoea is viral in origin (norovirus, rotavirus, and adenovirus), antibiotic therapy does not shorten the duration of symptoms, therefore should be discouraged.

When to consider empirical treatment for acute diarrhea?

- Immunocompetent host with high grade or persistent fever, or with dysentery or in sepsis
- Immunocompromised host
- Suspected enteric fever

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
EMPIRICAL THERAPY			
Empirical treatment	Ciprofloxacin 500mg PO q12h **OR** Azithromycin 500mg PO q24h		Duration: 3 days
PATHOGEN-DIRECTED THERAPY			
Non-shiga toxin producing (STEC), A*eromonas/Plesiomonas* *Yersinia* species	Trimethoprim/sulfamethoxazole 160/800mg PO q12h	Ciprofloxacin 500mg PO q12h	Duration: 3 days
Campylobacter jejuni	Azithromycin 500mg PO q24h		Duration: 3 days In immunocompromised: consider longer duration of therapy
Salmonella, non-typhi	Trimethoprim/sulfamethoxazole 160/800mg PO q12h	Ciprofloxacin 500mg PO q12h **OR** Azithromycin 500mg PO q24h **OR** Ceftriaxone 2gm IV q24h	Duration: Immunocompetent: 5-7 days Immunocompromised: 14 days Antibiotic is usually not indicated , except in patient - < 6 months old or >50 years old - with severe illness or in septic shock - with prostheses, valvular heart disease or severe atherosclerosis - with malignancy - who is immunocompromised
Salmonella, non-typhi (in HIV patients)	Refer to section (Infections in Immunocompromised Patients - HIV)		
Salmonella typhi	Refer to section (Tropical Infections)		
Vibrio cholera	Primary therapy is rehydration. Azithromycin 1gm PO single dose	Erythromycin Ethylsuccinate 800mg PO q12h for 3 days	Antibiotic is to reduce the shedding time

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	OR Doxycycline 300mg PO single dose		
Shigella sp. (Fever and bloody stool)	Ciprofloxacin 750mg PO q12h for 3 days	Azithromycin 500mg PO q24h for 3 days **OR** Trimethoprim/sulfamethoxazole 160/800mg PO q12h for 3 days **For severe disease:** Ceftriaxone 2gm IV q24h for 2-5 days	In immunocompromised patients duration of antibiotic is 7-10 days.
Giardiasis	Metronidazole 400mg PO q8h		Duration: 7 – 10 days
Entamoeba histolytica	Metronidazole 800mg PO q8h for 5–10 days **PLUS** *Paromomycin 500mg PO q8h for 7 days		*Requires DG's Approval
CLOSTRIDIUM DIFFICILE INFECTION			
Discontinue therapy with inciting antibiotic agent as soon as possible as may influence risk of CDI recurrence.			
Initial (Non-severe)	Vancomycin 125mg PO q6h	Metronidazole 400 mg PO q8h	Duration: 10 days
Initial (Severe)	Vancomycin 125mg PO q6h	Metronidazole 500mg IV q8h **PLUS** Vancomycin 125mg PO q6h	Symptoms to indicate severe colitis: • WCC >15 x 10^9 • Creatinine 50% increase from baseline • Temperature > 38.5ºC • Evidence of severe colitis (abdominal signs; radiography)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			Duration: 10 days
Initial (Fulminant/Severe with complications)	*Vancomycin 500mg PO q6h **PLUS** Metronidazole 500mg IV q8h		*If ileus, consider rectal instillation of Vancomycin (enema): Vancomycin 500mg (in 100 mL normal saline) q6h via enemas or by nasogastric tube Duration: 10 days
Recurrent	**If vancomycin was used for the initial episode:** Vancomycin pulsed-tapered regimen: 125mg PO q6h for 10-14 days, then 125mg PO q12h for 7 days, then 125mg PO q24h for 7 days, then 125mg PO q48-72h for 2-8 weeks	**If Metronidazole was used for the initial episode:** Vancomycin 125mg PO q6h for 10-14 days	Duration: 10 - 14 days

References :
1. Riddle et al. ACG clinical guideline: diagnosis, treatment, and prevention of acute diarrheal infections in adults. Am J Gastroenterol. 2016;111:602–622
2. Shane et al. 2017 IDSA CPG for the Diagnosis and Management of Infectious Diarrhea.CID 2017:65.
3. McDonald et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by IDSA and Society for Healthcare Epidemiology of America (SHEA).Clin Infect Dis.Feb 15,2018. doi:10.1093/cid/cix1085
4. UK: https://www.guidelines.co.uk/infection/phe-infectious-diarrhoea-guideline/252651.article
5. AUS: https://www.ncbi.nlm.nih.gov/pubmed/27062204

TRAVELLERS' DIARRHEA			
Mild Diarrhea Diarrhea that is tolerable, not distressing	Antibiotic is not indicated		
Moderate Diarrhea Diarrhea that is distressing or interferes with planned activities	Azithromycin 1gm PO single dose or 500mg PO q24h	Ciprofloxacin 750mg PO stat **OR** 500mg PO q12h	Antibiotic therapy may be considered Duration: 3 days

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Severe Diarrhea Diarrhea that incapacitating or completely prevents planned activities; Including all dysentery	Azithromycin 1gm PO single dose or 500mg PO	Ciprofloxacin 750mg stat **OR** 500mg PO q12h	Antibiotic therapy should be considered Duration: 3 days
References: 1. Riddle et al. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. J Travel Med 2017; 24:S57 2. https://www.racgp.org.au/afp/2015/januaryfebruary/advising-travellers-about-management-of-travellers%E2%80%99-diarrhoea/ (aus)			
LIVER ABSCESS			
Pyogenic liver abscess Common pathogens: Klebsiella spp *Escherichia coli*	**Empirical therapy** Ceftriaxone 2gm IV q24h **OR** Cefotaxime 2gm IV q8h **PLUS/MINUS** Metronidazole 500mg IV q8h	**Empirical therapy** Ceftriaxone 2gm IV q24h **PLUS/MINUS** *Metronidazole 500mg IV q8h	Duration : 4-6 weeks To consider drainage if abscess size is ≥5cm or impending rupture. *Metronidazole**:** Risk factors of anaerobic liver abscess: • acute and chronic inflammatory bowel disease with or without perforation • malignancy of gastrointestinal tract • surgery of the gastrointestinal • tract or pelvic organs Metronidazole has excellent bioavailability: consider IV to PO switch (refer to appendix 7).
Amoebic liver abscess *Entamoeba histolytica*	Amoebicidal agent: *Metronidazole 750mg IV q8h for 10 days followed by		*May switch to PO when there is satisfactory clinical improvement. dose: Metronidazole 800 mg PO q8h Drainage of amoebic liver abscess is not usually required but is necessary if:

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Luminal agent: -To eradicate intestinal colonization after Amoebicidal treatment **Paromomycin 25-35mg/kg/day PO q8h for 7 days		1. The patient does not respond to antibiotic therapy 2. The abscess is >5 cm in diameter 3. The abscess is in the left lobe of the liver 4. The diagnosis remains in doubt ** Requires DG's approval.

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1. Anesi,J and GluckmanS.Amebic Liver Abscess Clinical Liver Disease, Vol 6, No 2, August 2015
2. Stanley etal. Amoebiasis , *Lancet* 2003; 361: 1025–34
3. Hope etl. Optimal treatment of hepatic abscess. Am Surg. 2008;74:178-182

CHOLECYSTITIS AND CHOLANGITIS			
Community acquired Common organisms: • Enterobacteriaceae is the commonest organism(>50%)[1] • Bacteroides only comprise 4-20% of biliary infection	Amoxicillin/clavulanate 1.2gm q8h	3rd gen. Cephalosporins: Cefoperazone 1-2gm IV q12h **OR** Cefotaxime 2gm IV q8h **PLUS/MINUS** Metronidazole 500mg IV q8h (if biliary enteric anastomosis is present)	Duration: 4- 7 days Appropriate source control to drain infected foci and restoration of anatomic and physiological function is recommended for all patients, as antibiotics will not enter bile in the presence of obstruction. *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
Hospital acquired	*Piperacillin/tazobactam 4.5 gm IV q6-8h		

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1. Gomi,H. et al. Tokyo Guidelines 2018: antimicrobial therapy for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci, 25: 3–16. doi:10.1002/jhbp.518
2. Joseph et al, Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America , CID 2010; 50:133–64

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
SPONTANEOUS BACTERIAL PERITONITIS (SBP)			
Primary SBP Common organisms: *Enterobacteriacea (eg: E. coli, K. pneumoniae, and Streptococcus sp.)*	Cefotaxime 2gm IV q8h **OR** Ceftriaxone 1gm IV q12h	Amoxicillin/clavulanate 1.2gm IV q8h	Duration: 5 days
In cirrhotic with upper gastrointestinal hemorrhage	Ceftriaxone 1gm IV q12h **OR** Cefotaxime 2gm IV q8h	Norfloxacin 400mg PO q12h	Duration: 7 days

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1. Bhuva et al. Spontaneous bacterial peritonitis: An update on evaluation, management, and prevention *Am J Med* 1994;97:169–175.
2. Rimola et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. *Journal of Hepatology 2000; 32: 142-153*
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A5. INFECTIONS IN IMMUNOCOMPROMISED PATIENTS

A5.i HAEMATOLOGY – ONCOLOGY

1. Any infection in the immunocompromised host is life-threatening and needs immediate attention. Febrile neutropenia is defined as a temperature of >38.3°C on a single occasion or >38°C for 2 hours and ANC (Absolute Neutrophil Count) <500 cells/uL or <1000 cells/uL in those with anticipated declining counts.

2. Cultures maybe positive in less than 40% of cases. Patients have impaired inflammatory responses and hence may have no localizing signs. The usual sign is fever >38°C or hypothermia. The common portals of infection include the oral cavity, gastrointestinal tract, perianal region, lungs and IV lines.

3. Potential pathogens are dependent on the underlying defect, e.g.

Neutropenia	**Gram-negative organisms, Gram-positive organisms, Fungi**
Hypogammaglobulinaemia **Post splenectomy/hyposplenic patients**	Encapsulated organisms
Defective cellular immunity	Pneumocystis jirovecii, Toxoplasma, Fungi Viruses, Mycobacteria

4. The use of growth factors e.g. G-CSF may be considered as prophylactic use if the risk of febrile neutropenia is ≥ 20% due to chemotherapy which is used for treatment of hematological or solid tumour malignancy. The prophylactic use of growth factors significantly reduced the relative risk for severe neutropenia, febrile neutropenia and infection. It should be considered in high-risk patients with ANC<100/uL multiple organ dysfunction syndrome, pneumonia, invasive fungal infections or septic shock or patients with reduced bone marrow reserve due to extensive radiotherapy. However, there is no evidence that either G-CSF reduced the number of patients requiring intravenous antibiotics or lowered infection related mortality.

5. Attention must be paid to:

    a. Strict isolation measures.
    b. Patient's personal hygiene and diet.
    c. Modification of antibiotic regime if deterioration of clinical status or if there is no clinical improvement over 72-96 hours in a stable patient.
    d. The antibiotics are generally kept for a minimal duration of 5 to 7 days or stopped if afebrile for 2 days in patients who is asymptomatic with negative cultures and improving neutrophil *count ≥ $0.5x10^9$/l. (*refer to comment on low risk (out patient))
    e. Regular surveillance culture.
    f. Handwashing and strict aseptic technique.
    g. Venous cannula must be inspected daily for signs of phlebitis and changed every 72 hours or when necessary. Central devices are to be removed if there is clinical deterioration in spite of appropriate antibiotics for 48-72 hours, tunnel or pocket infections (implanted port system), atypical mycobacterial infection and candidemia

SUGGESTED EMPIRICAL ANTIBIOTIC THERAPY IN ADULT FEBRILE NEUTROPENIC PATIENTS

Low Risk (Outpatient)

Suitable low risk patients include:
- no evidence of dehydration or hypotension
- no evidence of pneumonia
- no COAD
- able to access prompt medical attention if deteriorates

Outpatient oral antibiotics may be considered after careful risk assessment and consultation with a hemato-oncologist:

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Low Risk (Outpatient)	Amoxicillin/clavulanate 625mg PO q8h **PLUS/MINUS** *Ciprofloxacin* 500mg PO q12h		Treat till counts > 0.5 x 10^9/L Can consider stopping the antibiotic after reassessing the patient following 2 days afebrile at the discretion of the treating hemato-oncologists – if the patient has stable vital signs, no evidence of ongoing infection, are educated about their condition and stay near to hospital facilities. *Add ciprofloxacin if patient is previously colonized by *Pseudomonas aeruginosa*

High Risk (Inpatient)

Risk assessment for complication of severe infection should be done during triage. Patient are deemed high risk if there is:
- prolonged and profound neutropenia with ANC <0.1x10^9/L
- hypotension
- pneumonia
- new onset abdominal pain or neurological signs

The administration of the first dose of empirical antibiotic with anti-pseudomonal coverage should be done as soon as possible following triage (within the first hour) after taking blood cultures. The suggested antibiotics are listed below.
Consider switch from intravenous to oral antibiotic in a clinically stable patient who has no gastrointestinal absorption issue.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
First line therapy	*Piperacillin/tazobactam 4.5gm IV q6-8h **PLUS/MINUS** **Amikacin 15mg/kg IV q24h	Cefepime 2gm IV q8h **PLUS/MINUS** **Amikacin 15mg/kg IV q24h **PLUS/MINUS** ***Metronidazole 500mg IV q8h	*Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours). **Amikacin may be added in patient with severe sepsis for broader gram negative coverage. It can be discontinued if microbiological cultures showed isolated organisms sensitive to Piperacillin/tazobactam or Cefepime and patient is clinically stable. ***Metronidazole may be added in the presence of: - severe mucositis - intra-abdominal infections - peri-anal abscesses - colitis
Severe sepsis or Second line therapy for persistent fever of 4 - 7 days and deterioration of clinical signs	Meropenem 1gm q8h **PLUS/MINUS** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose	Imipenem 500mg q6h or 1gm q8h (in severe sepsis) IV **PLUS/MINUS** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose	*Vancomycin loading dose refer to Appendix 1 *Vancomycin is not a routine in the initial antibiotic regime. Consider add vancomycin for patients: - colonized with MRSA - suspected to have catheter-related infection, skin and soft-tissue infection - in septic shock Stop vancomycin after 48 hours if no evidence of gram positive cocci. Linezolid is an alternative in those patients with no clinical response to vancomycin and in those

			with suspected or confirmed VRE, VISA or VRSA.

Antifungal therapy

It should be initiated earlier in the presence of:
- severe mucositis
- oral thrush
- dysphagia
- suspicious skin infiltrates or pulmonary infiltrates
- fundal exudates
- prolonged steroid use more than 2 weeks

IV Amphotericin B remains the empirical therapy of choice for invasive fungal infections. For patients who are intolerant, refractory or those with toxicity to conventional amphotericin B, the lipid formulations of amphotericin B, voriconazole and echinocandins are alternatives empirical therapy based on local availability and costs.

Voriconazole is an alternative to amphotericin B for preemptive and directed therapy for invasive aspergillosis.

In candidiasis, echinocandins, azoles and amphothericin B are antifungals of choice.

ANTIFUNGAL AGENT	DAILY DOSE
ABCD *(amphotericin B colloidal dispersion)*	3-4mg/kg (6mg/kg/day for IA) q24h
ABLC *(amphotericin B lipid complex)*	5mg/kg q24h
Ampho B deoxycholate *(conventional)*	0.7-1.0mg/kg q24h
Liposomal ampho B	3-5mg/kg q24h
Anidulafungin	200mg loading dose, followed by 100mg q24H
Caspofungin	70mg loading dose, followed by 50mg q24h
Micafungin	100mg q24h
Fluconazole	12mg/kg/day on Day 1, then 6mg/kg q24h
Itraconazole	200mg q8h for 3 days, followed by 200mg q12h
Posaconazole	800mg (syrup), 300mg (tablet) q12h for 1 day, followed by 300mg q24h
Voriconazole	6mg/kg q12h for 2 doses, followed by 3-4 mg/kg q12h

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
For patients on fluconazole or no antifungal prophylaxis, if **-** new clinical signs or symptoms suggestive of invasive fungal infections (IFI)* - fever persists ≥7days with no identified fever source	Micafungin 100mg IV q24H	Anidulafungin 200mg IV single dose, then 100mg IV q24H **OR** Caspofungin 70mg IV single dose, then 50mg IV q24H	*If sinus and/or chest CT scan findings not suggestive of fungal infection, it is less likely to be aspergillus or mold infections.
If signs and symptoms suggestive of invasive fungal infections (IFI)* AND Sinus ± chest CT suggestive of fungal infection.	Voriconazole 6mg/kg IV q12H for 2 doses, then 4mg/kg IV q12H	*Amphotericin B deoxycholate 0.7-1mg/kg IV q24H **OR** *Liposomal Amphotericin B 3-5mg/kg IV q24H	*For patients on voriconazole or posaconazole as prophylaxis, empirical antifungal of choice will be Amphothericin B.

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A5.ii OPPORTUNISTIC INFECTIONS (OI) IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Important cut-offs for CD4 T cells, above which particular AIDS illnesses are improbable. These CD4 counts are only reference values; exceptions are always possible.			
No cut-off	Kaposi's sarcoma, pulmonary tuberculosis, HZV, bacterial pneumonia, lymphoma, HSV		
< 250/µl	PCP, oesophageal candidiasis, PML, HIV encephalopathy		
< 100/µl	Cerebral toxoplasmosis, cryptococcosis, miliary tuberculosis		
< 50/µl	CMV end organ disease, cryptosporidiosis, atypical mycobacteriosis		
The treatment regimens are based on drugs available in the Ministry of Health National Formulary and hence in some instances may vary from internationally accepted treatments. Some regimes are chosen as preferred regimes due to cost considerations.			
***Pneumocystis jiroveci* (*carinii*) interstitial pneumonia (PJP/PCP)**			
Treatment	Trimethoprim/Sulfamethoxazole 15-20mg/kg/day [TMP component] IV/PO in 3-4 divided doses	**<u>For mild to moderate cases</u>:** **(PO_2 70-80mmHg)** Clindamycin 600mg IV/PO q8h **PLUS** Primaquine 30mg (base) PO q24h **OR** Dapsone 100mg PO q24h **PLUS** Trimethoprim 15mg/kg/day PO in 3-4 divided doses	Duration: 21 days Patients with severe disease should receive corticosteroids as soon as possible (within 72 hours of starting PCP treatment): **<u>Prednisolone dose:</u>** 40mg PO q12h for 5 days, then 40mg PO q24h for 5 days, then 20mg PO q24h for 11 days (Total duration is 21 days) Trimethoprim/sulfamethoxazole &

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		<u>For severe cases</u>: **(PO_2 < 70mmHg)** *Pentamidine 4mg/kg/day IV (in 1 pint D5% or NS run over 1-2 hours) **OR** Clindamycin 600mg IV q6h or 900mg IV q8h **PLUS** Primaquine 30mg (base) PO q24h	Clindamycin has excellent bioavailability, may switch to PO after clinical improvement. Patients given dapsone or primaquine should be tested for G6PD deficiency. *Requires DG's Approval
Prophylaxis (primary and secondary) <u>Indications</u>: • CD4 count <200 cells/μL • CD4 count 200-250 cells/μL if ART cannot be initiated	Trimethoprim/sulfamethoxazole (80/400mg) 1–2 tablets PO q24h	Dapsone 100mg PO q24h **OR** *Aerosolized Pentamidine 300mg monthly via ultrasonic nebulizer	**Discontinuation:** Can consider when CD4 100-200 cells/μL if HIV RNA is suppressed for 3-6 months with ART. **Restarting prophylaxis:** CD4 count falls to <200 cells/μL or PCP occurs at a CD4 >200 cells/μL (lifelong prophylaxis should be considered). Patients receiving Sulfadiazine/Pyrimethamine or Sulfadoxine/ Pyrimethamine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP. *Requires DG's Approval

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Toxoplasma Gondii Encephalitis			
Acute Infection (up to 97% patients are Toxo IgG +ve)	Trimethoprim/sulfamethoxazole 10mg/kg/day (TMP component) IV/PO in 2 divided doses	*Pyrimethamine 200mg PO loading dose followed by Pyrimethamine: • 50mg PO q24h (if BW≤60kg) • 75mg PO q24h (if BW>60kg) **PLUS** Folinic acid 10-25mg IV/PO q24h **PLUS** Clindamycin 600mg IV/PO q6h **OR** *Sulfadiazine 1gm PO q6h	Duration: At least 6 weeks **Adjunctive corticosteroids** (E.g. dexamethasone) should be administered when clinically indicated to treat mass effect associated with focal lesions or associated oedema but should be discontinued as soon as clinically feasible. *Pyrimethamine & Fansidar® (Sulfadoxine/Pyrimethamine) can be used interchangeably depending on availability; however Fansidar is associated with higher incidence of adverse drug reactions. 1 tab of Fansidar equals to 25mg of Pyrimethamine. *Requires DG's Approval

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Suppressive/ Maintenance Therapy	Trimethoprim/ Sulfamethoxazole (80/400mg) 2 tablets PO q12h	Dapsone 100mg PO q24h **OR** Clindamycin 600mg PO q8h **PLUS** *Pyrimethamine 50mg PO twice-weekly **PLUS/MINUS** Folinic acid 10-25mg PO twice-weekly **OR** *Sulfadiazine 0.5-1gm PO q6h **PLUS** *Pyrimethamine 25-50mg PO q24h **PLUS** Folinic acid 10-25mg PO q24h	**Discontinuation:** Consider when CD4 >200 cells/µL if HIV RNA is suppressed for 6 months with ART. *Requires DG's Approval
Primary Prophylaxis Indications: Toxoplasma IgG +ve with CD4<100	Trimethoprim/ Sulfamethoxazole (80/400mg) 2 tablets PO q24h	Dapsone 50mg PO q24h **PLUS** *Pyrimethamine 50mg PO once weekly **PLUS** Folinic acid 25mg PO once weekly **OR** Dapsone 200mg PO once weekly **PLUS** *Pyrimethamine 75mg PO once weekly **PLUS** Folinic Acid 25mg PO once weekly	**Discontinuation:** CD4>200 cells/µL for >3months CD4>100 cells/µL, if HIV viral load suppressed for 3 to 6 months *Requires DG's Approval

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Mucocutaneous Candidiasis			
Oropharyngeal (oral thrush)	Nystatin suspension 500,000units PO 4-5 times daily **OR** *Itraconazole 200mg PO q24h	Fluconazole 100mg PO q24h	Duration: 7-14 days Chronic suppressive therapy is usually not recommended. *Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (eg: Cola drinks). Avoid PPIs and H2 blockers. Significant drug-drug interaction with p450 enzyme inducers (eg: Rifampicin). Consider fluconazole if in doubt.
Oesophageal	Itraconazole 200mg PO q24h	Fluconazole 200-400mg PO/IV q24h **OR** Amphotericin B deoxycholate 0.6mg/kg IV q24h	Duration: 14-21 days Candidiasis is the most common cause of oesophagitis with HIV infection, but CMV, HSV and aphthous ulcerations can present with similar complaints. Endoscopy required with unusual presentations or lack of response to azole within several days.
Vulvovaginal	Refer to section (Obstetrics & Gynaecology Infections)		
Cryptococcal meningitis or meningoencephalitis (*Cryptococcus neoformans*)			
Induction therapy	*Amphotericin B deoxycholate 0.7-1mg/kg IV q24h **PLUS** Flucytosine 25mg/kg PO q6h	*Amphotericin B deoxycholate 0.7-1mg/kg IV q24h **PLUS**	Duration: At least 2 weeks *The lipid formulations (Amphotericin B lipid complex 5mg/kg or liposomal 3-4mg/kg IV

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		Fluconazole 800-1200mg IV/PO q24h (may be given in divided dosing)	q24h) may be used instead if available. For severe/recurrent infection, please refer to ID physician.
Consolidation therapy (continued after successful induction therapy; defined as substantial clinical improvement and negative CSF culture after repeat LP)	Fluconazole 400mg PO/IV q24h (if Flucytosine used in induction therapy) OR 800mg PO/IV q24h (if Fluconazole used in induction therapy)	Itraconazole 200mg PO q12h	Duration: 8 weeks
Maintenance Therapy (continued after consolidation therapy)	Fluconazole 200mg PO q24h	Itraconazole 200mg PO q24h for patients intolerant or failed fluconazole (however less effective and higher relapse rate)	**Discontinuation:** Completed initial (induction, consolidation) therapy **AND** at least 1 year on maintenance therapy **AND** Remains asymptomatic from cryptococcal infection **AND** CD4 count ≥100 cells/μL and suppressed HIV RNA in response to effective ART for ≥6 months
Secondary prophylaxis	Fluconazole 200mg PO q24h		**Restarting secondary prophylaxis:** CD4 count <100 cells/μL
Cryptococcosis (localized non-meningeal disease)			
Mild-moderate pulmonary infection or extra-pulmonary non-CNS disease **OR**	Fluconazole 400mg PO q24h for 6-12 months Then, consolidation: Fluconazole 400mg PO q24h for 8 weeks Then, maintenance (secondary prophylaxis):	*Itraconazole 200mg PO given q8h for 3 days Then, consolidation: Itraconazole 200mg PO given q12h for 8 weeks Then, maintenance (secondary prophylaxis):	**Discontinuation of maintenance:** At least 1 year of treatment **AND** CD4 count ≥100 cells/μL and suppressed HIV RNA in response to effective ART for ≥6 months

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Asymptomatic with positive lung/blood culture or positive antigen test (no CNS disease)	Fluconazole 200mg q24h	Itraconazole 200mg q24h	In the case of treatment failure, all patients initially treated with fluconazole should have their therapy changed to amphotericin-B until clinical response is achieved. *Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (eg: Cola drinks). Avoid PPIs and H2 blockers.
Severe pulmonary or extra-pulmonary non-CNS Disease	Treat as per cryptococcal meningitis		

References:
1. WHO Guidelines for the Diagnosis, Prevention and Management of Cryptococcal Disease in HIV-Infected Adults, Adolescents and Children, March 2018. (Supplement to the 2016 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection)
2. The BMJ Best Practices: HIV-related opportunistic infections

Histoplasmosis (*Histoplasma capsulatum*)			
Moderate to severe disseminated disease or CNS involvement	**Induction therapy** *Amphotericin B deoxycholate 0.7-1.0mg/kg IV q24h for at least 2 weeks followed by **Maintenance therapy** Itraconazole 200mg PO q8h for 3 days, then 200mg q12h for at least 12 months		*The lipid formulations of amphotericin B may be used instead if available. All the triazole antifungals have the potential to interact with certain ARV agents and other anti-infective agents.
Mild disseminated disease (Blood culture positive but patient is asymptomatic)	**Induction & maintenance therapy** *Itraconazole 200mg PO q8h for 3 days, then 200mg PO q12h	**For patients intolerant to Itraconazole:** Fluconazole 800mg PO q24h **OR**	Duration: At least 12 months

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		Voriconazole 400mg PO q12h on day 1, then 200mg PO q12h	*Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (eg: Cola drinks). Avoid PPIs and H2 blockers.
Chronic Suppressive therapy (Secondary prophylaxis) Indication: • Severe disseminated or CNS infection after completion of at least 12 months of treatment • Relapsed despite appropriate initial therapy	*Itraconazole 200mg PO q24h	Fluconazole 400mg PO q24h	**Discontinuation:** Received azole for >1 year, **AND** Negative fungal blood cultures, **AND** CD4 count >150 cells/µL for ≥6 months on ART **Restarting secondary prophylaxis:** CD4 count <150 cells/µL *Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (eg: cola drinks). Avoid PPIs and H2 blockers.
Penicilliosis (*Penicillium/Talaromyces marneffei*)			
Acute infection (Severely-ill patients)	**Induction therapy** *Amphotericin B deoxycholate 0.6-0.7mg/kg IV for 2 weeks Must be followed by consolidation therapy	Voriconazole 6mg/kg IV q12h on day 1, then 4mg/kg IV q12h for at least 3 days Must be followed by consolidation therapy.	*The lipid formulations of amphotericin B may be used instead if available All the triazole antifungals have the potential to interact with certain ARV agents and other anti-infective agents. **Itraconazole: Absorption depends on gut acidity: • Capsule: Take with food and acidic beverage (eg: cola drinks)
	Consolidation therapy **Itraconazole 200mg PO q12h for 10 weeks Must be followed by maintenance therapy	Fluconazole 400mg PO q12h for 10 weeks Must be followed by maintenance therapy	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute infection (Mild disease)	**Itraconazole 200mg PO q12h for at least 8-12 weeks Must be followed by maintenance therapy	Fluconazole 400mg PO q12h for at least 8-12 weeks Must be followed by maintenance therapy	• Liquid preparation: Take on empty stomach • Avoid PPIs and H2 blockers
Maintenance therapy/ Secondary prophylaxis	**Itraconazole 200mg PO q24h	Fluconazole 400mg PO q24h	**Discontinuation:** CD4 count >100 cells/µL for ≥6 months on ART
Mycobacterium tuberculosis infection and diseases			
Refer to (Ministry of Health's CPG on Management of Tuberculosis)			
***Mycobacterium Avium* Complex (MAC) Disease**			
Treatment	Clarithromycin 500mg PO q12h **PLUS** Ethambutol 15mg/kg PO q24h ****PLUS/MINUS** 3rd/ 4th drug: Amikacin 10-15mg/kg IV q24h **OR** Streptomycin 15mg/kg IM q24h **OR** Levofloxacin 500mg PO q24h **OR** Ciprofloxacin 500-750mg PO q12h	*Azithromycin 500mg PO q24h **PLUS** Ethambutol 15mg/kg PO q24h ****PLUS/MINUS** 3rd/ 4th drug: Amikacin 10-15mg/kg IV q24h **OR** Streptomycin 15mg/kg IM q24h **OR** Levofloxacin 500mg PO q24h **OR** Ciprofloxacin 500-750mg PO q12h	Duration: At least 12 months *Azithromycin: use if drug interaction or intolerance precludes the use of clarithromycin. **Addition of 3rd/4th drug should be considered for patients with disseminated disease, CD4 count <50 cells/µL or in the absence of effective ART. **Discontinuation:** Consider if patient is on ART and viral load is suppressed, CD4 >100 cells/µL >6 months, asymptomatic of MAC, and has completed >12 months of therapy.
Maintenance/ Secondary Prophylaxis	Same as the treatment regimen		**Restarting secondary prophylaxis:** CD4 <100 cells/µL again.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Primary Prophylaxis **<u>Indications</u>:** **CD4 < 50 cells/µL** **Ruled out active MAC and TB**	Azithromycin 1250mg PO once weekly	Clarithromycin 500mg PO q12h	**Discontinuation:** Consider if patient is on ART **AND** Viral load is suppressed, CD4 >100 cells/µL ≧ >3 months
Cytomegalovirus (CMV) Disease			
Treatment (CMV Retinitis) (Immediate Sight-Threatening Lesions (Adjacent to the Optic Nerve or Fovea))	Intravitreal injections of Ganciclovir (2mg/injection) biweekly until scarring **PLUS** Ganciclovir 5mg/kg IV q12h for **OR** Valganciclovir 900mg PO q12h Followed by maintenance	Intravitreal injections of Foscarnet (2.4mg/injection) biweekly until scarring **PLUS** Ganciclovir 5mg/kg IV q12h **OR** Valganciclovir 900mg PO q12h Followed by maintenance	Duration: 14-21 days Immune recovery is essential for successful treatment. Start ART within 2 weeks if possible
Treatment (CMV Retinitis) (For Small Peripheral Lesions)	Ganciclovir 5mg/kg IV q12h Followed by maintenance	Valganciclovir 900mg PO q12h Followed by maintenance	
Treatment (Extraocular CMV diseases) (Oesophagitis, colitis, interstitial pneumonitis, neurological disease)	Ganciclovir 5mg/kg IV q12h Followed by maintenance	May consider switch to Valganciclovir 900mg PO q12h once patient tolerate orally (in CMV oesophagitis and colitis only) Followed by maintenance	Duration: 21-42 days or until signs and symptoms have been resolved Immune recovery is essential for successful treatment. Start ART within 2 weeks if possible
Maintenance/ Secondary prophylaxis (CD4 <100 cells/µL)	Ganciclovir 5mg/kg IV q24h 5–7 times weekly	Valganciclovir 900mg PO q24h	**Discontinuation:** Consider if patient is on ART and viral load well suppressed, CD4 >100 cells/µL >3 months and after 3-6 months of CMV

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			treatment. Maintenance therapy is generally not necessary; ART offers best hope for prevention of relapses.
Herpes Simplex Virus (HSV) Infections			
Refer to section (Sexually Transmitted Infection)			
Varicella-Zoster Virus (VZV) Diseases			
Refer to section (Skin and Soft Tissue Infection (SSTI))			
Bacterial Enteric Infections			
Salmonellosis **Salmonella non-typhi**	Ciprofloxacin 500-750mg PO or 400 mg IV q12h **OR** Ceftriaxone 2gm IV q24h	Ampicillin 2gm IV q4-6h **OR** Trimethoprim/sulfamethoxazole (80/400mg) 2 tablets PO or 2 ampoules IV q12h	Susceptibility profile may help guide final choice. Duration: If CD4≥200: 7-14 days. If CD4< 200 and with bacteraemia: 6 weeks. Longer course with debridement and drainage needed for persistent bacteraemia or metastatic disease.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Rhodococcus infections (Rhodococcus equi, formerly *Corynebacterium equi*)			
Induction Treatment	*Vancomycin 15-20mg/kg (actual body weight) IV q8-12H; not to exceed 2gm/dose **PLUS (antibiotics with intracellular activity)** Azithromycin 500mg stat and then 250 mg IV/PO q24h **PLUS** Ciprofloxacin 500-750mg PO q12h or 400 mg IV q8-12h **OR** Levofloxacin 500-750mg IV/PO q24h	**Addition of 4th drug should be considered in non-responding patients or CNS involvement: ****4th drug:** Imipenem/Cilastatin 500mg IV q6h	Duration: 4-8 weeks Adjust antibiotics according to susceptibility data. Use at least two susceptible agents. *Consider Vancomycin loading dose 25-30mg/kg for critically ill/septic patient to achieve faster steady state. Aim trough of 15-20mcg/mL.
Maintenance/ Secondary prophylaxis	Azithromycin 250mg PO q24h **PLUS** Ciprofloxacin 500-750mg PO q12h **OR** Levofloxacin 500-750mg PO q24h	*Rifampicin 600mg PO q24h **PLUS** Azithromycin 250mg PO q24h **OR** Ciprofloxacin 500-750mg PO q12h **OR** Levofloxacin 500-750mg PO q24h	Duration: Until CD4>200 cells/µL *Alternative regime can be used if concomitant tuberculosis can be ruled out.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
PML (Progressive Multifocal Leucoencephalopathy)			
Polyoma virus JC virus (JCV)	No effective therapy exists		With ART, some patients improve and others stabilize. Few may deteriorate due to immune reconstitution
Isospora Belli Infection			
Initial Therapy	Trimethoprim/sulfamethoxazole (160/800mg) IV/PO q6h	Pyrimethamine 50-75mg PO q24h **PLUS** Folinic acid 10-25mg PO q24h **OR** Ciprofloxacin 500mg PO q12h	Duration: 10 days
Cryptosporidiosis			
Cryptosporidium sp.	Symptomatic treatment of diarrhoea		Effective ART (to increase CD4 >100 cells/μL) can result in complete, sustained clinical, microbiological and histologic resolution.
Microsporidiosis			
Microsporidium sp.	Albendazole 400mg PO q12h for 2-4 weeks **PLUS** Symptomatic treatment of diarrhoea (The best treatment option is ART and fluid support)		Effective ART (to increase CD4 >100 cells/μL) can result in complete, sustained clinical, microbiological and histologic resolution.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Syphilis (*Treponema pallidum* Infection)			
Refer to section (Sexually Transmitted Disease)			
Bartonellosis			
For Bacillary Angiomatosis, Peliosis Hepatis, Bacteraemia, and Osteomyelitis	Doxycycline 100mg PO q12h **OR** Erythromycin 500mg PO/IV q6h	Azithromycin 500mg PO q24h **OR** Clarithromycin 500mg PO q12h	Duration: At least 3 months If relapse occurs after initial (>3 month) course of therapy, long-term suppression with doxycycline or a macrolide is recommended as long as CD4 <200 cells/µL.
Other Severe Infections (or CNS involvement)	Doxycycline 100mg PO/IV q12h **PLUS/MINUS** Rifampicin 300mg PO/IV q12h **OR** Erythromycin 500mg PO/IV q6h **PLUS/MINUS** Rifampicin 300mg PO/IV q12h		
Confirmed *Bartonella* Endocarditis	refer to section (Cardiovascular infections)		

References:

1. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents by panel members of National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC) and HIV Medicine Association of the Infectious Disease Society of America (HIVMA/IDSA) 2017.
2. The BMJ Best Practices: HIV-related opportunistic infections
3. The Sanford Guide to Antimicrobial Therapy (updated 16/02/2018)
4. The John Hopkins POC-IT ABX Guide 2000-2017
5. European AIDS Clinical Society Guidelines

A6. OBSTETRICS & GYNEACOLOGICAL INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Preferred	
Septic Abortion Common organisms: *Bacteroides* sp *(especially Prevotella bivia)* *Streptococcus* sp *(Grp A, Grp B)* *Enterobacteriaceae* *Chlamydia trachomatis* *Ureaplasma urealyticum*	Ampicillin 2gm IV q4-6h **PLUS** Gentamicin 5mg/kg IV q24h **PLUS** Metronidazole 500mg IV q8h	Ampicillin/sulbactam 3gm IV q6h **PLUS** Doxycycline 100mg PO q12h **OR** Clindamycin 900mg IV q8h **PLUS** Gentamicin 5mg/kg IV q24h	Intravenous antibiotics are administered until the patient has improved and afebrile for 48 hours, then are typically followed by oral antibiotics **To complete a 10-14 days course.**
Intra-partum antibiotic prophylaxis (IAP) for Group B Streptococcus (GBS) positive mothers Indications of IAP: • Previous infant with invasive GBS disease • Preterm labour • GBS carriage in previous pregnancy • PPROM with known GBS carrier • GBS carriage in current pregnancy	Benzylpenicillin 5MU IV initial dose, then 2.5–3MU IV q4h until delivery	Ampicillin 2 gm IV initial dose, then 1 gm IV q4h until delivery. **Mild penicillin allergy** Cefazolin 2 gm IV initial dose, then 1 gm q8h until delivery **OR** Cefuroxime 1.5 gm IV stat and 750mg IV q8h until delivery **Severe penicillin allergy** Vancomycin 15-20 mg/kg IV q8-12h until delivery **OR** Clindamycin 900mg IV q8h until delivery	Prophylaxis begins at hospital admission for labour or rupture of membrane and continued every four hours until the infant is delivered. Penicillin allergy refer to Appendix 8 Treatment is NOT INDICATED if C-section performed before onset of labour with intact membrane (please use standard surgical prophylaxis) Antenatal treatment is **NOT RECOMMENDED** for GBS cultured from a vaginal or rectal swab.
Preterm Premature Rupture of Membranes (PPROM)	**If non-GBS carrier:** Erythromycin Ethylsuccinate 400mg PO q6h for 7-10 days		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Preferred	
	<u>If GBS carrier:</u> Ampicillin 2gm IV q6h for 48 hours followed by Amoxicillin 500mg PO q8h for an additional 5-7 days or until delivery whichever comes first **PLUS** One dose of Azithromycin 1gm PO upon admission (to cover for Ureaplasmas – important cause of chorioamnionitis & Chlamydia)		
Chorioamnionitis	Ampicillin 2gm IV q6h **PLUS** Gentamicin 5mg/kg IV q24h **<u>If the patient is undergoing a cesarean delivery:</u>** **PLUS** Metronidazole 500mg IV q8h	Ampicillin/sulbactam 3gm IV q6h **<u>Mild penicillin allergy:</u>** Cefazolin 2gm IV q8h **PLUS** Gentamicin 5mg/kg IV q24h **<u>Severe penicillin allergy:</u>** Clindamycin 900mg IV q8h	Antibiotic regimen is continued postpartum until patient is afebrile and asymptomatic for **AT LEAST 48 HOURS** There is NO evidence that continuation with oral antibiotic are beneficial after discontinuation of parenteral therapy Penicillin allergy refer to Appendix 8
Pelvic Inflammatory Disease <u>Common organisms:</u> *Neisseria gonorrhoeae* *Chlamydia trachomatis* *Bacteroides* sp *Enterobactericiae* *Haemophilus influenza*	**<u>Outpatient regimen (Mild-moderate):</u>** Ceftriaxone 500mg IM in a single dose **OR** Cefotaxime 1gm IM in a single dose **PLUS** Metronidazole 400mg PO q12h for 14 days		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Preferred	
Streptococcus sp *especially Streptococcus agalactiae (*GBS*)* *Gardnerella vaginalis* *Ureaplasma urealyticum* *Mycoplasma hominis*	**PLUS** Doxycycline 100mg PO q12h for 14 days **OR** Azithromycin 1gm PO once per week for 2 weeks		
	Inpatient regimen (Moderate-severe): Cefuroxime 1.5gm IV q8h **OR** Ceftriaxone 2gm IV q24h **PLUS** Doxycycline 100mg PO q12h **PLUS** Metronidazole 500mg IV/PO q8h **Duration of treatment: 14 days**	**Ampicillin/sulbactam** 3gm IV q6h **PLUS** **Doxycycline** 100mg PO q12h	**Tubo ovarian abscess:** Surgical intervention for source control may be required. May need to consider tuberculosis if not responding to standard treatment
Endometritis	**Non-pregnancy:** Follow antibiotic guide for severe PID		
	Post-partum endometritis: Clindamycin 900mg IV q8h **PLUS** *Gentamicin 5mg/kg q24h **OR** Cefotaxime 1gm IV q8h **PLUS** Metronidazole 500mg IV q8h	Amoxicillin/clavulanate 1.2gm IV q8h **OR** Ampicillin/sulbactam 3gm IV q6h	**Duration of treatment: 10-14 days** *TDM for gentamicin is required

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Preferred	
	PLUS *Gentamicin 5mg/kg IV x 1 dose		
Vaginitis Bacterial vaginosis	Metronidazole 400mg PO q8h for 7 days	Clindamycin 300mg PO q12h for 7 days	Metronidazole can be use in any stage of pregnancy
Vaginal Candidiasis *Candida albicans* **Uncomplicated infection**	Clotrimazole 500mg as a single vaginal pessary (Stat dose) **OR** Clotrimazole 200mg as vaginal pessary for 3 nights	Fluconazole 150-200mg PO for one dose	Pregnancy: If indicated, treat with topical therapy as oral therapy is **CONTRAINDICATED**.
Vaginal Candidiasis *Candida albicans* **Complicated infections:**	**Severe vaginitis symptoms:** Fluconazole 150-200mg PO q72h for 2 or 3 doses		
	Recurrent vulvovaginal candidiasis: Fluconazole 150-200mg PO q72h for 3 doses then weekly for 6 months	Clotrimazole 500mg vaginal suppository once weekly for 6 months	
Trichomoniasis *Trichomonas vaginalis*	Metronidazole 400mg PO q8h for 7 days **OR** Metronidazole 2gm PO as single dose		Metronidazole can be use in any stage of pregnancy(reference) If post-partum and breastfeeding, not advisable to breastfeed during treatment. May resume breastfeeding after 24 hrs of the last dose.
Cervicitis	Azithromycin 1gm single dose	Doxycycline 100mg PO q12h for 7 days	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Preferred	
Postpartum mastitis Common organisms: *Staphylococcus aureus (MSSA)* *Streptococcus pyogenes* (Grp A, B) *Escherichia coli* *Bacteroides* sp *Corynebacterium* sp *CoNS*	**Outpatient** Cephalexin 500mg PO q6h for 5-7 days		Duration of therapy for 5-7 days may be adequate but if poor response consider extending to 10-14days. Milk culture for less severe infection If severe infection (hemodynamic instability) blood culture required
	Inpatient Cloxacillin 2gm IV q6h	Cefazolin 1-2gm IV q8h	
Post episiotomy tear	**1st and 2nd degree tear:** Antibiotics not required		Penicillin allergy refer to Appendix 8
	3rd and 4th degree tear: Cefuroxime 1.5gm IV as single dose	**Penicillin Allergy** Clindamycin 600mg IV as single dose	
Manual removal of placenta	Ampicillin 2gm IV as single dose	Cefazolin 2gm IV as single dose	
Post Lower Segment Caesarean Section (LSCS) infection	In mild Surgical Site Infections (SSI), antibiotic is generally not indicated. Appropriate dressing is the primary treatment.		
	Cloxacillin 2gm q6h **OR** Cefazolin 1-2gm IV q8h	**Risk of Gram negative or anaerobic infection (eg: Diabetes):** Ampicillin/sulbactam 3gm IV q6-8h	

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11. Antibiotic prophylaxis for prevention of postpartum perineal wound complications: a randomized controlled trial, 2008
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A7. OCULAR INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Dosage alterations in Ophthalmology NAG: Dose alteration may be needed for systemic and intravitreal antibiotics in paediatric patients.			
Blepharitis Common organisms: *Staphylococcus aureus* *Staphylooccus epidermidis*	Eyelid hygiene/scrubs is the mainstay of therapy Topical antibiotics are not indicated as an initial therapy	Oxytetracycline with Polymyxin B eye ointment applied q12h to the lid margin **OR** Fusidic Acid 1% eye ointment applied q12h to the lid margin	
Meibomian Gland Dysfunction	Warm compresses and massage Systemic therapy is not indicated as an initial therapy	**In resistant cases:** *Doxycycline 100mg PO q12h for 4-6 weeks **OR** Azithromycin 500mg PO q24h for 3 days	*Tetracyclines are contraindicated in children <8 years.
Internal Hordeolum with Secondary Infection *Staphylococcus aureus* Systemic antibiotics are indicated in the presence of superficial cellulitis or abscess.	Warm compresses Cloxacillin 500mg PO q6h	 Amoxicillin/clavulanate 625mg PO q8h	Duration: 5 days
External Hordeolum (Stye) *Staphylococcus aureus* In the presence of superficial cellulitis or abscess.	Epilation of affected eye lash and warm compresses Cloxacillin 500mg PO q6h	 Amoxicillin/clavulanate 625mg PO q8h	Duration: 5 days
Bacterial Conjunctivitis Common organisms:	Chloramphenicol 0.5% eye drop q6h	Moxifloxacin 0.5% eye drop q6h **OR** Ciprofloxacin 0.3% eye drop q6h	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Staphylococcus aureus *Streptococcus pneumonia* *Haemophilus influenzae*		**OR** Levofloxacin 0.5% eye drop q6h	
Gonococcal Conjunctivitis (including neonates) *Neisseria Gonorrhoea*	Requires systemic therapy. Refer to Sexually Transmitted Infections & Neonatal Infection Sections		Copious irrigation with topical saline drops or artificial tears every 30-60 minutes. Topical antibiotics may be considered as ancillary therapy.
Chlamydial Conjunctivitis (including neonates) *Chlamydial Trachomatis*	Requires systemic therapy. Refer to Sexually Transmitted Infections & Neonatal Infection Sections		
Bacterial Keratitis No Growth	Ciprofloxacin 0.3% eye drop q1-2h **OR** Moxifloxacin 0 .5% eye drop q1-2h **OR** Levofloxacin 0.5% eye drop q1-2h	*Cefuroxime 5% eye drop q1-2h **PLUS** *Gentamicin 0.9% or 1.4% eye drop q1-2h	*Prepared extemporaneously using injectable forms
Contact Lens Related Bacterial Keratitis No Growth	Ciprofloxacin 0.3% eye drop q1-2h **OR** Levofloxacin 0.5% eye drop q1-2h	*Gentamicin 0.9% or 1.4% eye drop q1-2h **PLUS** *Ceftazidime 5% eye drop q1-2h	*Prepared extemporaneously using injectable forms
Bacterial Keratitis Gram-positive cocci	Moxifloxacin 0 .5% eye drop q1-2h	*Cefuroxime 5% eye drop q1-2h **For MRSA:** * Vancomycin 5% eye drop q1-2h	*Prepared extemporaneously using injectable forms

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Bacterial Keratitis Gram-negative rods	Ciprofloxacin 0.3% eye drop q1-2h **OR** Levofloxacin 0.5% eye drop q1-2h	*Gentamicin 0.9% or 1.4% eye drop q1-2h **PLUS** *Ceftazidime 5% eye drop q1-2h	*Prepared extemporaneously using injectable forms
Acanthamoeba Keratitis Acanthamoeba sp.	*Chlorhexidine 0.02% eye drop q1-2h **PLUS** **Propamidine isethionate 0.1% eye drop q1-2h		*Prepared extemporaneously using injectable forms **Requires DG's Approval
Fungal Keratitis	**Natamycin 5% eye drop q1-2h **OR** *Amphotericin B 0.15%-0.2% eye drop q1-2h	*/**Voriconazole 1% eye drop q1-2h **OR** *Fluconozole 0.2% eye drop q1-2h **<u>Oral Therapy:</u>** May be considered in the absence of contraindications Fluconozole 200mg PO q24h **OR** Ketoconazole 200mg PO q24h	Natamycin is the choice therapy for fusariam Amphotericin B is the choice therapy for candida In severe fungal keratitis – combination therapy may be used *Prepared extemporaneously using injectable forms **Requires DG's Approval
Herpes Simplex Keratitis **Herpes Simplex Type 1 & 2**	Acyclovir 3% eye ointment 5 times/day **In presence of stromal or endothelial disease:** Acyclovir 400mg PO 5 times/day for 7-14 days **Prophylaxis for recurrent cases:** Acyclovir 400mg PO q12h for 12 months		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Herpes Zoster Ophthalmicus *Herpes Zoster Virus*	Needs systemic therapy. Refer to Skin & Soft Tissue Infections Section		
Ocular Toxoplasmosis *Toxoplasma gondii*	Trimethoprim/sulfamethoxazole 160/800mg PO q12h for at least 6 weeks	Pyrimethamine 25-50mg PO q24H **PLUS** Folinic acid 10-25mg PO q24H **PLUS** Sulfadiazine 1gm PO q6H **OR** Azitromycin 500mg PO q24h **OR** Clindamycin 300mg PO q6h for 3-4 weeks, then 150mg q6h PO for 3-4 weeks	Pregnancy : May consider Intravitreal Clindamycin 1.0mg/0.1ml Systemic steroids are usually indicated in immunocompetent patients.
	Prophylaxis for recurrent lesions: Trimethoprim/sulfamethoxazole 80/400mg q12h PO for 3 times a week		
Acute Retinal Necrosis *Herpes Simplex*	Acyclovir 10mg/kg/dose IV q8h (not more than 800mg) for 10-14 days **FOLLOWED BY** Acyclovir 800mg PO 5 times/day for 6 weeks	** Valacyclovir 1gm PO q8H for 6 weeks	**Requires DG's Approval Systemic steroid is indicated depending on location or severity of the infection.
CMV Retinitis *Cytomegalovirus*	**Systemic therapy:** Ganciclovir 5mg/kg IV q12h for 2-3 weeks	**Systemic therapy:** ** Valganciclovir: 900mg PO q12h for 3 weeks (induction) followed by 900mg PO q24h (maintenance)	Systemic therapy is indicated in all cases. Maintenance may need to continue until CD4 count is >150 cells/mm3 for 3 consecutive months.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Intravitreal therapy: Intravitreal Ganciclovir 2mg/0.1ml biweekly	**Intravitreal therapy:** **Intravitreal Foscarnet 2.4mg/0.1ml (1-2weekly)	Intravitreal therapy is indicated in zone 1 and 2 lesions. Intravitreal to be tapered according to clinical response. Ganciclovir implant: 4.5gm an option for prolonged usage of intravitreal Ganciclovir. **Requires DG's Approval
Ocular Syphilis *Treponema Pallidum*	Ocular Syphilis (syphilitic uveitis) should be treated as Neurosyphilis. Refer to Sexually Transmitted Infections Section		Referral to Dermatologist/ ID Physician
Ocular Tuberculosis *Mycobacterium Tuberculosis*	Needs systemic therapy. Refer to Ministry of Health's CPG on Management of Tuberculosis (Extra pulmonary TB) *Ethambutol may cause optic neuropathy and should be avoided depending on the case.		**Ocular TB:** presents as a unilateral/ bilateral infective uveitis characterized by multifocal choroiditis/ granuloma and there may be supportive FFA findings of occlusive vasculitis. The diagnosis maybe clinical as vitreous sampling for AFB or TB PCR may not be very sensitive due to small sample size and sensitivity of the tests. Clinical response to anti-TB is often diagnostic. **Uveitis secondary to TB Hypersensitivity** is an immune response to acid fast bacilli in the eye and manifests predominantly as an inflammatory uveitis. Treatment includes anti-TB in combination with an immunosuppressive dose of systemic steroids for at least 6-9 months. Systemic steroids maybe indicated but is only for

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			- non-active systemic TB - immunocompetent patients - severe ocular inflammation developing after starting anti-TB treatment and - vision threatening condition Systemic steroids should not be started ALONE without anti-TB treatment.
Post Operative Bacterial Endophthalmitis Common organisms: *Staphylococcus epidermidis* *Staphylococcus aureus* *Pseudomonas aeruginosa* Bacteroids species *Streptococcus pneumoniae* *Alpha-haemolytic streptococcus*	**Intravitreal antibiotic injections:** Vancomycin 1-2mg/0.1ml **PLUS** Ceftazidime 2mg/0.1ml If suspicious of fungal endophthalmitis: **ADD** Intravitreal Amphotericin B 0.005mg/0.1ml	**Intravitreal antibiotic injections:** Vancomycin 1-2mg/0.1ml **PLUS** Amikacin 0.4mg/0.1ml	Systemic antibiotics are indicated in severe, virulent endophthalmitis. Repeat intravitreal antibiotics after 48 to 72 hours if indicated. *Prepared extemporaneously using injectable forms
	Topical treatment-options: - *Ceftazidime 5% eye drop - *Vancomycin 5% eye drop - *Gentamycin 1.4% eye drop - Moxifloxacin 0.5% eye drop - Levofloxacin 0.5% eye drop (monotherapy or combination)		
	Systemic treatment: Ciprofloxacin 750mg PO q12h for 10 days For culture negative cases: **ADD**	**Systemic treatment:** Vancomycin 15-20mg/kg IV q8-12h; not to exceed 2gm/dose **PLUS** Ceftazidime 1-2gm IV q8h	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Clarithromycin 250-500mg PO q12h for 7-14 days		
Post Operative Fungal Endophthalmitis	**Intravitreal therapy:** Intravitreal Amphotericin B 0.005mg/0.1ml	**Intravitreal therapy:** **Intravitreal Miconazole 0.01mg/0.1ml **OR** **Intravitreal Voriconazole 50ug-100ug/0.1ml	Intravitreal and Systemic therapy are indicated in all cases. **Requires DG's Approval
	Systemic therapy: Fluconazole 200mg PO q24h for 6 weeks (minimum)	**Systemic therapy:** ** Voriconazole 200mg PO q12h	
Endogenous Endophthalmitis Systemic treatment	**Systemic therapy:** Ciprofloxacin 750mg PO q12h for 10 days For culture negative cases: **ADD** Clarithromycin 250-500mg PO q12h for 7-14 days	**Systemic therapy:** Vancomycin 15-20mg/kg IV q8-12h; not to exceed 2gm/dose **PLUS** Ceftazidime 1-2gm IV q8h	Treatment is based on primary infection (bacterial/fungal etc) and culture and sensitivity results. All cases require systemic therapy. Intravitreal injection is indicated in cases with vitreous involvement and sight threatening choroidal lesions. Topical therapy may supplement therapy. Not to use systemic steroids in these cases. Review antibiotic regimen after microbiology results. Repeat intravitreal antibiotics after 48 to 72 hours if indicated. *Prepared extemporaneously using injectable forms
	Topical treatment-options: • *Ceftazidime 5% eye drop • *Vancomycin 5% eye drop • Gentamycin 0.3% eye drop • Moxifloxacin 0.5% eye drop • Levofloxacin 0.5% eye drop (monotherapy or combination)		
	Intravitreal antibiotic injections: Vancomycin 1-2mg/0.1ml	**Intravitreal antibiotic injections:** Vancomycin 1-2mg/0.1ml	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	PLUS Ceftazidime 2mg/0.1ml If suspicious of fungal endophthalmitis: **ADD** Intravitreal Amphotericin B 0.005mg/0.1ml	**PLUS** Amikacin 0.4mg/0.1ml	
Ocular Melioidosis	For ocular manifestations of Melioidosis, refer to treatment of Melioidosis infection.		
Ocular Bartonellosis	For ocular manifestations of Bartonella, refer to treatment of Bartonella infection.		
Ocular Leptospirosis	For ocular manifestations of Leptospira, refer to treatment of Leptospira infection.		
Dacryocystitis Common organisms: *Streptococcus pneumonia* *Staphylococcus aureus* Gram-negative anaerobes	Cefuroxime 250mg PO q12h	Amoxicillin/clavulanate 625mg PO q8h	Consider intravenous antibiotics in severe infections. Duration: 7 days
Preseptal Cellulitis Common organisms: *Streptococcus pneumoniae* *Staphylococcus aureus* Streptococcus sp.	Cloxacillin 500-1000mg PO q6h for 5 days	Amoxicillin/clavulanate 625mg PO q8h for 7 days **OR** Ceftriaxone 1-2gm IV q24h	Consider intravenous antibiotics in severe infections.
Orbital Cellulitis/abscess Common organisms: *Streptococcus pneumoniae* *Staphylococcus aureus* Streptococcus sp. Gram-negative anaerobes	Amoxicillin/clavulanate 1.2gm IV q8h	Ceftriaxone 1-2gm IV q24h If Anaerobes suspected: **ADD** Metronidazole 500mg IV q8h	Duration: 7-10 days

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A8. ORAL/DENTAL INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	AlternativeTreatment	
A. ANTIMICROBIAL USE FOR BACTERIAL INFECTIONS			
INFECTIONS OF THE TEETH AND SUPPORTING STRUCTURES			
Reversible/ Irreversible Pulpitis	Systemic antibiotic use not recommended	Systemic antibiotic use not recommended	
Localised Dentoalveolar Abscess	**Superficial** Systemic antibiotic use not recommended (unless medically compromised)	Systemic antibiotic use not recommended (unless medically compromised)	Penicillin allergy refer to Appendix 8
	Deep Infection/ Medically Compromised Amoxicillin 500mg PO q8h **PLUS** Metronidazole 400mg PO q8h **OR** Amoxicillin/clavulanate 625mg PO q8h	**Penicillin Allergy** Clindamycin 300mg PO q6h	
Dry Socket	Systemic antibiotic use not recommended	Systemic antibiotic use not recommended	Local treatment with saline irrigation and antiseptic/ analgesic dressings and symptomatic relief of pain
Localised Pericoronitis	Systemic antibiotic use not recommended in absence of regional or systemic signs and symptoms	Systemic antibiotic use not recommended in absence of regional or systemic signs and symptoms	Local treatment with antiseptic irrigation and mouthwash and symptomatic relief of pain
Chronic Gingivitis	Systemic antibiotic use not recommended	Systemic antibiotic use not recommended	1st line treatment-Mechanical and chemical plaque control. *0.2% Aqueous Chlorhexidine Gluconate not be used alone but as an adjunct to

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	AlternativeTreatment	
			mechanical debridement 2nd line treatment-Antimicrobial mouth rinse
Chronic Periodontitis Antibiotic use can be considered in cases of: 1. Unresponsive to conventional mechanical therapy. 2. Acute infection associated with systemic manifestation 3. Medically compromised	Systemic antibiotic use generally not recommended. Amoxicillin 500mg PO q8h **PLUS** Metronidazole 400mg PO q8h **OR** Amoxicillin/clavulanate 625mg PO q8h	Systemic antibiotic use generally not recommended. **Penicillin Allergy** Clindamycin 300mg PO q6h	1st line treatment-Mechanical plaque control Penicillin allergy refer to Appendix 8
Aggressive Periodontitis Common organisms: *Aggregatibacter actinomycetemcomitans* *Porphyromonas gingivalis* *Tannerellafor sythensis* *Prevotella intermedia* Spirochaetes	Amoxicillin 500mg PO q8h **PLUS** Metronidazole 400mg PO q8h	**Penicillin Allergy** Clindamycin 300mg PO q6h	Antibiotics are not used alone but are used as an adjunct to scaling and root debridement. Penicillin allergy refer to Appendix 8
Local missed Periodontal Abscess	Systemic antibiotic use not recommended	Systemic antibiotic use not recommended	Incision and drainage Management of cause of abscess and symptomatic relief of pain
INFECTIONS OF THE JAWS			
Osteomyelitis of the jaws of dental origin Different organisms maybe involved	For **acute cases**, start with: Amoxicillin 500mg PO q8h **PLUS** Metronidazole 400mg PO q8h	**Penicillin Allergy** Clindamycin 300-450mg PO/IV q6h	Culture and sensitivity is necessary to guide the antibiotic. For **chronic cases**, start with surgical

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	AlternativeTreatment	
	OR Amoxicillin/clavulanate 625mg PO q8h		treatment first. Antibiotics only when causative organisms are identified Duration of antibiotic therapy: can be 4-6 weeks depending on patient response / microbiological clearance of the pathogen. Penicillin allergy refer to Appendix 8
SPREADING INFECTIONS AND INFECTIONS OF FASCIAL SPACES (WITH/WITHOUT SYSTEMIC SIGNS)			
Cellulitis ±Abscess of dental origin Common organisms: Viridans Streptococci Staphylococci Prevotella Peptostreptococcus *Fusobacterium nucleatum* Clostridium sp **Surgical site infection &Traumatic wound infection** Infection is usually by endogenous organisms rather than exogenous Common organisms: Viridans Streptococci Staphylococci *Prevotella intermedia* Peptostreptococcus Eubacterium *Fusobacterium nucleatum*	Benzylpenicillin 2-4MU IV q4-6h **PLUS** Metronidazole 500mg IV q8h **OR** Amoxicillin/Clavulanate 1.2gm IV q6-8h (not more than1.2gm in a single dose-max 7.2gm daily) **OR** Cefuroxime 750mg-1.5gm IV q8h **PLUS** Metronidazole 500mg IV q8h **OR** <u>If not responding to above antibiotics:</u> Ceftriaxone 1-2gm IV q24h **PLUS** Metronidazole 500mg IV q8h	**<u>Penicillin Allergy</u>** Clindamycin 300-450mg IV/PO q6h	Empirical antibiotics are started Incision and drainage is advised and antibiotic is changed in accordance with result of culture and sensitivity. Penicillin allergy refer to Appendix 8
	<u>Step Down/Oral Therapy:</u> Amoxicillin 250-750mg PO q8h	**<u>Penicillin Allergy</u>** Clindamycin 300-450mg PO q6h	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	AlternativeTreatment	
	PLUS Metronidazole 400mg PO q8-12h **OR** Amoxicillin/Clavulanate 625mg PO q8h **OR** Cefuroxime 250-500mg PO q12h **PLUS** Metronidazole 400mg PO q8-12h		
Traumatic wound involving skin / Infection of skin origin	Cloxacillin 500-1000mg IV q6h (in skin involvement- if Staphylococcus expected) **OR** Clindamycin 300-450mg IV/PO q6h **OR** Amoxicillin 250-750mg PO q8h **PLUS** Metronidazole 400mg PO q8-12h		
POST IMPLANT INFECTIONS ("PERIIMPLANTITIS")			
Causative organisms: Actinomyces sp. Eubacterium sp. Propionibacterium sp. Lactobacillus sp. Veillonella sp. *Porphyromonas gingivalis* *Prevotella intermedia* *Fusobacterium nucleatum*	Amoxicillin/clavulanate 625mg PO q8h **OR** Amoxicillin 500mg PO q8h **PLUS** Metronidazole 400mg PO q8h	**Penicillin Allergy** Doxycycline 100mg PO q12h **OR** Clindamycin 300mg PO q6h	Bacteria associated with periimplantitis are extremely resistant to antibiotics. Antibiotics are not used alone but are used as an adjunct to local mechanical and chemical debridement. Also irrigation with Chlorhexidine and optimal oral hygiene by patient.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	AlternativeTreatment	
			Locally delivered antibiotics is preferred compared to systemic administration. Currently there is no reliable study to suggest most effective antibiotic therapy. Penicillin allergy refer to Appendix 8
B. ANTIMICROBIAL USE FOR FUNGAL INFECTIONS			
Oral Candidiasis	Refer to section [Infections in Immunicompromised patients – HIV]		
C. ANTIMICROBIAL USE FOR VIRAL INFECTIONS			
Common oral viral infections: **Herpes simplex virus type 1 (HSV-1)** Primary herpetic gingivostomatitis Herpes labialis **Herpes simplex virus type 2 (HSV-2)** **Epstein-Barr virus** Infectious mononucleosis, oral hairy leukoplakia **Varicella-zoster virus** **Coxsackie virus** Herpangina Hand, foot and mouth disease	Symptomatic treatment in most cases. Can also consider: 1) **Topical Acyclovir** 5% cream q4h for 5-10 days in prodromal phase for recurrent herpes labialis 2) **Systemic antiviral** Acyclovir 400-800mg PO 5 times daily for 7-14 days		
Severe Varicella/Herpes infections or in immunocompromised patients	Refer to section [Skin & Soft Tissue Infections – Viral Infections]		
Viral encephalitis	Refer to section [Central Nervous System (CNS)Infections – Viral Encephalitis]		

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
1. Sore Throat			

The modified Centor Score can be used to help physicians decide which patients need no testing, throat culture/rapid antigen detection testing, or empiric antibiotic therapy.

The cumulative score determines the likelihood of streptococcal pharyngitis and the need for antibiotics:

CRITERIA	SCORE	AGE	SCORE
Absence of cough	1	3 to 14 years	1
Swollen and tender anterior cervical lymph nodes	1	15 to 44 years	0
Temperature > 100.4° F (38° C)	1	45 years and older	-1
Tonsillar exudates or swelling	1		

Cumulative score:

TOTAL SCORE	RISK	COMMENT
<3	Low risk	Do not require antibiotic therapy
≥ 3	High risk	Treat with antibiotic therapy

References: A clinical score to reduce unnecessary antibiotic use in patients with sore throat. Can Med Assoc J, Jan. 13, 1998

2. Throat and Upper Respiratory Tract			
Tonsillitis/Pharyngitis Common organism: Group A Streptococcus	Phenoxymethylpenicillin (Pen V) 500mg PO q6h or 1gm PO q12h for 5-10 days **OR** Benzathine Penicillin 1.2MU IM, one single dose	Amoxicillin 500mg PO q8h for 5-10 days **Penicillin Allergy:** Erythromycin Ethylsuccinate 800mg q12h for 5-10 days	Antibiotics should be prescribed in suspected (Modified Centor Score ≥3)/proven bacterial infections, as sore throats are commonly viral in origin. Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute Peritonsillar Abscess Common organisms: Group A Streptococcus *Staphylococcus aureus* *Haemophilus influenza* *Fusobacterium necrophorum*	Ampicillin/sulbactam 3gm IV q6h **OR** Amoxicillin/clavulanate 1.2gm IV q8h **OR** Benzylpenicillin 2MU IV q6h **PLUS** Metronidazole 500mg IV q6-8h for 10-14 days	Amoxicillin/clavulanate 625mg PO q8h **OR** Phenoxymethylpenicillin (Pen V) 500mg PO q6h **PLUS** Metronidazole 500mg PO q6h **OR** Clindamycin 300-450mg PO q6h **Penicillin Allergy:** Clindamycin 600mg IV q8h	Abscess to be drained Penicillin allergy refer to Appendix 8
Diphteria *Corynebacterium diphtheriae*	*Antitoxin **PLUS** Erythromycin Lactobionate 500mg IV q6h followed by Erythromycin Ethylsuccinate 800 mg PO q12h for total of 14 days **OR** Benzylpenicillin 50,000 units/kg to a maximum of 1.2 MU IV q12h followed by Phenoxymethylpenicillin (Pen V) 250mg PO q6h for total of 14 days		***Diphtheria Antitoxin:** **Pharyngeal/ laryngeal disease of 2 days duration** 20,000 - 40,000 units **Nasopharyngeal disease** 40,000 – 60,000 units **Systemic disease of ≥3 days or any patient with diffuse neck swelling** 80,000 – 120,000 units Administer over 60 mins to inactivate toxin rapidly

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute Epiglottitis Common organisms: *Haemophilus influenzae* Type B virus *Streptococcus pneumonia*	Ceftriaxone 2gm IV q24h **OR** Ampicillin/sulbactam 3gm IV q6h **Oral step down therapy:** Amoxicillin/clavulanate 625mg PO q8h for 7–14 days	**Penicillin Allergy:** Clindamycin 600-900mg IV q8h **PLUS** Ciprofloxacin 400mg IV q12h	Urgent hospitalisation. May present with life threatening upper airway obstruction, especially in paediatrics. Penicillin allergy refer to Appendix 8 Consider adding Vancomycin for patients with moderate to severe sepsis, meningitis or previously colonized with MRSA.
Deep Neck Space Abscess Common organisms: *Streptococcus pyogenes* *Staphylococcus aureus* *Fusobacterium necrophorum*	Ampicillin/sulbactam 3gm IV q6h **OR** Ceftriaxone 2gm IV q24h **PLUS** Metronidazole 500mg IV q6h		Duration: 10-14 days
3. Rhinology			
Acute Bacterial Rhinosinusitis (ABRS) Common organisms: *Streptococcus pneumoniae,* *Haemophilus influenzae,* *Moraxella catarrhalis*	Amoxicillin 500mg PO q8h for 5-10 days **OR** Amoxicillin/clavulanate 625mg PO q8h for 5-7 days *If no improvement after 3 days of oral antibiotic, refer ENT.	**Penicillin allergy:** Doxycycline 100 mg q12h for 5-7 days Pregnant patients with penicillin allergy would need to be treated with Azithromycin 500mg PO q24hr for 3 days	Consider antibiotic if present at least 3 of below:[4] • Purulent/ greenish nasal discharge • Severe local pain (VAS 8-10) • Fever • Elevated ESR/CRP • Double sickening (becoming worse after initial recovery) *VAS: Visual Analogue Score.* The patient is asked: "How troublesome are your symptoms?" Not troublesome (0) to Worst thinkable troublesome (10) Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
4. Otology			
Acute otitis media (AOM) Common organisms: *Streptococcus pneumoniae,* *Haemophilus influenza,* *Moraxella catarrhalis*	***For non-severe AOM:** Amoxicillin 500mg PO q8h for 5days If symptoms not improved in 48-72 hours, treat as severe AOM ****For severe AOM or perforated tympanic membrane:** Amoxicillin/clavulanate 625mg PO q8h for 5 days	**Penicillin Allergy:** Azithromycin 500mg PO on day 1, followed by 250mg PO q24h until day 5	***Non-severe AOM:** • Mild otalgia • Temp <39ºC May consider 48-72hours of observation with symptomatic therapy before prescribing antibiotic. ****Severe AOM:** • Moderate to severe otalgia • Temperature >39ºC If symptoms not resolving after 48-72hours, refer ENT. Penicillin allergy refer to Appendix 8
Malignant Otitis Externa/ Necrotizing Otitis Externa Common organism: *Pseudomonas aeruginosa*	Ciprofloxacin 400mg IV q8h **OR** Ceftazidime 2gm IV q8h followed by Once showing clinical response, consider switching to oral therapy: Ciprofloxacin 750mg PO q12h to complete 6 weeks		
Acute Diffuse Otitis Externa Common organisms: *Pseudomonas aeruginosa* *Staphylococcus aureus*	Ofloxacin 0.3% otic solution Instill 10 drops into affected ear(s) q24h for 7 days		Aural toileting required in discharging ears

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Chronic Suppurative Otitis Media *Pseudomonas aeruginosa* *Staphylococcus aureus*	Ofloxacin 0.3% otic solution Instill 10 drops into affected ear(s) q12h for 10-14 days		Aural toileting required in discharging ears
Otomycosis Common organism: *Aspergillus* sp.	Clotrimazole 1% ear solution, applied q12h for 10 to 14 days		Aural toileting required.

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
LOWER RESPIRATORY TRACT INFECTIONS			
1. COMMUNITY ACQUIRED PNEUMONIA (CAP)			
• The diagnosis of CAP generally requires the demonstration of an infiltrate on chest radiograph in a patient with a clinically compatible syndrome (e.g; fever, dyspnoea, cough and sputum production) • CURB-65 is a clinical prediction rule that has been validated for predicting mortality in CAP. i. Confusion ii. BUN > 7 mmol/l iii. Respiratory rate of ≥ 30 BPM iv. Blood pressure ≤ 90/60 mmHg v. Age ≥ 65 Score 0-1 : Manage Outpatient (unless patient has co-morbidity or has difficult social circumstances) Score 2 and above : Consider Admission • Physicians should use CURB-65 prediction tools to support, not replace clinical judgments.			
Outpatient	Amoxicillin 500mg PO q8h for 5-7 days	Amoxicillin/clavulanate 625mg PO q8h for 5-7 days **OR** Doxycycline 100mg PO q12h for 7 days	
Inpatient (CURB ≥2)	Amoxicillin/clavulanate 1.2gm IV q8h for 5-7 days **PLUS** Azithromycin 500mg IV/PO q24h for 3-5 days	Ceftriaxone 2gm IV q24h for 5-7 days **PLUS** Azithromycin 500mg IV/PO q24h for 3-5 days **Penicillin Allergy** **Levofloxacin 500-750mg IV/PO q24h for 5-7 days	Penicillin allergy refer to Appendix 8 **Levofloxacin should be strictly reserved for penicillin allergy due to higher risk of adverse events. To switch to oral therapy when clinical condition improves and patient is able to tolerate orally. If suspected melioidosis infection, please refer to the section on tropical infections.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
2. VIRAL PNEUMONIA			
Influenza	Oseltamivir 75mg PO q12h for 5 days		
Varicella zoster	Acyclovir 10mg/kg IV q8h for 7 days		
3. LUNG ABSCESS AND EMPYEMA			
Empirical	Amoxicillin/clavulanate 1.2gm IV q6-8h	Ceftriaxone 2gm IV q24h **PLUS** *Metronidazole 500mg IV q8h **Penicillin Allergy** Clindamycin 600mg IV/PO q6h	Duration of treatment: - Drained abscess / empyema may require 2-4 weeks of antibiotics - Undrained abscess/ Empyema may require 4-6 weeks of antibiotics **Lung empyema:** Attempts should be made to drain the collection. May change to oral regime once clinical improvement seen *Metronidazole: in cases of lung abscess when aspiration is suspected If melioidosis is suspected, please refer to the section on tropical infections. Penicillin allergy refer to Appendix 8
Staphylococcus aureus	Cloxacillin 2gm IV q4-6h	Cefazolin 2gm IV q8h	Duration: 4-6 weeks, depending on clinical response. In rare cases (slow response to antibiotics) may need prolonged therapy. May change to oral therapy (e.g. Amoxicillin/clavulanate 625mg PO q8h) to complete the duration once patient stabilized and improved.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
4. INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)			
Antibiotics only considered if there is: Increased purulence in sputum **AND** one of the following: • Increased sputum volume • Increased dyspnoea **OR** Patient intubated (GOLD 2019)			
Outpatient	Amoxicillin/clavulanate 625mg PO q8h for 5-7 days	Cefuroxime 500mg PO q12h for 5-7 days **OR** Doxycycline 100mg PO q12h for 5-7 days	
Inpatient	Amoxycillin/clavulanate 1.2gm IV q8h for 5-7days **PLUS/MINUS** Azithromycin 500mg IV/PO for 3-5 days	Ceftriaxone 2gm IV q24h for 5-7 days **PLUS/MINUS** Azithromycin 500mg IV/PO for 3-5 days	
*If suspect Pseudomonas infection	**Piperacillin/tazobactam 4.5gm IV q6-8h **OR** Cefepime 2gm IV q8h **PLUS/MINUS** Azithromycin 500mg IV/PO for 3-5 days	Ceftazidime 2gm IV q8h **PLUS/MINUS** Azithromycin 500mg IV/PO for 3-5 days	*Pseudomonas sp risk factors: 1. Frequent exacerbation 2. Severe airflow limitation 3. Exacerbation requiring mechanical ventilation Reference: COPD (GOLD) 2019 Guideline **Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
5. HOSPITAL ACQUIRED PNEUMONIA (HAP/VAP)			
Risk factors for multi-drug resistance (MDR) organisms: 1. Prior intravenous antibiotic use within 90 days 2. More than 5 days of hospitalization in high risk ward (ICU, HDU) 3. Previous colonization with MDR pathogens Risk of MDR organisms is lower with early onset HAP/VAP.			
Early Onset HAP/VAP (2-4 days of admission/intubation)	Amoxicillin/clavulanate 1.2gm IV q8h for 5-7 days	Ceftriaxone 2gm IV q24h for 5-7 days	Need to adjust to local antibiogram/ prevalent organisms
Late Onset HAP/VAP (5 days or more of admission/intubation) Causative organism is determined by local prevalence.	*Piperacillin/tazobactam 4.5gm IV q6-8h for 7 days **OR** Cefepime 2gm IV q8h for 7 days	Imipenem/cilastatin 500mg IV q6h for 7 days **OR** Meropenem 1gm IV q8h for 7 days	Ideal empirical antibiotic coverage depends on local prevalence of organisms. Duration of antibiotics could be shortened to 7 days even for MDR *Pseudomonas aeruginosa* and *Acinetobacter baumanii* infections. Longer duration may be indicated depending upon clinical, radiological and laboratory parameters. To de-escalate antibiotics according to culture and sensitivity results *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
6. ASPIRATION PNEUMONIA			
	Amoxicillin/clavulanate 1.2gm IV q8h	Ceftriaxone 2gm IV q24h **PLUS** Metronidazole 500mg IV q8h	Duration: 7- 10 days To switch to oral therapy when clinical condition improves and patient is able to tolerate orally. Antibiotics are not indicated for aspiration (chemical) pneumonitis.

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
SEXUALLY TRANSMITTED INFECTIONS (STIs) • Ideally diagnosis of STI (apart from syphilis) should be Nucleic Acid Amplification Test (NAAT) based testing. • Contact tracing/partner notification is important in all STIs. • Duration of contact tracing/partner notification depends on the type of STIs			
Syphilis (*Treponema pallidum* Infection)			
Primary Syphilis **Secondary Syphilis** **Early Latent Syphilis** (History of syphilis infection within the last 2 years)	Benzathine Penicillin 2.4MU IM STAT **OR** Procaine Penicillin 600,000units IM q24h for 10 days	**<u>Penicillin Allergy</u>** Doxycycline 100mg PO q12h for 14 days	If drug administration is interrupted for ≥ 1 day at any point during the treatment course, it is recommended that the entire course is restarted. Patients should be warned of possible reactions to treatment: • Jarisch-Herxheimer reaction • Anaphylaxis/Allergy Abstain from sex for 2 weeks after they and their partner(s) have completed treatment. Screen for HIV. All sexual partners should be examined, investigated and treated epidemiologically. Partner notification: Primary syphilis (3 months), Others (6 months – 12 months). Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Late Latent Syphilis **Gummatous Syphilis** **Cardiovascular Syphilis**	Benzathine Penicillin 2.4MU IM weekly for 3 weeks (Day 1, 8, & 15) **OR** Procaine Penicillin 600,000units IM q24h for 14 days	**Penicillin Allergy** Doxycycline 100mg PO q12h for 28 days	For cardiovascular syphilis: Consider Prednisolone 40-60 mg OD for 3 days starting 24 hours before the antibiotics. If a patient defaults Benzathine Penicillin treatment by ≥ two weeks in between the weekly doses, the whole regime needs to be restarted. Contact tracing and partner notification as above. Penicillin allergy refer to Appendix 8
Neurosyphilis	Benzylpenicillin 4MU q4h IV for 14 days **OR** Procaine Penicillin 2.4MU IM q24h **PLUS** Probenecid 500mg PO q6h, both for 14 days	**Penicillin Allergy** Ceftriaxone 2gm IM or IV q24h for 14 days (if no anaphylaxis to penicillin) **OR** Doxycycline 200mg PO q12h for 28 days	Consider Prednisolone 40-60 mg OD for 3 days starting 24 hours before the antibiotics. CSF examination should be done in: 1. Patients with neurological and/or ocular symptoms or signs. 2. Nontreponemal test titres do not decrease by fourfold within 12 months of therapy. Contact tracing and partner notification as above. ** IM Ceftriaxone – dilute with Lidocaine Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Syphilis in HIV Primary, secondary, early and late latent and neurosyphilis	Treatment as appropriate for stage of infection	Treatment as appropriate for stage of infection	Perform full neurological examination Contact tracing and partner notification as above.
Syphilis in Pregnancy			
Primary, secondary, early latent	**1st & 2nd Trimesters** **(up to and including 27 weeks):** Benzathine penicillin G 2.4MU IM single dose **3rd Trimester** **(from week 28 to term):** Benzathine penicillin G 2.4MU IM weekly for 2 weeks (Day 1 & 8) **OR** **(All three trimesters)** Procaine penicillin G 600,000unit IM q24h for 10 days	**Penicillin Allergy** **(All three trimesters)** Ceftriaxone 500mg IM q24h for 10 days **OR** Azithromycin 500mg PO q24h for 10 days **OR** Erythromycin Ethylsuccinate 800mg PO q6h for 14 days	Tetracycline and Doxycycline are contraindicated in pregnancy Penicillin allergy refer to Appendix 8 If Macrolide therapy: Neonate require assessment and treatment at birth
Late latent, gummatous, cardiovascular	Treat as for non-pregnant patients (**DO NOT USE DOXYCYCLINE** in pregnancy)		
Neurosyphilis	Treat as for non-pregnant patients with Neurosyphilis (**DO NOT USE DOXYCYCLINE** in pregnancy)		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Gonorrhoea (*Neisseria Gonorrhoeae* Infection)			
Uncomplicated (Urogenital, Anorectal, Pharyngeal)	Ceftriaxone 500mg IM as a single dose **PLUS** *Azithromycin 1gm PO as a single dose	**β-lactam Allergy:** Gentamicin 240mg IM as a single dose **PLUS** *Azithromycin 2gm PO as a single dose **Pregnancy and breastfeeding:** Ceftriaxone 500mg I.M. as a single dose **PLUS** *Azithromycin 1gm P.O as a single dose	*Azithromycin: Dual therapy to treat for coexisting *Chlamydia trachomatis* infection (35-40%), synergistic effect & reduce cephalosporin resistance Avoid unprotected sexual intercourse for 1 week following treatment (partner(s) need to be treated as well) Test of cure in 2 weeks post treatment with NAAT is advisable Partner notification: Symptomatic partners in last 2 weeks. Asymptomatic partners in last 3 months Sexual partners should be treated for gonorrhoea even though they are asymptomatic. **β-lactam** allergy refer to Appendix 8
Gonococcal Conjunctivitis	IM Ceftriaxone 500mg q24h for 3 days	**Anaphylaxis to Penicillin or established allergy to Cephalosporin** Azithromycin 2gm PO single dose **PLUS** Doxycycline 100mg PO q12h for 7 days **PLUS** Ciprofloxacin 250mg PO q24h for 3 days	Penicillin or cephalosporin allergy refer to Appendix 8
Epididymitis/ Epididymo-orchitis	**Caused by gonorrhoea and chlamydia:** Ceftriaxone 500mg IM STAT		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
	PLUS Azithromycin 1gm PO STAT **PLUS** Doxycycline 100mg PO q12h for 14 days **STI related but unlikely gonorrhoea**: Doxycycline 100mg q12h for 14 days **Non-STI related (Enteric organisms)**: Ciprofloxacin 500mg q12h for 10 days		
Disseminated Gonorrhoea	Ceftriaxone 1-2gm IV q24h for 7 days	Cefotaxime 1gm IV q8h for 7 days	May be switched to Ciprofloxacin 500mg PO q12h 24-48hrs after symptoms improve.
Chlamydia Infections (*Chlamydia trachomatis*)			
Uncomplicated (urogenital, pharyngeal and rectal infection)	Doxycycline 100mg PO q12h for 7 days	Azithromycin 1gm PO stat, then 500mg PO q24h for 2 days	Avoid unprotected sexual intercourse for 1 week following treatment (partner(s) need to be treated as well) Test of cure (TOC) is not routinely recommended. Only consider TOC in pregnancy, poor compliance, and persistent symptoms. TOC ideally between 4-6 weeks post treatment with NAAT test Partner notification: Symptomatic partners in last 6 weeks. Asymptomatic partners in last 6 months Sexual partners should be treated for chlamydia even though they are

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			asymptomatic
Chlamydia in pregnancy	Azithromycin 1gm PO stat, then 500mg PO q24h for 2 days	Amoxicillin 500mg PO q8h for 7 days **OR** Erythromycin Ethylsuccinate 800mg PO q6h for 7 days	Doxycycline is contraindicated in pregnancy
Non-Gonococcal Urethritis (NGU)			
First episode of Non-gonococcal urethritis (NGU)	Doxycycline 100mg PO q12h for 7 days	Azithromycin 500mg PO STAT then 250mg q24h for 4 days	
Recurrent and persistent Non-gonococcal urethritis (NGU)	**If treated with Doxycycline first line**: Azithromycin 500mg PO stat then 250mg PO q24h for the next 4 days **PLUS** Metronidazole 400mg PO q12h for 5 days **If treated with Azithromycin first line**: Moxifloxacin 400mg PO q24h for 10-14 days **PLUS** Metronidazole 400mg PO q24h for 5 days		Most common cause of recurrent or persistent NGU is *Mycoplasma genitalium*. Also consider infection with *Trichomonas vaginalis* Partner notification: preceding 6 months from diagnosis Abstain from sexual intercourse until has completed therapy and his partner(s) have been treated – at least 1 week Follow-up is recommended after 2-3 weeks TOC in asymptomatic patient not recommended For confirmed *Mycoplasma genitalium* infection, TOC in 3 weeks post treatment is recommended using PCR

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Herpes Simplex Virus Type-1 and 2 (HSV-1 & 2) Infections			
Herpes Genitalis	**First episode:** Acyclovir 400mg PO q8h for 5 days	Valaciclovir 500mg PO q12h for 5 days	Physical supportive measures: saline bathing, analgesia, local anaesthetics and psychological support. Oral antiviral drugs indicated within 5 days of the start of the episode and while new lesions are still forming. Topical antivirals are less effective than oral agents and not recommended, due to the association with acyclovir resistant strain. Addition of topical antivirals to oral treatment is of no benefit.
	Recurrent episode: **Short-course** Acyclovir 800mg PO q8h for 2 days **5-day regimens** Acyclovir 400mg PO q8h	Valaciclovir 500mg PO q12h for 3-5 days	
Herpes Genitalis **Suppressive therapy:** (Indicated if ≥ 6 recurrences per year, severe, prolonged, or with psychosocial problems)	Acyclovir 400mg PO q12h	Valaciclovir 500mg PO q24h	Duration: All for up to 1 year, then reassess If breakthrough recurrences occur, dosage should be increased (refer: Recurrent episode dose)
Herpes Genitalis in pregnancy First episode	**First or second trimester acquisition (until 27+6 weeks):** Acyclovir 400mg PO q8h for 5 days	Valaciclovir 500mg PO q12h for 5 days	Do not delay treatment whilst awaiting results (HSV PCR recommended) **Third trimester acquisition:** No additional monitoring of the pregnancy is required Continue daily suppressive Acyclovir 400 mg PO q8h until delivery
	Third trimester acquisition (from 28 weeks): Acyclovir 400mg PO q8h for 5 days	Valaciclovir 500mg PO q12h for 5 days	
Suppressive therapy for recurrent	Acyclovir 400mg PO q8h		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Herpes Genitalis in pregnancy	Treatment recommended starting at 36 weeks of gestation until delivery		
Other Sexually Transmitted Infections			
Chancroid *Haemophilus ducreyi*	Azithromycin 1gm PO in a single dose **OR** Ceftriaxone 250mg IM in a single dose **OR** *Ciprofloxacin 500mg PO q12h for 3 days **preferred in HIV +ve patients*		Avoid unprotected sexual intercourse until they and their partner(s) have completed treatment and follow-up. Sexual contacts within 10 days before onset of the patient's symptoms should be examined and treated even in the absence of symptoms. Patients should be re-examined 3-7 days after initiation of therapy. Successful treatment; ulcers improve symptomatically within 3 days and substantial re-epithelisation occurs within 7 days after onset of therapy.
Lymphogranuloma Venereum *Chlamydia trachomatis Serovars L1,2,3*	Doxycycline 100mg PO q12h for 21 days	Azithromycin 1gm PO weekly for 3 weeks	Fluctuant buboes: Should be aspirated through healthy adjacent skin. Surgical incision contraindicated. Sexual contacts within 1 month prior to patient's symptoms, or the last 3 months of detected asymptomatic LGV, should be examined and tested for chlamydial infection and treated with the same regimen. Should be followed up until symptoms resolve.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			Routine TOC not necessary if recommended regimen is used and completed. If TOC is required (tetracycline allergy or pregnant), should be performed 2 weeks post completion of treatment.
Granuloma Inguinale (Donovanosis) *Klebsiella granulomatis*	Azithromycin 1gm PO weekly or 500mg q24h **PLUS/MINUS** Gentamicin 1mg/kg IM/IV q8h (in patients whose lesions do not respond in the first few days to other agents)	Doxycycline 100mg PO q12h **OR** Trimethoprim/Sulfamethoxazole 160/800mg PO q12h **OR** Ciprofloxacin 750mg PO q12h **PLUS/MINUS** Gentamicin 1mg/kg IM/IV q8h (in patients whose lesions do not respond in the first few days to other agents)	**Treatment duration**: for at least 3 weeks or until all lesions completely heal In the absence of any reliable screening test and the long incubation period, all sexual contacts in the last 6 months should be examined for possible lesions by clinical examination. Patients should be followed up until lesions have healed completely.
Trichomoniasis *Trichomonas vaginalis*	Metronidazole 2gm PO in a single dose **OR** 400mg PO q12h for 5 days		Screen other STIs Sexual contact(s) should be treated simultaneously and patients should be advised to abstain for at least one week until they and their partner(s) have

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Treatment failure (Second regimen)	Metronidazole 400mg PO q12h for 7 days		completed treatment and follow-up. Any partners within the 4 weeks prior to presentation should be screened for the full range of STIs and treated for TV. TOC only recommended if the patient remains symptomatic following treatment, or if symptoms recur. **Higher-dose of metronidazole is required if failing second regimen.
Bacterial vaginosis Common organisms: Anaerobic bacteria *(*e.g., *Prevotella sp., Mobiluncus sp., Gardnerella vaginalis*, and *Mycoplasma hominis)*	Metronidazole 400mg PO BD for 5-7 days **OR** 2gm PO as single dose	Clindamycin 300mg PO q12h for 7 days	Not an STI but frequently detected during STI screening

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A12. SKIN & SOFT TISSUE INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
1. PURULENT SKIN & SOFT TISSUE INFECTION			
Localised Impetigo Common Organisms: *Staphylococcus aureus* *Streptococcus pyogenes*	*Topical 2% Fusidic acid q8-12h for 5 days (Outpatient use only) **OR** Cloxacillin 500-1000mg PO q6h for 5-7 days **OR** Cephalexin 250-500mg PO q6h for 5-7 days		*Only can be used by Dermatologist
Generalised Impetigo/Ecthyma	Cephalexin 250-500mg PO q6h	Amoxicillin/clavulanate 625mg PO q8h	**Duration : 5-7 days**
	Penicillin Allergy: Erythromycin Ethylsuccinate 800mg PO q12h	**Other alternative/ in case of CA-MRSA :** Clindamycin 600mg PO q8h **OR** Trimethoprim/sulfamethoxazole 160/800mg PO q12h	Penicillin allergy refer to Appendix 8
Ecthyma gangrenosum Most common causative organism is *Pseudomonas sp*. however antibiotics need to be tailored according to culture result	Ciprofloxacin 500mg PO q12h **OR** *Piperacillin/tazobactam 4.5gm IV q6-8h	Ceftazidime 2gm IV q8h **OR** Cefepime 2gm IV q8h	Consider adding aminoglycoside in selected cases such as in immunocompromised/neutropenic and septic shock patients. Use synergistic combination therapy with aminoglycosides until susceptibilities are known. *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
2. NON-PURULENT SKIN & SOFT TISSUE INFECTION			
Furuncles	Cloxacillin 500mg PO q6h for 5-7days	Amoxicillin/clavulanate 625mg PO q8h for 5-7days	
Carbuncles Common organism: *Staphylococcus aureus*	Cloxacillin 1-2gm IV q6h	Amoxicillin/clavulanate 1.2gm IV q8h **OR** Cefazolin 1gm IV q8h	Surgical drainage is the mainstay of treatment. **Duration : 7-10 days**
Erysipelas Common organism: *Streptococcus pyogenes*	Phenoxymethylpenicillin 500mg PO q6h **OR** Amoxicillin 500mg PO q8h	Cephalexin 500mg PO q6h	**Duration : 7-10 days**
	If severe: Benzylpenicillin 2-4MU IV q4-6h	**If severe:** Cefazolin 1gm IV q8h **OR** Cefuroxime 750mg IV q8h	
	MRSA: *Vancomycin 15-20mg/kg q8-12h; not to exceed 2gm/dose		*Vancomycin loading dose refer to Appendix 1
Diabetic Foot Infections	Refer to section Surgical Infection - Bone and Joint Infections		
Gas Gangrene/ Myonecrosis/ Necrotizing Fasciitis	Refer to section Surgical Infection - Bone and Joint Infections		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Yaws ***Treponema pertenue***	Benzathine Penicillin 1.2MU IM single dose	Doxycycline 100mg PO q12h for 15 days **OR** Azithromycin 30mg/kg (max 2gm) single dose **<u>Penicillin Allergy:</u>** Tetracycline 500mg PO q6h for 15 days **OR** Erythromycin Ethylsuccinate 800mg PO q12h for 15 days	Penicillin allergy refer to Appendix 8
CELLULITIS			
Mild: Common organisms: *Staphylococcus aureus* & *Streptococcus pyogenes*	Cephalexin 500mg PO q6h	Cefuroxime 250-500mg PO q12h **OR** Amoxicillin/clavulanate 625mg PO q8h	**Duration : 5-10 days according to clinical response** Change to oral once condition improves. Gram negative coverage may be necessary in the following circumstances: 1. Potential relation of the cellulitis to a decubitus ulcer 2. Crepitant cellulitis 3. Prominent skin necrosis/gangrene 4. Location : a. Perioral b. Perirectal cellulitis 5. Clinical condition : a. Septicaemic shock b. Suspecting necrotizing fasciitis 6. Immunocompromised patients. 7. Specific exposures**
Moderate: Common organisms: *Staphylococcus aureus* & *Streptococcus pyogenes*	Cloxacillin 1-2gm IV q6h	Cefazolin 1-2gm IV q8h	
Severe : Common organisms: *Staphylococcus aureus* & *Streptococcus pyogenes*	Ampicillin/sulbactam 3gm IV q6-8h **PLUS/MINUS** Clindamycin 600mg IV q6h (Deescalate once cultures are available/ Necrotizing fasciitis ruled out)	*Piperacillin/tazobactam 4.5gm IV q6-8h **PLUS/MINUS** Clindamycin 600mg IV q6h (Deescalate once cultures are available/ Necrotizing fasciitis ruled out)	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
****Consider alternative organisms in the following circumstances:**			
Dog/cat bite: Common organisms: *Pasteurella multocida, Capnocytophaga canimorsus*	Amoxicillin/clavulanate 625mg PO q8h		
Cat scratch disease *Bartonella henselae*	Azithromycin 500mg PO on Day 1, then 250mg PO q24h for 4 days		
Human bite: Common organisms: *Eikenella corrodens*, anaerobes, *Staphylococcus aureus*	Amoxicillin/Clavulanate 625mg PO q8h		
Salt water exposure: Common organism: *Vibrio sp.*	Doxycycline 200mg stat then 100mg PO q12h **PLUS/MINUS** ***Ceftriaxone 2gm IV q24h		***Consider adding 3rd Generation Cephalosporin in severe infection
Fresh or brackish water exposure: Common organisms: *Aeromonas sp., Plesiomonas*	Ciprofloxacin 400mg IV q12h **OR** Ciprofloxacin 750mg PO q12h		
Neutropenic patients: Common organisms: *Pseudomonas aeruginosa*, other Gram negatives	*Piperacillin/tazobactam 4.5gm IV q6-8h	Ceftazidime 2gm IV q8h **OR** Cefepime 2gm IV q8h	*Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours). Vancomycin loading dose refer to Appendix 1

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
MRSA	Vancomycin 15-20mg/kg IV q8-12h **In severe infections:** To load with Vancomycin 25-30mg/kg IV, followed by 15-20mg/kg (actual body weight) IV q8-12h; not exceeding 2gm/dose	Linezolid 600mg IV/PO q12h	******Consider CA-MRSA if :** **1. Outbreaks of known CA-MRSA** **2. If non-resolving cellulitis**
******If CA-MRSA suspected**	Clindamycin 300-450mg IV/PO q8h **OR** Doxycyline 100mg PO q12h **OR** Trimethoprim/sulfamethoxazole 160/800mg PO q12h		
3. PERIPHERAL PHLEBITIS/THROMBOPHLEBITIS			
Common organisms: *Staphylococcus aureus,* Coagulase negative *Staphylococcus,* Gram negative rods	**Early stage phlebitis:** Remove the intravenous cannula		Peripheral intravenous catheters with associated pain, induration, erythema, or exudate should be removed.
	Medium and advanced stage phlebitis or thrombophlebitis: Remove the intravenous cannula and take blood culture Can consider empirical treatment if persistent fever: Cephalexin 500mg PO q6h **OR** Cloxacillin 1-2gm IV q6h		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
4. BED SORE/PRESSURE SORE/DECUBITUS ULCER			
	Local treatment is preferred. **If there is surrounding cellulitis/signs of bacteremia/ fasciitis/ surrounding intramuscular abscess/ OM changes:** Ampicillin/Sulbactam 3gm IV q6-8h		
5. MYCOBACTERIAL INFECTIONS			
Hansen's Disease (Leprosy) ***Mycobacterium Leprae***	**Paucibacillary** Rifampicin 600mg PO monthly (supervised) **PLUS** Dapsone 100mg PO q24h Duration: 6 months (Completion of 6 doses within 9 months) Surveillance: 5 years	***Bacterial resistance or hypersensitivity to first line** Can be substituted with one of the following: Ofloxacin 400mg PO q24h **OR** Minocycline 100mg PO q24h **OR** Clarithromycin 500mg PO q24h **OR** Ethionamide 250mg PO q24h	*Second line can only be initiated by a dermatologist.
	Multibacillary Rifampicin 600mg PO monthly **PLUS** Clofazimine 300mg PO monthly and 50-100mg PO q24h **PLUS** Dapsone 100mg PO q24h Duration: 1 year (if initial BI<4) or 2 years (if BI≥4)		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Completion of 12 doses within 18 months (BI<4) Completion of 18 doses within 36 months (BI≥4) Surveillance: 15 years		
Hansen's Disease (Leprosy) in HIV	Same as non HIV patients		
NON-TUBERCULOUS MYCOBACTERIAL INFECTIONS			
Mycobacterium marinum	Clarithromycin 500mg PO q12h **PLUS** Minocycline/Doxycycline 100mg PO q12h Duration: At least 2 months of treatment until clearance	Rifampicin 600mg PO q24h **PLUS** Ethambutol 15mg/kg PO q24h for 4-6 months, and continue for at least 1 month after lesions have been cleared **OR** Monotherapy Doxycyline 100mg PO q12h for 1-2 months after lesion clearance (3-4 months)	Often resistant to Isoniazid.
Mycobacterium kansasii	Isoniazid 300mg PO q24h **PLUS** Rifampicin 600mg PO q24h **PLUS** Ethambutol 15mg/kg PO q24h for 18 months		
Mycobacterium ulcerans (Buruli ulcer)	Rifampicin 10mg/kg PO q24h **PLUS** Streptomycin 15mg/kg IM q24h for 8 weeks	Rifampicin 10mg/kg PO q24h **PLUS** Streptomycin 15mg/kg IM q24h for 4 weeks followed by:	Wide surgical excision and debridement are important. **Duration:** For 4-6 months, and continue for at least 1 month after lesions have been cleared.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		Rifampicin 10mg/kg PO q24h **PLUS** Clarithromycin 7.5mg/kg PO q12h	
Mycobacterium fortuitum/ chelonei	**Combination therapy (2 of the following:** Clarithromycin 500mg PO q12h **OR** Doxycycline/Minocycline 100mg PO q12h **OR** Ciprofloxacin 500-750mg PO q12h **PLUS/MINUS** *Amikacin 15mg/kg IV q24h		*Amikacin: Started for severe infection until clinical improvement (together with 2 oral agents), then continue with just 2 oral agents.
6. FUNGAL INFECTIONS			
Tinea capitis *Trichophyton, Microsporum*	Griseofulvin 500mg PO q12h for 6 to 12 weeks or longer till fungal cultures are negative **OR** Terbinafine 250mg PO q24h **PLUS** 2.5% Selenium sulphide shampoo **OR** 2% Ketoconazole shampoo, 2 – 3 times per week for 2 weeks	Itraconazole 200mg PO q24h **OR** Fluconazole 6mg/kg PO q24h Duration is based on mycological agent: *Trichophyton sp* : 2-4 weeks *Microsporum sp* : 8-12 weeks	**Other recommendations:** 1. For kerion, Griseofulvin should be considered as first line unless *Tricophyton* has been cultured as the pathogen. Duration of treatment may be longer. 2. Contacts of patient may be treated with 2% Ketoconazole shampoo 2 – 3 times per week for 2 weeks. 3. Surgical excision is to be avoided. 4. Topical therapy alone is not recommended for the management of tinea capitis. 5. Consider adding oral prednisolone in selected cases. 6.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Tinea barbae	Same as treatment of **Tinea capitis**		
Tinea corporis/ Tinea cruris/ Tinea faciei *Trichophyton, Microsporum, Epidermophyton*	**Mild infections:** Topical imidazoles or allylamines cream/lotion: e.g.: Clotrimazole 1% **OR** Miconazole 2% **OR** Ketoconazole **OR** Terbinafine Duration: till clinical clearance with additional 2 weeks		**Recommendations:** 1. In patients with renal or hepatic impairment, caution should be exercised while prescribing systemic antifungals. 2. Terbinafine clearance significantly reduced in patient with renal impairment. Other systemic antifungals are preferred in these patients. 3. Topical Nystatin should not be used in dermatophytosis as they are not effective against dermatophytes
	Extensive infections: Terbinafine 250mg PO q24h for 2 weeks **OR** Itraconazole 200mg PO q24h for 2 weeks **OR** Griseofulvin 500mg PO q12h or q24h for 4-6 weeks	Fluconazole 150-300mg per week PO for 3-4 weeks	
Tinea manuum/ Tinea pedis *Trichophyton, Microsporum, Epidermophyton*	**First line:** Topical antifungals as mentioned in tinea corporis for 4-8 weeks		**Recommendations:** 1) Topical keratolytic agents can be used in conjunction with antifungals for hyperkeratotic type of tinea pedis/manuum. 2) KM_nO_4 in 1:10,000 dilution wet dressings, applied for 20 min 2–3 times/day, may be helpful
	Resistant cases: Terbinafine 250mg PO q24h for 2-4	Fluconazole 150mg/week PO for 4	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	weeks **OR** Itraconazole 200mg PO q24h for 2-4 weeks **OR** Griseofulvin 500mg PO q12h for 6-12 weeks	weeks	if vesiculation or maceration is present. 3) Systemic antifungals can be prescribed as first line treatment in severe moccasin-type tinea pedis or severe recurrent tinea with blisters.
Tinea unguium *Trichophyton, Microsporum, Epidermophyton*	Amorolfine 5% Nail Lacquer weekly application **Duration:** For 6 months (fingernails) For 12 months (toenails) **OR** Pulse Itraconazole 200mg PO q12h for 1 week per month **Duration:** For 2 months (fingernails) For 3 months (toenails) **OR** Terbinafine 250mg PO q24h **Duration:** For 6 weeks (fingernails) For 12 weeks (toenails)	Griseofulvin 500mg PO q12h **Duration:** For 6 months (fingernails) For 12 months (toenails) **OR** Fluconazole 150mg PO once weekly **Duration:** For ≥ 3 months (fingernails) For 6-12 months (toenails)	Amorolfine 5% Nail Lacquer is not indicated for children less than 12 years old. Patients with contraindications to systemic agents may consider topical antifungal agents. Diagnosis of onychomycosis should be confirmed with a KOH preparation, culture, or PAS Stain. Empirical treatment is not recommended.
Tinea versicolor *Malassezia Furfur, Pityrosporum Orbiculare*	**First line:** Topical treatment only Selenium Sulphide 2% shampoo Apply to affected areas 10 minutes before bathing **OR** Dilute to 1:1 with water, apply and leave overnight (treat for 1-2 weeks) **OR**	Sulfur + salicylic solution	**Recommendations:** Ketoconazole shampoo or Selenium sulphide shampoo can be used once every two to four weeks for approximately six months in order to try and prevent recurrence.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	2% Ketoconazole shampoo apply to affected areas 10 minutes before bathing **<u>For face</u>:** Topical Imidazole for 4-6 weeks e.g.: Miconazole 2% cream, Clotrimazole 1% cream, Tioconazole 1% cream		
	For recurrent or resistant cases: Itraconazole 200mg PO q24h for 1 week **OR** Fluconazole 150-300mg PO weekly dose for 2 to 4 weeks		
Candidiasis *Candida albicans*	**Mild cutaneous candidiasis:** Topical Imidazole q12h till clear e.g., Miconazole 2% cream, Clotrimazole 1% cream, Tioconazole 1% cream		Treatment of sexual partner is advisable in case of recurrent infection. *Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (e.g.: Cola drinks). Avoid PPIs and H2 blockers.
	Extensive cutaneous candidiasis: *Itraconazole 200mg PO q24h for 1 week	Fluconazole 100mg PO q24h for 1 week (in severe and immunocompromised patients)	
Subcutaneous Fungal Infections Lymphocutaneous and Cutaneous Sporotrichosis	*Itraconazole 200mg PO q12h until all lesions have resolved (usually for a total of 3–6 months)	**For patients not able to tolerate Itraconazole:** Terbinafine 250mg PO q12h **OR** Fluconazole 400-800mg q24h	In some immunocompromised condition such as AIDS, longer treatment may be necessary. Refer to Opportunistic Infections In HIV Patients. *Itraconazole: Absorption depends on gut acidity. Take capsule with food and acidic beverage (e.g.: Cola drinks). Avoid PPIs and H2 blockers.
Systemic sporotrichosis (pulmonary, osteoarticular, meningeal, or disseminated	Amphotericin B deoxycholate 0.7-1mg/kg q24h for 2 weeks followed by,		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
sporotrichosis)	*Itraconazole 200mg PO q12-24h for 12 months		**Avoid azole in pregnancy
Sporotrichosis In Pregnancy**	Tebinafine 250mg PO q24h	Amphotericin B deoxycholate 0.7-1mg/kg q24h	
Cutaneous fungal infection in immunocompromised patients	Refer to treatment of disseminated fungal infection in immunocompromised/HIV patients		Skin biopsy for HPE and culture are advised before commencing treatment.
Aspergillus sp, Scedosporium apiospermum, and Fusarium sp infection	Voriconazole 6mg/kg IV q12h for 2 doses, followed by 4mg/kg IV q12h	Amphotericin B (deoxycholate) 0.7–1mg/kg q24h **OR** Amphotericin B (lipid formulation) 3–5mg/kg q24h	
Cryptococcal infections **1)Mild** **2) Life threatening**	Fluconazole 100–400mg PO q24 h Refer to Treatment of disseminated fungal infection in immunocompromised/HIV patients		
Penciciliosis and life threatening acute severe disseminated Histoplasmosis	Refer to Treatment of disseminated fungal infection in immunocompromised/HIV patients		
7. VIRAL INFECTIONS			
Herpes Simplex Infections	**i) Mild infection:** Acyclovir 400mg PO q8h for 5 days		
	ii) Severe life threatening: Acyclovir 5-10mg/kg IV q8h for 5 days or until able to take orally, then change to oral		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	iii) Genitalia: Refer to section [Sexually Transmitted Infections]		
Chickenpox (Varicella zoster)	**i) Immunocompetent** Acyclovir 800mg PO 5 times daily for 7 days		Advisable to start treatment early within 48 hours.
	ii) Immunocompromised Acyclovir 10mg/kg IV q8h for 7 days (change to oral once there is an improvement)		
Herpes Zoster	Please refer to varicella zoster treatment		Topical antiviral treatment is not recommended for Herpes Zoster. Systemic antiviral treatment is recommended for all immunocompromised patient or for immunocompetent patients with following criteria: (1) >50 years of age (2) have moderate or severe pain (3) have moderate or severe rash; (4) have non-truncal involvement Advisable to start treatment early within 48-72 hours
8. PARASITIC INFESTATION			
Scabies *Sarcoptes scabiei*	Benzyl Benzoate emulsion 25% (EBB) apply from neck down and leave for 24 hours for 2-3 days **OR**		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Permethrin 5% lotion/cream apply and leave for 8 hours Repeat application after 1 week		
	In pregnancy/ Immunocompromised: Permethrin 5% lotion/cream apply and leave for 8 hours Repeat application after 1 week		
Head Lice *Pediculus humanus Capitis*	Permethrin 1% lotion apply to scalp for 10 min and wash off **OR** Malathion 1% shampoo Repeat application after 1 week		
Body Lice/pubic Lice *Pediculus humanus*	Malathion lotion 0.5% for 8-12 hours and wash off **OR** Permethrin 1% cream apply to affected area for 10 min and wash off		

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
1. GENERAL SURGERY			
Acute Pancreatitis			
Mild to moderate	No antibiotics		Antibiotics should be given for an extra-pancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections & pneumonia.
Severe Antibiotic mainly indicated for infected pancreatic necrosis. Possible causative organisms: Enterobacteriaceae Enterococci *Staphylococcus aureus* Streptococcus *Staphylococcus epidermidis* Anaerobes Candida spp (rarely)	*Piperacillin/tazobactam 4.5gm IV q6-8h	Cefoperazone 1-2gm IV q12h **PLUS** Metronidazole 500mg IV q8h	Modify antibiotics once culture and sensitivity is available. Reserve carbapenem for infections caused by resistant pathogens. *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
Diverticulitis Antibiotics considered for patients with the following: Fever, elevated WBC, patients who have failed to respond to conservative management			
Diverticulitis (Not undergoing a source control procedure)	Amoxicillin/clavulanic Acid 625mg PO q8h for 5 days **OR** Ampicillin/sulbactam IV 3gm q6h	**Non-severe penicillin allergy:** Cefuroxime 1.5gm IV q8h **PLUS** Metronidazole 500mg IV q8h	Penicillin allergy refer to Appendix 8
Diverticulitis (Severe infection/life threatening infection)	*Piperacillin/tazobactam 4.5gm IV q6-8h for 7 days	****Severe penicillin allergy:** Ciprofloxacin 400mg IV q12h **PLUS** Metronidazole 500mg IV q8h	* Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours). Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Breast abscess/Mastitis Common organism: *Staphylococcus aureus*	Cloxacillin 1-2gm IV q6h **OR** Cefazolin 1-2gm IV q8h	Amoxicillin/clavulanate 625mg PO q8h **OR** Ampicillin/sulbactam 750mg PO q12h **Penicillin Allergy:** Clindamycin 600mg IV/PO q8h	Drainage may be required for abscess For lactating mastitis: Consider sending breast milk for C&S if not responding after 48h of initial antibiotic therapy or recurring mastitis. Duration: 10 to 14 days but shorter courses (5 to 7 days) can be used if the response to therapy is rapid and complete. Penicillin allergy refer to Appendix 8
Hernia repair with mesh	Refer to section Chemoprophylaxis-Surgical		
Appendicitis Common organisms: Enterobacteriaceae Enterococci Bacteroides	Cefuroxime 1.5gm IV q8h **PLUS** Metronidazole 500mg IV q8h	Ampicillin/sulbactam 1.5gm IV q6-8h **OR** Amoxicillin/clavulanate 1.2gm IV q8h	Acute appendicitis without evidence of perforation, abscess, or local peritonitis; treatment should be discontinued within 24 hrs. For patients with various forms of appendicitis not undergoing a source control procedure, change to early oral therapy. Duration: 4-7 days.
Perforated Appendix /Appendicular Mass	Cefuroxime 1.5gm IV q8h **OR** Cefoperazone 1-2gm IV q12h **PLUS** Metronidazole 500mg IV q8h	Ampicillin/sulbactam 1.5-3gm IV q6-8h **OR** Amoxicillin/clavulanate 1.2gm IV q8h	Duration: 4-7 days
Perforated Viscus Peritonitis	Cefuroxime 1.5gm IV q8h **OR**	Ampicillin/sulbactam 1.5-3gm IV q6-8h **OR**	Duration: 4-7 days (if adequate source control, no delay in surgical intervention and patient has rapid

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
	Cefoperazone 1-2gm IV q12h **PLUS** Metronidazole 500mg IV q8h	Amoxicillin/clavulanate 1.2gm IV q8h	clinical recovery).
Abdominal trauma **Stab Wound** **Suspected bowel or solid organ injury** Common organisms: Gram negative enteric aerobes and anaerobes	Amoxicillin/clavulanate 1.2gm IV q8h	Cefuroxime 1.5gm IV q8h **PLUS** Metronidazole 500mg IV q8h	Duration: 4-7 days (if adequate source control, no delay in surgical intervention and patient has rapid clinical recovery). * Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
	Severe / Infected wound: Cefazolin 2gm IV q8h **PLUS** Metronidazole 500mg IV q8h **OR** *Piperacillin/tazobactam 4.5gm IV q6-8h	**Severe / Infected wound :** Ciprofloxacin 400mg IV q12h **PLUS** Clindamycin 450-600mg IV q8h	
Anal/Rectal abscess	Amoxicillin/clavulanate 1.2gm IV or 625mg PO q8h		Drainage is required. Duration: 4-7 days (if adequate source control, no delay in surgical intervention and patient has rapid clinical recovery). Routine antibiotic is not recommended in otherwise healthy patients.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
VASCULAR			
Mycotic aneurysm (Initial Treatment) Vascular prosthesis infection Common organisms: *Streptococcus pneumoniae* *Staphylococcus aureus* (30%) *Salmonella sp* (50%)	Ceftriaxone 2gm IV q24h	*Piperacillin/tazobactam 4.5gm IV q6-8h	Duration: At least six weeks (IV then oral based on clinical response and cultures) *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours). Consider adding Vancomycin if suspecting MRSA/CoNS or Vascular prosthesis infection If *Burkholderia pseudomallei* is suspected, refer to Tropical Infection section *CRP monitoring upon follow-up
	***Step down therapy:** Ciprofloxacin 250mg PO q12h **OR** Amoxycillin/clavulanate 625mg PO q8h		
Ischaemic limb ulcers with infection	Ampicillin/sulbactam 1.5-3gm IV q6-8h for 7 days (to continue until C&S available)	Amoxicillin/clavulanate 1.2 gm IV q8h for 7 days (to continue until C&S available)	Duration: depends on the extend of the infection (longer if bone involved)
BITES (penetrating injuries)			
Animal bite Common organisms: *Staphylococcus aureus* Streptococcus Gram negative Bacilli Anaerobes Pasturella (50% dog bites and 75% cat bites) *Eikenella corrodens* Pseudomonas sp.	Amoxicillin/clavulanate 625mg PO q8h	Doxycycline 100mg PO q12h **PLUS** Clindamycin 300mg PO q6h	Prophylactic duration: 3-5 days - Associated crush injury - In the hands or proximity to a joint - Associated edema If wound is infected: 10 days or longer is recommended * Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
	If severe/life threatening: Ampicillin/sulbactam 1.5-3gm IV q6-8h	**If severe/life threatening**: *Piperacillin/tazobactam 4.5gm IV q6-8h	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Human bite Common organisms: *Staphylococcus aureus* Anaerobes *Eikenella corrodens* Strep. (esp.viridans)	Amoxicillin/clavulanate 625mg PO q8h	**Penicillin Allergy:** Clindamycin 300mg PO q6h **PLUS** Ciprofloxacin 500-750mg PO q12h **OR** Trimethoprim/sulfamethoxazole 160/800mg PO q12h	Penicillin allergy refer to Appendix 8

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2. BONE AND JOINT INFECTIONS

OSTEOMYELITIS

Acute Osteomyelitis Common organisms: *Staphylococcus aureus* (80%) Group A *Streptococcus pyogenes* Rarely gram negative bacilli	Empirical coverage: Cloxacillin 2gm IV q6h To tailor antibiotics according to definitive cultures.	**Penicillin Allergy:** Cefazolin 2 gm IV q6-8h	**Duration:** Initial IV therapy for 2-4 weeks followed by oral therapy. Minimum 6 weeks. Modify according to clinical response. A shorter duration of antibiotics can be considered if the osteomyelitis is fully resected (e.g. amputation

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			with a clear margin): - No surrounding soft tissue infection: 5 days. - Evidence of soft tissue infection: 10-14 days. Penicillin allergy refer to Appendix 8
Chronic Osteomyelitis[2,6] Definition • Relapsing infection despite adequate duration of appropriate antibiotic • Chronic pain/swelling/bone tenderness associated with tissue necrosis, increased drainage or persistent sinus tracts. • Presence of bone destruction and presence of sequestra on imaging Commonest organism: *Staphylococcus aureus*	Empirical treatment before taking adequate cultures is not recommended. Choice of antibiotic depends on C&S result from tissue/bone as swab culture NOT reliable. Thorough Surgical debridement required (Removal of deadbone/ orthopaedic hardware)		Duration: 6 weeks but usually > 3 months. Treat until inflammatory parameters are normal
Vertebral Osteomyelitis[3,4] **Epidural Abscess** Common organisms: *Staphylococcus aureus* (main) Brucella Salmonella Gram negative Bacilli	Empirical therapy should be withheld unless patient is septic or in patients with neurologic compromise. Cloxacillin 2gm IV q4h To tailor antibiotics according to definitive cultures	Cefazolin 2gm IV q6-8h	Empiric gram negative should be covered if patient had: - Recent spinal hardware inserted or surgery - Intraabdominal infections -Coexisting or synchronous genitourinary infection - HIV infection Surgical therapy is necessary in: - Spinal cord compression/instability - Persistence of epidural abscess despite adequate antibiotic - Considering TB spine/ MDR organisms
	Duration: Minimum 6 weeks. Minimum 8 weeks if undrained paravertebral abscess(es) and/or infection due to drug-resistant organisms.		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
	Up to 12 weeks if extensive bone destruction.		
SEPTIC ARTHRITIS			
Acute monoarticular [In person who do not have any risk factors for STD (Staphylococcus/ Streptococcus)]	Cloxacillin 2gm IV q4-6h Duration: Parenteral therapy 2-4 weeks Oral therapy to complete total 4-6 weeks	**Penicillin Allergy:** Cefazolin 2gm IV q6-8h **OR** Clindamycin 600mg IV q6h, followed by oral therapy (same dose) **OR** **Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose Duration: Parenteral therapy 2-4 weeks Oral therapy to complete total 4-6 weeks	Drainage, debridement and washout of infected joint is important to limit further damage. A shorter duration of therapy is possible in immunocompetent patients who have had adequate surgical drainage. Penicillin allergy refer to Appendix 8 ** Vancomycin: If suspected/confirmed MRSA. Consider loading dose 25-30mg/kg for critically ill/septic patient to achieve faster steady state. Empirical therapy wherever possible should be directed by the result of the Gram stain of the joint aspirate.
Acute monoarticular [In person who have risk factors for STD (Gonorrhea/Streptococcus/Staphylococcus/Gram negative Bacilli)]	Ceftriaxone 2gm IV q24h for 1-2 weeks **PLUS** Azithromycin 1gm PO stat **OR** Doxycycline 100mg PO q12h for 7 days	Cefotaxime 2gm IV q8h for 1-2 weeks **PLUS** Azithromycin 1gm PO stat **OR** Doxycycline 100mg PO q12h for 7 days	
Polyarticular Gonorrhoea	Ceftriaxone 2gm IV q24h for 7 days		

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
PROSTHETIC JOINT INFECTIONS			
Prosthetic Joint Infections (Empirical) Early: <3 months after surgery *Staphylococcus aureus* Gram negative Bacilli Delayed onset : from 3 to 12 months after surgery) Less virulent organism; CONS/Enterococcus/anaerobes Late Onset : >12 months after surgery *Staphylococcus aureus* Enterobacteraeciae B hemolytic Streptococcus Anaerobes			**Treatment concepts :** 1. Empirical therapy is not recommended 2. Treatment is based on culture and sensitivity 3. Rifampicin should never be used alone and should be started only after the clearance of bacteraemia. 4. Treatment strategy and duration of treatment depends on surgical strategy.
Definitive Prosthetic Joint infection treatment Methicillin-sensitive *Staphylococcus aureus* (MSSA)	**Initial Treatment:** Cloxacillin 2gm IV q4-6h **OR** Cefazolin 2gm IV q6-8h **PLUS** Rifampicin 600mg PO q24h or 450mg PO q12h		Duration: 2-6 weeks (according to treatment strategy) Followed by an oral combination therapy according to susceptibility. Rifampicin should be included if implant is in situ.
Definitive Prosthetic Joint infection treatment Methicillin-resistant *Staphylococcus aureus* (MRSA)	**Initial treatment:** *Vancomycin 15-20mg/kg (actual body weight) IV q8-12h; not to exceed 2gm/dose **PLUS** Rifampicin 300-450mg PO q12h		Duration: 2-6 weeks (according to treatment strategy) Followed by an oral combination therapy according to susceptibility. Rifampicin should be included if implant is in situ.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			*Vancomycin loading dose refer to Appendix 1
DIABETIC FOOT INFECTIONS			
Antibiotics should not be used unless there are local or systemic symptoms of infection. Local treatment including surgical debridement is important. Antibiotic selection should be based on the most recent culture and sensitivity report.			
Mild Infections: a. Local infection involving skin & SC tissues b. Erythema, less than 2 cm around the ulcer c. No systemic signs of infection	Amoxicillin/clavulanate 625mg PO q8h **OR** Ampicillin/sulbactam 375-750mg PO q12h	Cephalexin 500mg PO q6H **PLUS** Metronidazole 400mg PO q8h	Duration: 5-7 days
Moderate Infections: a. Deep tissue infection b. Erythema more than 2 cm around ulcer c. No SIRS	Ampicillin/sulbactam 3gm IV q6-8h	Cefazolin 2gm IV q8hrly **PLUS** Metronidazole 500mg IV q8h **Penicillin Allergy:** Ciprofloxacin 400mg IV q8-12h **PLUS** Clindamycin 600mg IV q8h	Duration: 7-14 days Modify according to clinical response. If proven osteomyelitis or margin of resection is inadequate: at least 4-6 weeks. However, a shorter duration (1 to 2 weeks) is sufficient if margin of surgical resection is adequate. Penicillin allergy refer to Appendix 8 **Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
	If pseudomonas is suspected: **Piperacillin/tazobactam 4.5gm IV q6-8h		
Severe Infections: All of the above 2 or more SIRS • History of previous antibiotics exposure • Recurrent admission • Risk of pseudomonas infection • Immunocompromised	*Piperacillin/tazobactam 4.5gm IV q6-8h If given as q8h, to be given as extended infusion (over 3-4 hours).	Cefepime 2gm IV q8h **PLUS** Metronidazole 500mg IV q8h	Surgical debridement is URGENT. Based on intra-operative culture and sensitivity, antibiotic should be streamlined. Duration: 7- 14 days (subjected to clinical improvement) If proven osteomyelitis or margin of resection is

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			inadequate: at least 4-6 weeks. A shorter duration of antibiotics can be considered if the osteomyelitis is fully resected (i.e., amputation with a clear margin): • No surrounding soft tissue infection: 5 days. • Evidence of soft tissue infection: 10-14 days.
NECROTIZING FASCIITIS			
Type 1 **Polymicrobial infection.** Primarily occurs in patients who are immunocompromised or have certain chronic diseases such as diabetes	*Piperacillin/tazobactam 4.5gm IV q6-8h **PLUS/MINUS** **Clindamycin 600-900mg IV q8h	Cefotaxime 2 gm IV q8h **PLUS** Metronidazole 500 mg IV q8h **OR** **Clindamycin 600-900 mg IV q8h **OR** Ampicillin/Sulbactam 3 gm IV q6-8h **PLUS /MINUS** **Clindamycin 600-900 mg IV q8h	* Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours). **Clindamycin: only necessary if risk of group A streptococcus/ presence of gas crepitus. Immediate aggressive surgical debridement is the primary treatment modality. Repeated surgical debridement for source control are normally necessary. Urgent gram stain. Based on intra-operative culture and sensitivity, antibiotic should be streamlined.
Type 2 **Monomicrobial infection** Group A *streptococcus(most common)*	Benzylpenicillin 2-4MU IV q4h **PLUS** *Clindamycin 600-900mg IV q8h		*Clindamycin: only necessary if risk of group A streptococcus/ presence of gas crepitus.
Vibrio vulnificus *Aeromonas hydrophilia*	Ceftriaxone 1gm IV q12h **PLUS**	Ciprofloxacin 400mg IV q8h	Duration**:** 7-14 days (subjected to clinical assessment)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Consider in water related injuries and patients with liver cirrhosis and ingestion of raw oysters	Doxycycline 100mg PO q12h		
Fournier's Gangrene Common organisms: *Escherichia coli* Klebsiella Proteus Enterococcus Pseudomonas Anaerobes	*Piperacillin/tazobactam 4.5gm IV q6-8h **OR** Ceftriaxone 2gm IV q24h **PLUS** Metronidazole 500mg IV q8h	Ampicillin/sulbactam 3gm IV q6-8h	Aggressive surgical debridement is necessary to remove all necrotic tissue. *Piperacillin/tazobactam: If given as q8h, to be given as extended infusion (over 3-4 hours).
SOFT TISSUE INFECTION SECONDARY TO GAS PRODUCING ORGANISM			
Common organisms: Clostridium sp Gram negative organism	Benzylpenicillin 4MU IV q4h **PLUS** Clindamycin 600-900mg IV q6h **PLUS/MINUS** *Gentamicin 5mg/kg IV q24h	Cefotaxime 2gm IV q8h **PLUS** Clindamycin 600-900mg IV q6h	Duration: 10-28 days *Gentamicin: If suspects Gram negative infection. Early aggressive surgical debridement is essential.
SUPPURATIVE WOUND INFECTIONS, SURGICAL OR TRAUMATIC			
Suppurative wound infections, surgical or traumatic	If there is surrounding cellulitis and/or systemic symptoms are present: Cloxacillin 500mg PO/IV q6h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h (If gram negative organisms suspected or known to be involved)		Change antibiotics accordingly after C&S result are available. Topical antibiotics are not recommended for treatment of wound infections as it may result in the emergence of resistant organisms. Patient tetanus immunization status should be assessed in all cases.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
	OR As a monotherapy: Cefuroxime 1.5gm IV q8h		
MUSCULAR, SKELETAL AND SOFT TISSUE TRAUMA, CRUSH INJURIES AND STAB WOUNDS			
Muscular, skeletal and soft tissue trauma, crush injuries and stab wounds	Cloxacillin 2gm IV q6h **PLUS/MINUS** *Metronidazole 500mg IV q8h **PLUS/MINUS** **Gentamicin 5mg/kg IV q24h	Cefazolin 2gm IV q6-8h **OR** Cefuroxime 1.5gm as a loading dose, followed by 750mg IV q8h **PLUS** *Metronidazole 500mg IV q8h	*Metronidazole: In soil/rust contamination or heavy machinery. **Gentamicin: If there's extensive skin & soft tissue involvement. Thorough surgical debridement, soft tissue and fracture stabilization. For severe penetrating injuries, especially those involving joints and/or tendons, antibiotics must be given for at least **5 days**
COMPOUND FRACTURES/ OPEN FRACTURES			
Compound fractures: Antibiotics are administered as prophylaxis within 3 hours of injury.			
Gustilo 1 & 2 fractures	Cefazolin 1-2gm IV q8h **OR** Cefuroxime 1.5gm IV q8h	Amoxicillin/clavulanate 1.2gm IV q8h	Pre-debridement and post debridement cultures are not representative of actual infection. Duration of antibiotic for open fractures classification: - Gustillo type I : stop after 24 hrs - Gustilo type II: discontinue after 24 hours to 48 hrs - Gustillo type III: 24 hrs after wound closure or up to a maximum of 72 hrs (whichever is earlier) *Gentamicin: If initial debridement is expected to last more than 2 hours will need higher dose of gentamicin 5mg/kg IV stat dose. **Metronidazole: In soil/rust contamination or heavy
Gustilo 3 fractures Mostly nosocomial and gram positive	As per Gustilo 1 & 2 fractures **PLUS** *Gentamicin 3-5mg/kg IV stat dose **PLUS/MINUS** **Metronidazole 500mg IV q8h		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
			machinery. If soft tissue injury is of concern, to follow antibiotic guide for soft tissue injury.

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3. UROLOGY			
Pyonephrosis/ Perinephric Abscess/ Renal Abscess Common organisms: Enterobacteriaceae Enterococci Pseudomonas sp *Staphylococcus aureus*	Amoxicillin/clavulanate 1.2gm IV q8h **OR** Cefuroxime 750mg IV q8h **OR** Ampicillin/sulbactam 3gm IV q6-8h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Ceftriaxone 2gm IV q24h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Obtain blood and urine cultures before starting treatment. Drainage is the mainstay of treatment followed by definitive surgical therapy if warranted. Send pus for culture and sensitivity. Step down to oral antibiotic guided by culture and sensitivity result once can tolerate orally and afebrile > 48 hours following catheter removal. Duration: 2-3 weeks (of both IV and oral) Longer course of antibiotic if: - Difficult to drain abscess -Slow resolution on follow- up imaging.
Acute Prostatitis Common organisms: Enterobacteriaceae	**Outpatient treatment :** Trimethoprim/ Sulfamethoxazole 160/800mg PO q12h **OR**		Obtain urine culture before starting treatment. May step down to oral antibiotic once can tolerate orally and afebrile > 48 hours.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
Enterococci Pseudomonas sp Fever, chills, malaise, myalgia, dysuria, irritative urinary symptoms (frequency, urgency, urge incontinence), pelvic or perineal pain, and cloudy urine	Ciprofloxacin 500mg PO q12h **Inpatient treatment:** Amoxicillin/clavulanate 1.2gm IV q8h **OR** Ampicillin/sulbactam 3gm IV q6-8h **OR** Cefuroxime 750mg IV q8h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Ceftriaxone 1-2gm IV q24h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Duration: 2 weeks or up to 4 weeks in severe illness or concomitant bacteremia.
Chronic Bacterial Prostatitis (NIH Type II) Chronic or recurrent urogenital symptoms that persist for at least 3 months. Relapsing UTI with repeated isolation of same organism from urine is the hallmark	Ciprofloxacin 500mg PO q12h	Trimethoprim/ Sulfamethoxazole 160/800mg PO q12h	Reassess after 2 weeks of antimicrobial therapy. Only continue antibiotics if pre-treatment cultures are positive and/or symptoms improve. Duration: 4-6 weeks
Epididymo-orchitis (non-STD related) Common organisms: Enterobacteriaceae Enterococci Pseudomonas sp Acute onset, usually unilateral scrotal pain swelling with or without fever, rigors,	Ciprofloxacin 500mg PO q12h for minimum of 2 weeks		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred Treatment	Alternative Treatment	
and lower urinary tract symptoms			
Epididymo-orchitis (STD related)	Refer to Sexually Transmitted Infections Section		
Testicular Abscess Common organisms: Enterobacteriaceae Enterococci Pseudomonas sp	Amoxicillin/clavulanate 1.2gm IV q8h **OR** Ampicillin/sulbactam 3gm IV q6-8h **OR** Cefuroxime 750mg IV q8h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Ceftriaxone 2gm IV q24h **PLUS/MINUS** Gentamicin 5mg/kg IV q24h	Drainage is the mainstay of treatment. Send pus for culture and sensitivity.
Fournier's Gangrene	Refer to section Necrotizing Fasciitis		
4. NEUROSURGERY			
Antibiotic prophylaxis NOT RECOMMENDED for: • Basal skull fractures • Traumatic CSF fistula • Post surgical CSF leak			
Depressed skull fractures	Cefuroxime 1.5gm IV q8h **PLUS** Metronidazole 500mg IV q8h		Duration: 5-7 days Review tetanus status of patient and consider vaccination.
Penetrating craniocerebral injuries	Ceftriaxone 2gm IV q12h **PLUS** Metronidazole 400mg PO q8h		Duration: 2 weeks initially and then review with microbiology

Reference:
1. Salford Royal, NHS. Antibiotic Prophylaxis in Cranial Neurosurgery Antibiotic Guidelines, Unique ID: 144TD(C)25(F4) Issue number: 6, 2018

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
1. TYPHOID FEVER (*Salmonella enterica* serovar Typhi and Paratyphi)			
Uncomplicated	Ceftriaxone 50-75mg/kg/24h (2-4 gm/day) IV q12-24h for 5-7 days	Ciprofloxacin 500mg PO q12h for 5-7 days	Ceftriaxone recommended for quinolone resistance. Recommend for early IV to Oral switch once symptoms improve or stable.
Complicated/severe (patients with systemic toxicity, depressed consciousness or organ system dysfunction)	Ceftriaxone 50-75mg/kg/24h (2-4 gm/day) IV q12-24h for 10-14 days **OR** Cefotaxime 40-80mg/kg/24h (2-6 gm/day) IV q8-12h for 10-14 days **PLUS/MINUS** *Dexamethasone 3mg/kg IV loading, then 1mg/kg IV q6h for 2 days	Ciprofloxacin 400mg IV q12h for 10-14 days **PLUS/MINUS** *Dexamethasone 3mg/kg IV loading, then 1mg/kg IV q6h for 2 days	*Indication of Dexamethasone: i) Typhoid psychosis ii) Septic shock and other indications (discuss with ID physician) Recommend for early IV to Oral switch once symptoms improve or stable.
2. CHOLERA *(Vibrio cholerae)*			
Non-Tetracycline resistance	Doxycycline 300mg PO stat	Ciprofloxacin 1gm PO stat	**Indication for antibiotics:** i) Oral or intravenous hydration is the mainstay of cholera treatment. ii) Antibiotics is recommended for severely ill patients, especially who are severely or moderately dehydrated and continue to pass a large volume of stool during rehydration treatment. Antibiotic treatment is also recommended for all patients who are hospitalized and moderate to severe cases. *Azithromycin/Erythromycin:
Tetracycline resistance	Ciprofloxacin 1gm PO stat **OR** *Azithromycin 1gm PO stat	*Erythromycin Ethylsuccinate 800mg PO q12h for 3 days	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			Recommended alternative for pregnant woman
3. SCRUB TYPHUS (*Orientia tsutsugamushi* (*rickettsia tsutsugamushi*))			
Uncomplicated	Doxycycline 100mg PO q12h for 7 days	*Azithromycin 500mg PO stat	*Azithromycin: Recommended for pregnant woman
Complicated (ARDS, septic shock, myocarditis, meningoencephalitis, hepatitis, renal failure)	*Azithromycin 500mg IV q24h for 5 days	**<u>If not responding to Azithromycin:</u>** Rifampicin 600mg PO q24h for 5 days	*Recommend for early IV to Oral switch once symptoms improve or stable.
4. BRUCELLOSIS			
Brucella melitensis, Brucella abortus, Brucella suis and Brucella canis	Doxycycline 100mg PO q12h for 6 weeks **PLUS** Streptomycin 1gm (15 mg/kg) IM q24h for 2-3 weeks	Doxycycline 100mg PO q12h for 6 weeks **PLUS** Gentamicin 5mg/kg/24h IV for 7 days **OR** Doxycycline 100mg PO q12h for 6 weeks **PLUS** Rifampicin 600-900mg (15mg/kg) PO q24h for 6 weeks **OR** **<u>Recommended alternative for pregnant woman:</u>** Rifampicin 600-900mg (15 mg/kg) PO q24h for 6 weeks	Longer duration (up to 12 weeks) is required in complicated cases i.e. spondylitis, neurobrucellosis, IE, localized suppurated lesions.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		PLUS Trimethoprim/ Sulphamethoxazole 160/800mg PO q12h for 6 weeks	
5. LEPTOSPIROSIS (*Leptospira* sp.)			
Mild to Moderate disease	Doxycycline 100mg PO q12h for 5-7 days	Azithromycin 500mg PO q24h for 3 days	
Severe disease (Leptospiral pulmonary syndrome, multiorgan involvement, sepsis)	Ceftriaxone 2gm IV q24h for 7 days (to deescalate to Benzylpenicillin once symptoms improve/stable) **OR** Benzylpenicillin 1.5MU IV q6h for 7 days		May consider Methylprednisolone 500-1000 mg IV for 3 days if pulmonary haemorrhage present. However, there is insufficient evidence to support the routine use corticosteroid.
6. TETANUS			
Clostridium tetani	Metronidazole 500mg IV q6-8h for 7-10 days **PLUS** Human Tetanus Immunoglobulin 3000-6000IU IM stat **PLUS** Anti-tetanus toxoid vaccine IM (initiate age appropriate active immunization at a different site)	Benzylpenicillin 100,000-200,000 unit/kg/24h IV q6h for 7-10 days **PLUS** Human Tetanus Immunoglobulin 3000-6000IU IM stat **PLUS** Anti-tetanus toxoid vaccine IM (initiate age appropriate active immunization at a different site)	Human Tetanus Immunoglobulin 500IU might be as effective as higher doses of 3,000 to 6,000IU and causes less discomfort. All patients with tetanus should undergo wound debridement to eradicate spores and necrotic tissue.
7. MELIOIDOSIS (*Burkholderia pseudomallei)*			
Intensive Therapy (Uncomplicated)	Ceftazidime 100-120mg/kg/24h IV q6-8h (usual dose: 2gm IV q6h)		*Add on Trimethoprim/ Sulphamethoxazole in eye, neurologic, testicular, prostatic, pericardium, bone

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	PLUS/MINUS *Trimethoprim/ Sulphamethoxazole • < 40 kg: 160/800mg PO q12h • 40-60kg: 240/1200mg PO q12h • >60kg: 320/1600 mg PO q12h		and joint melioidosis. Dose as per eradication therapy. Drainage of abscesses should be attempted where ever appropriate such as prostatic, empyema and pericardium.
Intensive Therapy **(Complicated)** (Severe melioidosis or neuromelioidosis)	Meropenem 75mg/kg/24h IV q8h (usual dose: 1gm IV q8h; if neurologic, 2gm IV q8h) **OR** Imipenem 50mg/kg/24h IV q6h (usual dose: 500-1000mg q6h) **PLUS/MINUS** *Trimethoprim/ Sulphamethoxazole (to deescalate to Ceftazidime once symptoms improve/stable)		**Duration of intensive therapy:** • Skin, bacteraemia with no foci, mild pneumonia: 2 weeks • Complicated pneumonia, prostatic, deep-seated foci, septic arthritis: 4 weeks • Osteomyelitis: 6 weeks • Neurologic/CNS: 8 weeks To use clinical judgement to guide prolongation of intensive phase if improvement is slow/persistent bacteraemia.
Eradication/Maintenance Therapy	Trimethoprim/ Sulphamethoxazole • < 40 kg: 160/800mg PO q12h • 40-60kg: 240/1200mg PO q12h • >60kg: 320/1600 mg PO q12h	Amoxicillin/clavulanate • <60kg: 1250mg (2 tabs of 625 mg) PO q8h • >60kg: 1875mg (3 tabs of 625 mg) PO q8h	**Duration of eradication therapy:** • Osteomyelitis, Neurologic/CNS: 24 weeks • Others: minimum 12 weeks
8. MALARIA			
Refer to the Ministry of Health's latest guideline on management of malaria.			

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
1. CYSTITIS			
Uncomplicated Cystitis Common organisms: *Escherichia coli* *Staphylococcus saprophyticus* Enterobacteriaceae: *Klebsiella, Proteus* In non-pregnant, pre-menopausal women with structurally and functionally normal urinary tract.	*Nitrofurantoin 50-100mg PO q6h (macrocrystals) or 100mg PO q12h (monohydrate/macrocrystals) **OR** Cephalexin 500mg PO q12h	Cefuroxime 250mg PO q12h **OR** Amoxicillin/clavulanate 625mg PO q8h **OR** Ampicillin/sulbactam 375-750mg PO q12h **OR** **Fosfomycin 3gm PO x 1 dose	Urine culture is indicated only if symptoms unresolved or recur. *Avoid Nitrofurantoin if GFR < 30ml/min. Ciprofloxacin and other quinolones are not recommended as empirical treatment in UTIs due to ; • selection of resistance, and • potential serious adverse events i.e. aortic aneurysm or dissection, tendinopathy or tendon rupture and peripheral neuropathy Consider use of quinolones only in patient with history of anaphylactic reaction to β-lactam antibiotics. **Consider Fosfomycin for patients suspected to have MDR Gram Negative Infection. Duration: 5-7 days
Cystitis in Pregnancy	*Nitrofurantoin 50-100mg PO q6h (macrocrystals) or 100mg PO q12h (monohydrate/macrocrystals) **OR** Cephalexin 500mg PO q12h	Cefuroxime 250mg PO q12h **OR** #Amoxicillin/clavulanate 625mg PO q8h **OR** Ampicillin/sulbactam 375-750mg PO q12h	Obtain urine culture before starting treatment and repeat 1-2 weeks after completion of antibiotics to ensure eradication. Duration: 5-7 days

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		OR **Fosfomycin 3gm PO x 1 dose	Treat for 7 days if recurrent. *Avoid Nitrofurantoin at third trimester if another option available due to small risk of haemolyticanaemia in newborn. #Amoxicillin/clavulanate is generally safe in pregnancy (Category B), but there may be an increased risk of necrotising enterocolitis associated with use in preterm, premature rupture of membranes. **Consider Fosfomycin for patients suspected to have MDR Gram-negative Infection.
2. PYELONEPHRITIS			
Uncomplicated Pyelonephritis Common organisms: Enterobacteriaceae Enterococci In non-pregnant, pre-menopausal women without urological abnormalities or comorbidities.	**Outpatient treatment :** Amoxicillin/clavulanate 625mg PO q8h for 14 days **OR** Ampicillin/sulbactam 375-750mg PO q12h for 14 days		Obtain urine culture before starting treatment. Perform ultrasound of the upper urinary tract to exclude obstructive pyelonephritis. May step down to oral antibiotic guided by culture and sensitivity result once can tolerate orally and afebrile ≥ 48 hours.
	Inpatient treatment: Amoxicillin/clavulanate 1.2gm IV q8h **OR** Cefuroxime 750mg IV q8h **OR** Ampicillin/sulbactam 1.5-3gm IV q8h	Ceftriaxone 1gm IV q24h	
Pyelonephritis in other categories (eg: Pregnancy)	Treat as In-patient treatment for Uncomplicated Pyelonephritis.		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
3. OTHER URINARY TRACT INFECTIONS (UTI)			
Complicated UTIs Common organisms: Enterobacteriaceae Enterococci Pseudomonas sp. UTI symptoms in men OR presence of a structural or functional abnormality: - Urinary tract obstruction - Chronic kidney disease - Poorly-controlled type 2 diabetes - Immunosuppression - Urinary catheter in situ - Neurogenic bladder - Post-menopausal women - History of recurrent UTIs - Nephrolithiasis	**Oral Therapy:** Amoxicillin/clavulanate 625mg PO q8h for 7 days **OR** Cephalexin 500mg PO q6h for 7 days		Obtain urine culture before starting treatment. Treat for 10-14 days in patients with upper tract symptoms, delayed response or sepsis. May step down to oral antibiotic guided by culture and sensitivity result once can tolerate orally and afebrile ≥ 48 hours.
	Parenteral Therapy: Amoxicillin/clavulanate 1.2gm IV q8h **OR** Ampicillin/sulbactam 1.5-3gm IV q8h **OR** Cefuroxime 750mg IV q8h **PLUS/MINUS** Aminoglycoside	Ceftriaxone 1gm IV q24h **PLUS/MINUS** Aminoglycoside	
Asymptomatic Bacteriuria (ABU) Urine bacterial growth ≥ 10^5cfu/mL in 2 serial samples in women or a single sample in men without UTI symptoms.	Screening for, and treating asymptomatic bacteriuria is not recommended, except; - in pregnant women, OR - prior to transurethral resection of prostate (TURP) or urological procedures breaching the mucosa *(refer "surgical prophylaxis" for treatment)* Whenever indicated, treatment should be guided by urine culture and sensitivity result.		Duration of treatment for pregnant women: 5-7 days
Catheter-associated UTIs (CA-UTI) Urine colony count ≥ 10^3cfu/mL with at least one sign or symptom compatible with UTI, with no other identifiable source of infection.	Refer to *"Complicated UTIs"*		Routine screening and treating asymptomatic catheterized patients is not recommended. Pyuria alone in the absence of other symptoms is not diagnostic of CA-UTI. Remove unnecessary catheters.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			Whenever indicated, change catheter prior to starting treatment. Treat for 10-14 days in patients with delayed response or sepsis.
Prophylaxis for Recurrent Urinary Tract Infections (rUTIs) 2 episodes/6 months OR ≥3 episodes/year	Nitrofurantoin 50-100mg PO ON (macrocrystals) or 100mg PO ON (monohydrate/macrocrystals) **OR** Cephalexin 250mg PO ON	Trimethoprim/sulfamethoxazole 80/400mg PO ON **OR** Trimethoprim 100mg PO ON	Antimicrobial prophylaxis is indicated if non-antimicrobial measures fail. Post-coital prophylaxis may be appropriate for sexually related rUTIs. Duration: 3-6 months

#The ORACLE trials demonstrated an increased risk of necrotising enterocolitis in women with preterm, premature rupture of membranes (and to a lesser extent for those with preterm labour) who received Amoxicillin/clavulanate compared to those who did not[13]. A much smaller study also reported an increased risk of necrotizing enterocolitis with Amoxicillin/clavulanate[14], but a retrospective study of Ampicillin/sulbactam+Amoxicillin/clavulanate compared with Cefazolin/Cephalexin/Erythromycin demonstrated no difference in rates of necrotising enterocolitis[15]. Many expert sources do not suggest avoiding Amoxicillin/clavulanate in pregnancy[16-20].

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SECTION B
PEADIATRICS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute Myocarditis			
Viral (commonest cause) Enteroviruses Adenovirus Influenza HIV etc.	Treatment mainly supportive		Among the viruses implicated are enteroviruses including Coxsackie & EV71. For severe HFMD with cardiopulmonary failure stage, use of IVIG may be considered if not used during CNS involvement or autonomic nervous system dysregulation stage.
Acute pericarditis			
Viral (commonest cause) Bacterial: *Staphylococcus aureus* *Haemophilus influenza* *Salmonella spp.* *M. tuberculosis*	Treatment mainly supportive. **Empiric for purulent pericarditis:** Cloxacillin 200mg/kg/day IV in 4-6 divided doses **PLUS** Cefotaxime 200-300mg/kg/day IV in 4 divided doses	**Penicillin allergy:** Cefazolin 100mg/kg/day IV in 3 divided doses (max. 6gm/day)	Need pericardial fluid to differentiate between different etiologic agent & C&S to adjust antibiotic. Consider surgical drainage for tamponade, pre-tamponade & ineffective conservative management. Duration of therapy: 4 weeks. Penicillin allergy refer to Appendix 8
Infective Endocarditis			
Empirical therapy for infective endocarditis			
Community-acquired organisms: *Streptococcus, Enterococcus* HACEK Gram-negative organisms	Ampicillin 200-300mg/kg/day in 4-6 divided doses **PLUS** Gentamicin 1mg/kg/dose IV q8h	**PLUS/MINUS** *Cloxacillin 200 mg/kg/day IV in 4-6 divided doses	*For acute presentation, need to cover for MSSA since *Streptococcus* & *Enterococcus* HACEK presentations are usually sub-acute.
Healthcare-associated organisms: MRSA Non-HACEK Gram-negative organisms *Enterococcus sp.*	Vancomycin 60mg/kg/day IV in 2- 3 divided doses (max. 2gm/day if unable to achieve therapeutic level) **PLUS**		*Rifampicin IS ONLY for prosthetic valve AND added after 3-5 days later than vancomycin & gentamicin.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Gentamicin 1mg/kg/dose IV q8h **PLUS/MINUS** *Rifampicin 20mg/kg/day in 3 divided doses (max. 900mg/day)		If non-HACEK Gram-negative organism like pseudomonas is suspected epidemiologically, add cefepime 50mg/kg/dose IV q8h until cultures are known. Once cultures are available, adjust accordingly.
Specific Organisms :			
Infective Endocarditis (*Streptococcus viridans)*			
Strains fully susceptible to penicillin (MIC<0.125 mg/l)	Benzylpenicillin 200,000-300,00 units/kg/day IV in 4-6 divided doses (up to 12-18MU/day)	Ampicillin 300mg/kg/day IV in 4-6 divided doses (max. 12gm/day) **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 4gm/day) **OR** **Penicillin Allergy** **Vancomycin 40mg/kg/day IV in 2-3 divided doses (max. 2gm/ day)	Duration: • 4 weeks for native valve • 6 weeks for prosthetic valve Vancomycin dose adjusted for trough concentration of 10-15 mg/ml. Penicillin allergy refer to Appendix 8
Strains with MIC>0.125 to 2 µg/ml	**PLUS** Gentamicin 1mg/kg/dose IV q8h for 2 weeks (add to first line regimen of penicillin/ceftriaxone) **Do not use ampicillin.**		***Vancomycin therapy is recommended only for patients with immediate type penicillin hypersensitivity.** For this strain (MIC>0.125): Antibiotic of choice is either penicillin with gentamicin or ceftriaxone with gentamicin.
Infective Endocarditis *(Enterococcus sp.)*			
Penicillin-sensitive (MIC≤ 8 mg/l)	Ampicillin 200-300mg/kg/day IV in 4-6 divided doses for *4-6 weeks **PLUS** Gentamicin 1mg/kg/dose IV q8h for *2-6 weeks	Ampicillin 200-300mg/kg/day IV in 4-6 equally-divided doses **PLUS** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses	*Duration: • If symptoms less than 3 months & native valve: ampicillin for 4 weeks & gentamicin for 2 weeks. • If symptoms more than 3 months:

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Sensitive to penicillin & vancomycin but high-level resistance to gentamicin (MIC>500 mg/l)	Ampicillin 300mg/kg/day IV in 4-6 divided doses **PLUS** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 4gm/day) Duration: 6 weeks		ampicillin & gentamicin for 6 weeks. Ampicillin plus ceftriaxone is preferred for individuals with renal impairment (CrCl ≤50ml/min) ONLY. Can not use ceftriaxone alone since enterococcus is intrinsically resistant to this drug. This combination is NOT ACTIVE against *E. faecium.* **Maximum dose of vancomycin: 2gm/day unless not able to achieve therapeutic range. Aim for serum trough of 10-20mg/l.
Resistant to penicillin but susceptible to vancomycin & gentamicin	**Vancomycin 40mg/kg/day IV in 3 divided doses **PLUS** Gentamicin 1mg/kg/dose IV q8h Duration: 6 weeks		
Infective Endocarditis (*Staphylococcus aureus)*			
Methicillin-sensitive (left-sided)	Cloxacillin 200-300mg/kg/day IV in 4-6 divided doses for 4-6 weeks	**Penicillin allergy** Cefazolin 100mg/kg/day IV in 3 divided doses for 4-6 weeks **OR** Vancomycin 60mg/kg/day IV in 2-3 divided doses for 4-6 weeks	If allergy to penicillin but not immediate type hypersensitivity, use cefazolin. Penicillin allergy refer to Appendix 8 Methicillin-sensitive (right sided): Can shorten duration to 2 weeks if good response, no metastatic sites, no cardiac or extracardiac complications with size of vegetation less than 20mm.
Methicillin-sensitive (right-sided)	Cloxacillin 200-300mg/kg/day IV in 4-6 divided doses for 4 weeks		
Methicillin-resistant (left & right)	Vancomycin 60mg/kg/day IV in 2-3 divided doses (max. 2gm/day) for 4-6 weeks	Daptomycin 10 mg/kg IV daily for 4-6 weeks	Daptomycin is superior to vancomycin for MRSA bacteremia with MIC >1 mg/l.
Methicillin-sensitive (prosthetic valve)	Cloxacillin 200-300mg/kg/day in 4-6 divided doses for ≥6 weeks **PLUS** Gentamicin 1mg/kg/dose IV q8h for 2		*Rifampicin has better penetration but to protect against development of resistance, use only after 3-5 days of cloxacillin &/or bacteremia has been

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	weeks **PLUS** *Rifampicin 20mg/kg/day PO in 3 divided doses for ≥6 weeks		cleared. MRSA (prosthetic valve): Vancomycin & rifampicin for 6 weeks or more.
Methicillin-resistant (prosthetic valve)	Vancomycin 60mg/kg/day in 2-3 divided doses for ≥ 6 weeks **PLUS** Gentamicin 1mg/kg/dose IV q8h for 2 weeks **PLUS** *Rifampicin 20mg/kg/day PO in 3 divided doses ≥6 weeks		
Culture-negative endocarditis	Ampicillin/sulbactam 300mg/kg/day IV in 4-6 divided doses for 4-6 weeks **PLUS** Gentamicin 1mg/kg/dose IV q8h for 4-6 weeks		Culture-negative endocarditis (CNE) is diagnosed when a child has clinical & echocardiogram evidence of IE but persistent negative cultures. This is in individuals with no prior antimicrobial use. If fungi or fastidious organism is suspected, need to ask microbiologist to prolong incubation. **Patients with culture-negative endocarditis should be treated in consultation with an ID specialist**.

References :
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2. Malaysian Clinical Practise Guideline for the Prevention, Diagnosis and Management of Infective Endocarditis 2017.

B2. CENTRAL NERVOUS INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Meningitis empirical treatment Age groups: **1-3 months:** *Group B streptococcus (GBS), E. coli, S. pneumoniae & N. meningitidis* **>3 months:** *S. pneumoniae, Hib, E. coli, Salmonellosis & N. meningitidis*	Cefotaxime 200-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4gm/day) **PLUS** Benzylpenicillin 300,000-400,000 units/kg/day IV in 4-6 divided doses (max. 24MU/day)		For children below 3 months of age: Cefotaxime is the preferred third generation cephalosporin since less drug-drug interactions (in terms of interaction with calcium-containing infusion & bilirubin displacement). Once organism is known, please refer below to adjust antibiotics.
Specific Organisms			
Haemophilus influenza (HI)	Cefotaxime 200-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100mg/kg/day IV in 1 or 2 divided doses (max. 2gm/dose; 4gm/day)	Ampicillin 300mg/kg/day q6h (if MIC <1mcg/ml)	Duration: 10 days (HI)
Neisseria meningitidis	Benzylpenicillin 300,000-400,000 units/kg/day; max. 12MU/day) IV in 4-6 divided doses for 7 days	Cefotaxime 200-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) for 7 days **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4gm/day) for 7 days	Prophylaxis for all household contacts & health care workers involved in unprotected contact during intubation & suctioning of airway/mouth-to-mouth resuscitation.
Strepcoccus pneumonia (SP)			
Penicillin-susceptible (MIC≤0.06 mcg/ml)	Benzylpenicillin 300,00-400,000 units/kg/day in 4-6 divided doses (max. 24MU/day)		Duration: 14 days (SP)

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Penicillin-resistant (MIC≥0.12 mcg/ml) & cefotaxime/ ceftriaxone- sensitive (MIC ≤0.5 mcg/ml)	Cefotaxime 200-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100mg/kg/day IV in 1 or 2 divided doses (max. 2gm/dose; 4gm/day)		
Penicillin & cefotaxime/ceftriazone-resistant (MIC ≥2.0 mcg/ml) (drug-resistant *Streptococcus pneumoniae,* DRSP)	High dose cefotaxime or ceftriaxone **PLUS** Vancomycin 60mg/kg/day in 4 divided doses		Treat in consultation with ID specialist.
Cryptococcal meningitis *Cryptococcus neoformans*	**Induction Therapy**: Amphotericin B 1.0mg/kg/day IV q24h **PLUS/MINUS** 5-flucytosine 25mg/kg/dose (max. 2gm/dose) PO q6h for 2-4 weeks		Duration of induction with 5-flucytosine (5-FU) is at least 2 weeks & until CSF repeat culture is NEGATIVE.
	Consolidation Therapy: Fluconazole 6mg/kg/dose (max. 400mg/dose) IV/PO q12h for 8 weeks		
***Herpes simplex* encephalitis**	**4 months to 12 years old:** Acyclovir 30-45mg/kg/day IV in 3 divided doses		Duration: 14-21 days. Doses of 60mg/kg/day OR dosing exceeding 15mg/kg or 500mg/m^2 is associated with acute kidney injury.
Brain abscess	Cefotaxime 200-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4gm/day)	If secondary to trauma: **PLUS** Cloxacillin 200-300mg/kg/day in 4-6 divided doses (add to third generation cephalosporin)	Surgical drainage may be indicated if appropriate. Duration: 6-8 weeks, depending on response based on neuroimaging & clinical presentations.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	PLUS Metronidazole 15mg/kg IV stat then 7.5mg/kg IV q8h		

References:
1. American Academy of Paediatrics. Committee on Infectious Diseases. Red Book: Report of the Committee on Infectious Diseases (2018).
2. Sanford Guide to antimicrobial therapy 2018

B3. CHEMOPROPHYLAXIS

B3.i SURGICAL

Guidelines for prevention of surgical site infections (SSIs) have been published. General principles:

1. Agent used for antimicrobial prophylaxis should prevent SSIs and related morbidity and mortality
2. Reduce duration and cost of care
3. Produce no adverse effect
4. Minimize adverse consequences to the microbial flora

Timing:
Effective chemoprophylaxis occurs only when the appropriate antimicrobial drug is present in tissues at sufficient local concentration at the time of intra-operative bacterial contamination. Administration of antimicrobial agent is recommended within 60 minutes before surgical incision to ensure adequate tissue concentration at the start of the procedure. Agents that require longer administration time such as vancomycin should begin within 120 minutes before surgery begins. Adequate antimicrobial concentration should be maintained throughout the surgical procedure and in most instances, single dose of antimicrobial agent is sufficient and the duration of prophylaxis after any procedure should not exceed 24 hours. Intra-operative dosing is required if the duration of the procedure is greater than two times the half-life of the antimicrobial agent or if there is excessive blood loss.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Cardiac surgery			
S. epidermidis, S. aureus, Corynebacterium sp., Enteric Gram-negative bacilli	Cefazolin 30 mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	If known to have MRSA/MRSE colonisation, use Vancomycin 15mg/kg IV	**<u>β-lactam Allergy:</u>** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre-operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Thoracic surgery			
Non-cardiac including lobectomy, pneumonectomy, lung resection & thoracotomy	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose:every 4 hours*	Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre -operative dose: every 2 hours*	**<u>β-lactam Allergy:</u>** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre-operative dose: every 6 hours*

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			β-lactam allergy refer to Appendix 8
Abdominal Surgery			
Gastroduodenale	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre -operative dose: every 2 hours*	**β-lactam Allergy:** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* **AND** Gentamicin 2.5 mg/kg IV β-lactam allergy refer to Appendix 8
Biliary tract (Open procedure/Laparoscopic procedure/Appendectomy/Small intestine/Hernia repair (hernioplasty & herniorrhaphy) /Colorectal)	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours* **OR** Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre -operative dose: every 2 hours*	Ceftriaxone 50-75mg/kg IV; max. 2gm **OR** Cefotaxime 50mg/kg; max. 1gm *Recommended re-dosing interval from initiation of pre -operative dose: every 3 hours* **PLUS** Metronidazole 15 mg/kg IV *(For neonates less than 1200gm, to give 7.5 mg/kg)*	**β-lactam Allergy:** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* **PLUS** Gentamicin 2.5 mg/kg IV β-lactam allergy refer to Appendix 8
Head & neck			
Clean (tonsillectomy, adenoidectomy, tracheostomy, thyroglossal cyst excision, precauricular sinus, dermoid cyst, brachial anomaly, thyroidectomy, paroidectoy, lymph node biopsy etc.)	No antibiotic routinely	No antibiotic routinely	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Clean with placement of prosthesis (excludes tympanostomy tubes	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre-operative dose: every 2 hours* **OR** Cefuroxime 50mg/kg IV; max. 1.5gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	**β-lactam Allergy:** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre-operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Clean-contaminated procedures with the exception of tonsillectomy & functional endoscopic sinus procedure	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours* **PLUS** Metronidazole 15mg/kg IV	Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre -operative dose: every 2 hours* **OR** Cefuroxime 50mg/kg IV; max. 1.5gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours* **PLUS** Metronidazole 15mg/kg IV	**β-lactam Allergy:** Clindamycin 10mg/kg IV; max 900mg *Recommended re-dosing interval from initiation of pre-operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Clean-contaminated cancer surgery	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours* **PLUS** Metronidazole 15mg/kg IV	Ampicillin/sulbactam 50mg/kg (of ampicillin component) IV *Recommended re-dosing interval from initiation of pre -operative dose: every 2 hours* **OR** Cefuroxime 50mg/kg IV; max. 1.5gm	**β-lactam Allergy:** Clindamycin 10mg/kg IV; max. 900mg *Recommended re-dosing interval from initiation of pre-operative dose: every 6 hours* β-lactam allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours **PLUS** Metronidazole 15mg/kg IV	
Neurosurgery			
Elective craniotomy & cerebrospinal fluid-shunting procedures	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	If known to have MRSA/MRSE colonisation, use Vancomycin 15mg/kg IV	**<u>β-lactam Allergy:</u>** Clindamycin 10mg/kg; max. 900 mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Orthopaedics			
Clean operations involving hand, knee, or foot & not involving implantation of foreign materials	None	None	
Spinal procedure with or without instrumentation/hip surgery/ Implantation of internal fixation devices (e.g. nails, screws, plates, wires)	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*		**<u>β-lactam Allergy:</u>** Clindamycin 10mg/kg; max. 900 mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* β-lactam allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Urology			
Low tract instrumentation with risk factors for infections	Trimethoprim 2mg/kg PO; max. 150mg	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	**β-lactam Allergy:** Gentamicin 2.5mg/kg IV β-lactam allergy refer to Appendix 8
Clean without entry into urinary tract/clean with entry into urinary tract (e.g. hypospadia surgery)	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	Amoxicillin/clavulanate 30mg/kg IV; max 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	UTI should be treated before procedure when possible. Medical literature does not support continuing antimicrobial prophylaxis until urinary catheter have been removed.
Clean-contaminated (entering gastrointestinal tract)	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours* **PLUS** Metronidazole 15 mg/kg IV	Amoxicillin/clavulanate 30mg/kg IV; max 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	**β-lactam Allergy:** Gentamicin 2.5mg/kg IV β-lactam allergy refer to Appendix 8
Plastic Surgery			
Elective soft tissue surgery	No prophylaxis unless complex prolonged procedure If complex, Cloxacillin 25mg/kg IV; max 1gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Elective hand or foot surgery involving bone	Cloxacillin 25mg/kg IV; max 1gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*		**β-lactam Allergy:** Clindamycin 10mg/kg IV; max. 900mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Cleft lip & palate surgery	Amoxicillin/clavulanate 30mg/kg; max. 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*		**β-lactam Allergy:** Clindamycin 10mg/kg; max. 900mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Excision & grafting surgery	Amoxicillin/clavulanate 30mg/kg; max. 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*		**β-lactam Allergy:** Clindamycin 10mg/kg; max. 900mg *Recommended re-dosing interval from initiation of pre -operative dose: every 6 hours* β-lactam allergy refer to Appendix 8
Interventional radiology			
Percutaneous endoscpic gastrostomy (PEG) or jejunostomy (PEJ) or nephrostomy tube placement	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	Amoxicillin/clavulanate 30mg/kg IV; max. 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	
Micturating cystourethrogram (MCUG)	Trimethoprim 2mg/kg PO; max. 150 mg (if patient is already on existing antibiotic UTI prophylaxis, increase antibiotic to		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	therapeutic dose for a single dose prior procedure)		
Tenckhoff peritoneal dialysis cathether insertion	Cefazolin 30mg/kg IV; max. 2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	Amoxicillin/clavulanate 30 mg/kg IV; max. 1.2gm *Recommended re-dosing interval from initiation of pre -operative dose: every 4 hours*	
Burns	No prophylaxis required		

References:

1. Clinical Practical Guideline for Antimicrobial Prophylaxis for Surgery 2013. American Society of Hospital Pharmacists (ASHP) guideline, IDSA, Surgical Infection Society (SIS) and Society of Healthcare Epidemiology of America (SHEA). Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA. American Journal of Health-system Pharmacy 2013. 70(3):195-283.
2. Antibiotic Prophylaxis for Paediatric Surgery. Royal Hospital for Children Glasgow. 2018.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Rheumatic fever (Secondary prevention)	Benzathine penicillin 1.2MU (>27kg); 0.6MU (≤ 27 kg) IM every 3-4 weeks Duration 1. **With carditis & residual heart disease (persistent valvular disease)**: 10 years since the last episode of ARF or 40 years of age whichever is longer. Consider lifelong prophylaxis. 2. **With carditis but no residual heart disease (no valvular disease):** 10 years since the last episode of ARF or 21 years of age whichever is longer. 3. **Without carditis:** 5 years since last ARF or until 21 years of age whichever is longer.	Phenoxymethylpenicillin (Penicillin V) 250 mg PO q12h **Penicillin Allergy**: Erythromycin Ethylsuccinate 15-20mg/kg/dose PO q12h	Penicillin allergy refer to Appendix 8
Infective Endocarditis (IE)	Amoxicillin 50mg/kg PO 30-60 minutes before procedure **OR** Ampicillin 50mg/kg IV 30-60 minutes before procedure	**Penicillin Allergy**: Clindamycin 20mg/kg IV/PO 30-60 minutes before procedure Other alternative: Cefazolin 50mg/kg IV (cephalosporin should not be used in children with anaphylaxis, angioedema or urticaria)	IE prophylaxis is recommended for patients with the highest risk cardiac conditions undergoing procedures likely to result in bacteremia with a microorganism that has the potential ability to cause bacterial endocarditis. Prophylaxis always required for: 1. Dental procedures that involve • Extraction

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			• Periodontal procedure including surgery • Subgingival scaling • Root planning • Re-planting avulsed teeth • Other surgical procedure e.g. implant placement & apicectomy 2. Incision & drainage of local abscess in the brain, skin, subcutaneous tissue (boils & carbuncle, eye (dacryo cystitis), epidural, lung, orbital area, per rectal area, liver (pyogenic liver), tooth & surgical procedure through infected skin. 3. Percutaneous endoscopic gastrotomy. Prophylaxis is required in some circumstances. Please refer page 132 CPG for Infective Endocarditis 2017. Maintenance of optimal oral hygiene may reduce the incidence of bacteremia from daily activities & is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE. Penicillin allergy refer to Appendix 8
Post splenectomy At risk for Pneumococcus, Meningococcus, Haemophilus	Phenoxymethylpenicillin (Penicillin V) 125mg PO q12h for ≤5 years old 250mg PO q12h for >5 years old	Amoxicillin: 20mg/kg/day (250 – 500mg PO q12h; 500mg daily if poor compliance i.e. adult dose)	Risk of sepsis is lifelong but especially high in the first 2 years after splenectomy. Important adjunct:

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Duration of chemoprophylaxis: - Minimum 3 years post splenectomy or until 18 years of age (some expert) OR at least 1 year post splenectomy Asplenia attributable to other causes unknown most expert recommend throughout childhood & into adulthood	**Penicillin Allergy:** Erythromycin Ethylsuccinate 15-20mg/kg/dose PO q12h	Immunisation against Pneumococcus, Haemophilus, Meningococcus at least 14 days prior to splenectomy (if not possible then as soon as possible, 14 days or more after surgery). Yearly influenza vaccine is also recommended. Not all pneumococcal isolates are sensitive to these antibiotics. Limitation stressed to parents so that all febrile illness in this group of children are taken seriously since initial signs & symptoms of fulminant spticaemia can be subtle. Penicillin allergy refer to Appendix 8
***Haemophilus influenza* b exposure**	Rifampicin < 1 month of age: 10mg/kg/dose PO q24h for 4 days Children: 20mg/kg/dose PO q24h for 4 days		Chemoprophylaxis is indicated for: 1. ALL household contacts in the following circumstances (household contact is defined as a person who resides with the index patient or who spent ≥4 hours with the index patient for at least five of the seven days before the day of hospital admission of the index case): • Household with at least one contact <4 years old who is unimmunised or incompletely immunised. • Household with a contact who is an immunocompromised child, regardless of that child's Hib immunisation status.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			• Household with a child younger than 12 months who has not complete the primary Hib series. 2. Nursery Contact For ALL attendees in childcare & preschool (regardless of age or vaccination status) when unimmunised or incompletely immunised children attend the facility & two or more cases of Hib invasive disease have occurred within 60 days. 3. Index case Prior to discharge if did not receive at least ONE dose of cefotaxime/ ceftriaxone & infants younger than 2 years. For contacts <2 years old who are not immunised: complete immunisation.
Meningococcal exposure	Rifampicin **<1 month old:** 5mg/kg/dose PO q12h for 2 days **≥1 month old:** 15-20mg/kg/dose (max. 600mg) PO q12h for 2 days	Ceftriaxone IM <15 years old: 125mg stat >15 years old: 250mg stat	Chemoprophylaxis is provided to close contact at **HIGH RISK** which include: - All household especially children younger than 2 years old. - Childcare or preschool contact at anytime during 7 days before onset of illness. - Direct exposure to index patient's secretion through kissing or through sharing toothbrushes or eating utensils at any time during 7 days before onset of illness.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			- Frequently slept in same place as index patient during 7 days before onset of illness. <u>Healthcare staff</u> Routine prophylaxis is not recommended unless there is intimate exposure to respiratory secretion during mouth-to-mouth resuscitation, unprotected contact during intubation/suctioning at any time 7 days before onset of illness or within 24 hours of initiation of effective antimicrobial therapy. Give chemoprophylaxis to index case prior to discharge if treated with regimens other than cefotaxime or ceftriaxone. Chemoprophylaxis is ideally initiated within 24 hours after index patient is identified; prophylaxis is not indicated more than 2 weeks after exposure.
Neonatal Group B *Streptococcus* infection	Intrapartum maternal prophylaxis: Benzylpenicillin 5MU IV loading, then 2.5-3.0MU IV q6h till delivery	Ampicillin 2gm IV loading, then 1gm q6h till delivery **<u>Penicillin Allergy:</u>** *Clindamycin 2gm IV loading, then 1gm IV q8h till delivery (according to susceptibility)	Treat during labour if previously delivered infant with invasive GBS, GBS bacteriuria or antenatal screening swabs positive OR if GBS status is not known AND any of the following: • Preterm <37 weeks • PROM >18 hours • Intrapartum temperature >38ºC Penicillin allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			*For high risk of anaphylaxis from β-lactam antibiotics.
Malaria prophylaxis	Chloroquine dose (chloroquine-sensitive area) 5mg/kg base (8.3mg/kg salt) orally, once weekly, up to maximum adult dose of 300mg base (begin 1-2 weeks before travelling & take weekly through-out & 4 weeks after leaving area) Artemether-lumefantrine (20/120mg) <5 kg : Not recommended 5-15 kg : 1 tablet in a single dose, then 1 tablet again after 8 hours, then 1 tablet q12h for 2 days 15-25 kg : 2 tablets in a single dose, then 2 tablets again after 8 hours, then 2 tablets q12h for 2 days 25-<35 kg: 3 tablets* in a single dose, then 3 tablets again after 8 hours, then 3 tablets q12h for 2 days. >35 kg : as per adult dose.	For prophylaxis (chloroquine- resistant): Paediatrics: Atovaquone-proguanil (Malarone®)¥ Age >8 years old: Doxycycline 2.2mg/kg once daily up to 100mg/day. Take 1-2 days before, during & 4 weeks after travelling. Mefloquine∞: weekly dose by weight in kg (tablet with 250 mg base, 274 mg salt) <9 kg : 5mg/kg weekly >-9-19 kg : 1/4 adult tablet weekly >19-30 kg : 1/2 adult tablet weekly>30-45 kg : ¾ adult tablet weekly >45 kg : 1 adult tablet weekly Start 2-3 weeks efore, continue weekly during exposure & for 4 weeks thereafter.	¥ Atovaquone/proguanil is another drug used in malaria prophylaxis in children (for chloroquine-resistance) BUT not yet registered in Blue Book (available commercially in Malaysia). ∞ Mefloquine: Not recommended if there are cardiac conduction abnormalities, seizures or psychiatric disorders e.g. depression, psychosis (Black box warning: Neuropsychiatric reactions may persist even after discontinuation). If using Mefloquine: Start 2-3 weeks before, continue weekly during exposure & 4 weeks thereafter. To carefully assess risk and benefit of starting antimalarial prophylaxis to any children to prevent development of drug resistant.
Pertussis (Post-exposure prophylaxis, PEP)	<1 month old: Azithromycin 10mg/kg/day in a single dose q24h for 5 days.	Erythromycin is not preferred in young infants. *Use only if azithromycin is not available.	Drug of choice for PEP & treatment is a macrolide. Azithromycin is the preferred macrolide. *Association between orally-admistered azithromycin & erythromycin

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	1-5 months old: Azithromycin 10mg/kg/day as single dose q24h for 5 days. 6 months & older: Erythromycin Ethylsuccinate 15-20mg/kg/dose PO q12h for 14 days. **OR** Azithromycin 10mg/kg/day in a single dose on Day 1, then 5mg/kg/dose on Day 2-Day 5.	Erythromycin Ethylsuccinate: 15-20mg/kg/dose PO q12h for 14 days. 2 months & older: Trimethoprim/sulfamethoxazole 8mg/kg/day in 2 divided doses for 14 days.	with infantile hypertrophic pyloric stenosis (especially in infant <6 weeks) has been reported but azithromycin remains the drug of choice in very young infants because the risk of developing severe disease outweights the potential risk. Antimicrobial prophylaxis is recommended for: 1. ALL household contacts of the index cases & other close contacts, including children in childcare, regardless of immunisation status. When considering borderline degree of exposure for a non-household contact, PEP should be administered if contact personally is at high risk[∞] or lives in a household with person at high risk of severe disease (e.g. young infant, pregnant women, person who has contact with infants) Close contacts who are unimmunised or underimmunised should have pertussis immunisation initiated or continued using age-appropiate products according to the recommended schedule as soon as possible (this include off-label Tdap in children 7-9 years old who did not complete DTaP series.) [∞]High risk: Infant, women at third trimester of pregnancy & people with pre-existing health conditions that may be exacerbated by pertussis infection (not limited to

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			immunocompromised individuals & those with moderate to severe asthma).
Chicken pox (Post-exposure prophylaxis) Potential interventions for people without evidence of immunity exposed to varicella (chicken pox) following significant exposure¥: **1. Vaccine**	**Varicella vaccine:** Within 3-5 days of exposure for susceptible healthy adult/child 12 months old or older (followed by a second dose at age-appropriate interval)		¥ Exposure is significant if: 1. Household: Residing in the same household 2. Playmate: Face-to-face indoor play ≥1 hour 3. Hospital: In same 2 to 4-bed room or adjacent beds in a large ward, face-to-face contact with an infectious staff member or patient, or visit by a person deemed contagious 4. Newborn infant
2. When indicated & available, *Varicella zoster* immune globulin (VZIG) **3. When VZIG not available**	For patients who are at high risk for severe infection & complications*∞ & significant exposure¥ (& have contraindications to vaccine): VZIG dose as per product information; weight-based as soon as possible after exposure up to10 days after **OR** IVIG (400mg/kg) IV **once** if VZIG not available **OR** Acyclovir 20mg/kg/dose PO q6h (max. 3200mg of daily dose) beginning 7-10 days after exposure & continue for 7 days.	Patients receiving monthly high dose IVIG (≥400 mg/kg) are likely to be protected & probably do not require VZIG	*∞ Susceptible hosts include: 1. Immunocompromised children 2. Pregnant women Newborns of mothers with *Varicella* shortly before or after delivery (i.e. 5 days before or within 2 days after delivery) 3. Premature infants born at ≥28 weeks of gestation who are exposed during their hospitalization & whose mothers do not have evidence of immunity 4. Premature infants born at <28 weeks of gestation or birth weight ≤1000 g regardless of their mothers' immunity.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		if the most recent dose of IVIG was administered ≤3 weeks before exposure.	

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B4. GASTROINTESTINAL INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute gastroenteritis Usually viruses e.g. rotavirus	Antibiotics not recommended		Oral rehydration is the cornerstone of treatment. Antibiotic therapy may prolong carriage state of salmonellosis.
Dysentery			
Dysentery *Shigella, E. coli, Campylobacter*	Most are mild infections which resolve spontaneously without antibiotics		Resistance patterns towards amoxicillin, trimethoprim sulphamethazole, ciprofloxacin & azithromycin are in the rise. Adjust antibiotic once culture & sensitivity (C&S) results are available. For immunocompromised host-treat longer (7-10 days). Reserve fluoroquinolone only for isolate where there is no other antibiotic option available due to its many side effects.
Mild or uncomplicated	No treatment required	Ampicillin 100mg/kg/day PO in 4 divided doses for 5-7 days for hospitalized children	
Severe illness (hospitalisation, invasive or other complications) or immunocompromised patients	**Empiric:** Ceftriaxone 50-75mg/kg/day IV q24h for 5 days (origin of infections: Asia)	Ciprofloxacin 20-30mg/kg/day IV in 2 divided doses for 3 days **OR** Azithromycin 10mg/kg/dose IV q24h (max. 500mg/dose). Total course: 3 days	
Dysentery *Amoebiasis*	Metronidazole 30-50mg/kg/day PO in 3 divided doses for 7-10 days		Similar dosage for extraintestinal disease.
Giardiasis	Metronidazole 15mg/kg/day PO (max. 250mg) in 3 divided dose for 5-7 days		
Typhoid fever			
Typhoid fever *Salmonella typhi* *S. paratyphi A & B*	**Empirical treatment:** Ceftriaxone 50-75mg/kg/day IV q24h (max. 2gm) for 7-14 days		Adjust antibiotic once C&S results are known. Duration of antibiotics: 7 days (uncomplicated) to 14 days (severe disease or if using ampicillin or trimethoprim/ sulphamethoxazole).
Mild or uncomplicated	Ciprofloxacin 20-40mg/kg/day (max. 1.5gm per day) PO in 2 divided doses for 5-7 days	Chloramphenicol 50-100mg/kg/day PO in 4 divided doses for minimum 14 days	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Severe infection or suspected resistant organism	Ceftriaxone 60-80mg/kg/day IV q24h for 7-14 days	Ciprofloxacin 20-30mg/kg/day IV (max. 0.8-1.2gm/day) in 2 divided doses for 7-10 days	Choice of antibiotics & duration depends on disease, C&S results & whether oral route is preferred. Fluoroquinolones need to be used with caution in children due to possible arthropathy & rapid development of resistance. There is now increasing data of other side effects e.g hypoglycaemia & neuropsychiatric d/o. Ampicillin & trimethoprim/ sulphamethaxazole may be consided for susceptible strain. More strains now becoming sensitive to these agents except for certain countries
Chronic carrier state (> 1 year)	Ampicillin 100mg/kg/day PO in 4 divided doses for 6 weeks **OR** Amoxicillin 100mg/kg/day PO in 2 divided doses for 6 weeks **OR** Trimethoprim/sulfamethoxazole 8mg (TMP)/kg/day PO in two divided doses for 6 weeks	Ciprofloxacin 20-30mg/kg/day PO in 2 divided doses for 4 weeks. **OR** Ampicillin 200-300mg/kg/day IV maximum in 4-6 divided doses. (If oral therapy not tolerated & strain is susceptible)	
Cholera	Azithromycin 20mg/kg/day PO in a single dose (max. 1gm) **OR** Erythromycin Ethylsuccinate 12.5mg/kg/dose PO q6h for 3 days (max. 250mg/dose) **OR** Doxycycline 4.4mg/kg/day (max. 200mg/day) PO daily (children > 8 years old) **OR** Tetracycline 12.5mg/kg/dose PO in q6h (max. 500mg/dose) for 3 days (children > 8 years old)		Oral or IV rehydration is the cornerstone of treatment. Prompt initiation of antibiotic therapy reduces the volume & duration of diarrhoea. Antimicrobials should be considered for people who are moderately to severely ill. Choice dependent on age & pattern of resistance. Monitor antimicrobial sensitivity pattern at beginning of & during the outbreak as it can change. Avoid using tetracycline or doxycycline for young children as they can cause staining of the teeth. Use of doxycycline should be considered in an epidemic caused by susceptible isolate.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			Fluoroquinolones are not approved for children younger than 18 years old for this indication.
Liver abscess (amoebic) *Entamoeba histolytica*	Metronidazole 35-50mg/kg/day PO in 3 divided doses for 7-10 days		Amoebic abscess tends to be solitary lesion. Consider surgical drainage if needed.
Liver abscess (pyogenic) *Klebsiella spp., E. coli, Streptococcus milleri*, other Gram-negative organisms, anaerobes, *S. aureus*	Cefotaxime 200mg-300mg/kg/day IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4 g/day) **PLUS** Metronidazole 22.5-40mg/kg/day IV in 3 divided doses (max. 4gm/day)	Piperacillin/tazobactam 300mg/kg/day (of piperacillin component) IV in 3-4 divided doses (max. 16gm/day) *ESBL-Klebsiella* Ertapenem 30mg/kg/day in 2 divided doses (max. 1gm/day) (above 3 months of age)	Surgical drainage is needed in most cases. Duration: 4-6 weeks
Acute cholangitis Gram-positive & Gram-negative organisms, anaerobes	Cefotaxime 200mg -300mg/kg IV in 4 divided doses (max. 2gm/dose) **OR** Ceftriaxone 100 mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4gm/day) **PLUS** Metronidazole 22.5-40 mg/kg/day IV in 3 divided doses (max. 4gm/day)	Piperacillin/tazobactam 300mg/kg/day (of piperacillin component) in 3-4 divided doses IV (max. 16gm/day) **OR** Ampicillin/sulbactam 200-300mg/kg/day (of ampicillin component) IV in 4-6 equally-divided doses	Duration ∽ 7 days. Outcome is similar with less than 7 days to those with longer duration >7 days in patients treated with percutaneuous cholecystectomy. In treatment failure, need source control.
Peritonitis Gram-positive & Gram-negative organisms, anaerobes	**Primary/spontaneous bacterial peritonitis** Cefotaxime 200mg -300mg/kg IV in 4 divided doses (max. 2gm/dose) **Secondary (nosocomial) peritonitis** Piperacillin/tazobactam IV 300mg/kg/day in 3-4 divided doses (max. 16gm/day)	Ampicillin 100mg/kg/day PO in 4 divided doses **PLUS** Gentamicin 5mg/kg/day IV OD **PLUS** Metronidazole 7.5mg/kg/dose IV 8h for 7-14 days	May omit metronidazole in primary peritonitis. In immunocompetent patient with mild to moderate peritonitis & source control, suggest 5 days of therapy. Ertapenem is not licenced to be used in infants less than 3 months old.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	If culture proven ESBL: Imipenem/cilastatin 60-100mg/kg/day IV in 4 divided doses Meropenem 60-100mg/kg/day IV in 3 divided doses De-escalate treatment to ertapenem 30mg/kg/day IV in 2 divided doses (max. 1gm/day) once patient is stable.		

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B5. INFECTIONS IN IMMUNOCOMPROMISED PATIENTS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
First line: **Febrile neutropenia** Fever >38°C, neutrophil<500mm³ *Enterobacteriaceae (Klebsiella* sp., *E. coli* etc.), *Pseudomonas*, aerobic Gram-positive *(Staphylococci, Streptococci)*	Cefepime 50mg/kg/dose IV in q8h	Piperacillin/tazobactam 300 mg/kg/day IV in 3-4 divided doses (max. 16gm/day of piperacillin component)	Use monotherapy with an anti-pseudomonal β–lactam agents. Meta-analysis has shown that there is no clinical advantage with β-lactam & aminoglycoside combination therapy. Also need to look at local epidemiological data.
Second line: Persistent fever > 72 hours* *Enterobacteriaceae (Klebsiella sp, E. coli* etc.), *Pseudomonas*, aerobic Gram-positive *(Staphylococci, Streptococci), Enterococci* or other resistant organisms ***DO NOT MODIFY INITIAL COVERAGE BASED SOLELY ON PERSISTENCE OF FEVER.**	Meropenem 60-120mg/kg/day IV in 3 divided doses (max. 6gm/day) **PLUS/MINUS** Vancomycin 60 mg/kg/day in 3-4 divided doses (max. 2gm/day)		Escalate to second line if patient unstable to cover resistant Gram- negative, Gram-positive & anaerobes. Consider adding vancomycin in suspected catheter-related infections, positive blood culture for Gram-positive cocci, hypotensive patients & patients who are known to be colonised with MRSA. In patients responding to initial empiric antibiotic therapy, discontinue double coverage (empirical vancomycin, if initiated) or double gram negative after 24-72 hours if there is no specific microbiologic indication to continue combination therapy.
Third line: Fever > 4-7 days with no identified source of fever *Candida sp. Aspergillus sp., Fusarium sp.* Viral: Respiratory viruses are the most	Imipenem/cilastatin 60-100 mg/kg/day IV in 4 divided doses (max. 4gm/day) **PLUS** Amphotericin B 0.5mg/kg/dose IV q24h & gradually escalate by (0.25-1mg/kg/dose) q24h	Imipenem/cilastatin 60-100 mg/kg/day IV in 4 divided doses (max. 4gm/day) **PLUS** Caspofungin 70mg/m^2/dose IV q24h at Day 1, then 50mg/m^2/dose IV q24h	1/3 of febrile neutropenic patients with persistent fever >1 week have systemic fungal infections[2] In patients at high risk of invasive fungal disease with prolonged (≥96 hours) febrile neutropenia unresponsive to broad spectrum antibacterial agents, initiate antifungal.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
common, HSV, VZV	(max. 1.5mg/kg/day) **OR** Lipid formulation of amphotericin B 3-5mg/kg/day		Amphotericin based anti-fungal is considered more broad spectrum than echinocandin (eg Caspofungin)

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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Congenital & Perinatal Infections			
Meningitis GBS *E. coli* Listeria other Gram-negative bacilli/rod (GNR)	Empirical therapy. Benzylpenicillin (Penicillin G) **GA <34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q12h postnatal age >7 days: q8h **GA >34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q8h postnatal age >7 days: q6h **OR** **< 1 week of age:** Ampicillin 200-300mg/kg/day IV in 3 divided doses **>1 week of age:** Ampicillin 300mg/kg/day IV in 4 divided doses **PLUS** Cefotaxime 50mg/kg/dose IV < 1 week of age: q12h > 1 week of age: q8h		Once cultures are known, adjust antibiotics accordingly.
Necrotising enterocolitis (NEC) Klebsiella, *E. coli,* Clostridia, Coagulase-negative Staphylococci,	Ampicillin 100mg/kg/dose IV <1 week of age: q12h >1 week of age: q8h **PLUS** Gentamicin 5mg/kg/dose IV		There is insufficient evidence regarding duration of antibiotic treatment for NEC. This suggested regimen for NEC is empirical. Once culture is known,

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Enterococci, Bacteroides	< 30 weeks of CGA: q48h 30-34 weeks of CGA: q36h ≥35 weeks CGA: q24h **PLUS** Metronidazole Loading dose:15mg/kg/dose IV Maintainence dose: <34 weeks of age: 7.5mg/kg/dose IV q12h 35-40 weeks of age: 7.5mg/kg/dose IV q8h >40 weeks of age: 10mg/kg/dose IV q8h Duration: 10-14 days		decisions regarding choice of antibiotics are best guided by culture results. Use vancomycin if CoNS/MRSA is suspected (substitute ampicillin with vancomycin).
Early onset sepsis (<48 hrs) Group B Streptococcus (GBS), Listeria, Streptococcus sp., *E. coli,* *Haemophilus influenza*, Klebsiella sp. etc.	Benzylpenicillin (Penicillin G) **GA<34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q12h postnatal age >7 days: q8h **GA >34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q8h postnatal age >7 days: q6h **OR** **< 1 week of age:** Ampicillin 200-300mg/kg/day IV in 3 divided doses **> 1 week of age:**		If negative blood culture, initial clinical suspicion not strong & reassuring baby's condition with low CRP, consider stopping antibiotics at 48 hours. If positive blood culture or strong clinical suspicion of sepsis but negative culture, may give 5-7 days of antibiotics. Consider antibiotics for more than 5-7 days if baby not fully recovered & based on pathogen identified on blood culture. In this empiric therapy-meningitis is not a consideration

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Ampicillin 200-300mg/kg/day IV in 4 divided doses **PLUS** Gentamicin 5mg/kg/dose IV <30 weeks of CGA: q48h 30-34 weeks of CGA: q36h ≥35 weeks CGA: q24h		Once cultures are known; adjust antibiotics accordingly.
Late onset sepsis >48 hours Methicillin-sensitive/resistant *S. aureus* (MSSA/MRSA), Coagulase- negative Staphylococci (CONS), Gram-negative rods (depending on local epidemiological data)	**First line:** Cloxacillin 50mg/kg/dose IV <1 week of age: q12h >1 week of age: q8h **PLUS** Gentamicin 5mg/kg/dose IV < 30 weeks of CGA: q48h 30-34 weeks of CGA: q36h ≥35 weeks of CGA: q24h		For late onset sepsis, the most common organisms are predominantly Gram-positive cocci, namely Staphylococci, especially CONS, in premature neonates & also neonates with central catheters. Piperacillin/tazobactam is a good second line option in pneumonia & intra-abdominal sepsis(non–CONS sepsis with good coverage against Gram-positive, Gram-negative & anaerobes) There is possibility of Gram-negative rods with inducible β-lactamases & ESBL producing organism such as Klebsiella, Serratia & E. coli in some NICU in Malaysia hence need to look at local epidemiology before deciding on suitable second line.
	Second line: Piperacillin/tazobactam IV PMA <30 weeks: 100mg/kg/dose q8h PMA >30 weeks: 80mg/kg/dose q6h		
	Other options: Cefepime GA < 36 weeks: 30mg/kg/dose q12h GA ≥36 weeks: 50mg/kg/dose q12h **OR**		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Meropenem GA **<32 weeks:** 20mg/kg/dose IV PNA<14 days: q12h PNA 14 days: q8h GA > **32 weeks:** PNA <14 days: 20mg/kg/dose IV q8h PNA >14 days: 30mg/kg/dose IV q8h **OR** Imipenem/cilastatin 25mg/kg/dose IV PNA<1 week: q12h PNA>1 week q8h	Meropenem for CNS infections: 40mg/kg/dose q8h for ALL Age groups.	Cefepime is the preferred agent when there are Gram-negative bacteria with extended spectrum cephalosporin resistance due to AmpC-β-lactamases (also termed Class C or Group 1). Studies comparing imipenem/ cilastin & meropenem for indication other than meningitis found no significant differences in efficacy or safety between the two. However, a recent meta-analysis suggested that meropenem may be better than imipenem/cilastin in efficacy & safety especially due to more cases of seizure with imipenem (WHO Subcommittee Meeting of the Expert Committee on the Selection & Use of Essential Medicine 2008).
Congenital syphilis *T. pallidum*	Benzylpenicillin (Penicillin G) 50,000units/kg/dose IV for first 7 days of life: q12h thereafter: q8h Duration : 10 days If diagnosed with congenital syphilis after one month of age: Benzylpenicillin (Penicillin G) : 200,000-300,000units/kg/day IV in 4-6 divided doses for 10-14 days.	Procaine penicillin 50,000units/kg/dose IM in a single daily dose for 10 days.	Only severe cases are clinically apparent at birth. Refer to algorithm for diagnosing & evaluation. Re-evaluate & possibly re-treat. Please refer Red Book 2018.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	In infants considered less likely to have syphilis & normal CSF examination including normal physical examination & long bone radiograph: Benzathine penicillin 50,000units/kg/dose IM in a single dose can be given.		
Congenital toxoplasmosis *T. gondii*	Pyrimethamine/sulfadoxine (Fansidar®) Pyrimethamine (1.25mg/kg/dose PO every 10 days) **PLUS** Sulfadoxine (25mg/kg/dose PO every 10 days) **PLUS** Folinic acid 50mg PO every 7 days for 12 months	Pyrimethamine 1mg/kg/day PO for 2 months, followed by 0.5 mg/kg/day PO for 10 months **PLUS** Sulfadiazine 100mg/kg/day PO in 2 divided doses for 12 months **PLUS** Folinic Acid 50 mg PO every 7 days for 12 months	Drug regimen is not definitively established. Clinical trials are ongoing. Prednisolone 0.5 mg/kg (max. 20 mg/dose) q12h can be added if CSF protein ≥1g/dL or active severe chorioretinitis. Streoids given till CSF protein<1g/dL or resolution of severe chorioretinitis. Fansidar is currently an “orphan” drug that need special procurement measures to buy. Refer to paediatric ID consultant for treatment and availability of drug.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Herpes simplex neonatal • Localised skin, eye & mouth (SEM) • Central nervous system (CNS) with or without SEM • Disseminated disease involving multiple organs	Acyclovir 60mg/kg/day IV in 3 divided doses Duration: Skin, eyes, mouth: 14 days CNS/disseminated: minimum of 21 days All infants surviving neonatal HSV infection of any classification should receive oral acyclovir suppression at 300 mg/m^2/dose administered 3 times daily for 6 months after completion of parenteral therapy.		Screen for other STDs. For CNS disease: Repeat lumbar puncture at end of therapy for HSV PCR. If PCR remains positive, continue IV acyclovir for another one week. Recurrence of HSV can occur & may be a lifelong problem.
Tetanus neonatorum	Metronidazole **PMA≤34 weeks:** 7.5 mg/kg/dose IV q12h **PMA 35-40 weeks:** 7.5 mg/kg/dose IV q8h **PMA >40 weeks:** 10mg/kg/dose IV q8h Duration : 10 days	Benzylpenicillin (Penicillin G) **GA<34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q12h postnatal age >7 days: q8h **GA >34 weeks:** 100,000units/kg/dose IV postnatal age <7 days: q8h postnatal age >7 days: q6h	
Congenital gonococcal ophthalmitis/conjunctivitis	Immediate & frequent saline eye irrigation. **Non-disseminated disease:** Cefotaxime 100mg/kg/dose IV in a single dose.	If penicillin-sensitive, may give benzylpenicillin **GA <34 weeks:** 100,000units/kg/dose IV	Evaluate for signs of disseminated infection (e.g. sepsis, arthritis & meningitis).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	May need to continue for 48-72 hours until systemic infection has been ruled out. **Disseminated disease:** Cefotaxime 50 mg/kg/dose IV < 1 week of age: q12h > 1 week of age: q8h For 7 days, with a duration of 10–14 days, if meningitis is documented.	-postnatal age <7 days: q12h -postnatal age >7 days: q8h **GA >34 weeks:** 100,000units/kg/dose IV -postnatal age <7 days: q8h -postnatal age >7 days: q6h	Screen mother & baby for chlamydial infection. Screen for other STDs. Investigate & treat parents.
***Chlamydia trachomatis* conjunctivitis**	Erythromycin Ethylsuccinate 10 mg/kg/dose PO <1 week of age: q12h >1 week of age: q8h Duration : 14 days. Local eye toilet until discharge stops.	Azithromycin 20 mg/kg/day PO, once daily for 3 days.	Initial treatment for chlamydial conjunctivitis should be based upon a positive diagnostic test. Re-swab after treatment; 20-30% will need a second course to clear infection.
GBS *Streptococcus agalactiae*			
Sepsis	Benzylpenicillin (Penicillin G) **GA<34 weeks:** 100,000 units/kg/dose IV postnatal age ≤7 days: q12h postnatal age >7 days: q8h **GA >34 weeks:** 100,000 units/kg/dose IV postnatal age ≤7 days: q8h postnatal age >7 days: q6h **OR**		Duration of treatment for GBS: Uncomplicated: 14 days (bacteremia without a defined focus). Meningitis: 21 days. Gentamicin can be discontinued once the infection is under control.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	< 1 week of age: Ampicillin 200-300 mg/kg/day IV in 3 divided doses **> 1 week of age:** Ampicillin 300 mg/kg/day IV in 4 divided doses **PLUS** Gentamicin 5 mg/kg/dose IV < 30 weeks of CGA: q48h > 30-34 weeks of CGA: q36h ≥35 weeks of CGA: q24h		
Meningitis	Benzylpenicillin (Penicillin G) **<34 weeks of age:** 100,000 units/kg/dose IV postnatal age <7 days: q12h postnatal age >7 days: q8h **>34 weeks of age:** 100,000 units/kg/dose IV postnatal age <7 days: q8h postnatal age >7 days: q6h **OR** Ampicillin **<1 week of age:** 200-300 mg/kg/day IV in 3 divided doses **>1 week of age:** 300 mg/kg/day IV in 4 divided doses **PLUS**		Duration for treatment Meningitis: 21 days. Doses of penicillin for meningitis is higher as recommended by experts (as high as 500,000 unit/kg/day (> 7 days of age).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Gentamicin 5 mg/kg/dose IV < 30 weeks of CGA: q48h > 30-34 weeks of CGA: q36h ≥35 weeks CGA: q24h		
E. coli Sepsis/Meningitis	Cefotaxime 50 mg/kg/dose IV < 1 week of age: q12h > 1 week of age: q8h Cefotaxime (Red Book 2018) **GA <32 weeks** 50mg/kg/dose IV PNA < 14 days: q12h PNA ≥ 14 days: q8h **GA ≥32 weeks** 50mg/kg/dose IV PNA ≤ 7 days: q12h PNA >7 days: q8h **PLUS** Gentamicin 5 mg/kg/dose IV < 30 weeks of CGA: q48h > 30-34 weeks of CGA: q36h ≥35 weeks CGA: q24h		Duration in bacteremia: 14 days. Duration for meningitis: 21 days. All cases of bacteremia need lumbar puncture to exclude meningitis. Treatment duration of 14 days can be decided on case-by-case basis if meningitis excluded & good clinical response.

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3. Swetha G. Pinninti, David W. Kimberlin.Neonaal Herpes Simplex Virus Infections. Seminars in Perinatology 42(2018) 168-175.
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5. American Academy of Paediatrics. Commitee on Infectious Diseases. Red Book: Report of the Committee on Infectious Diseases (2018).
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B7. OCULAR INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Preseptal cellulitis *Streptococcus pneumoniae* *Staphylococcus aureus* *Streptococcus pyogenes* *Haemophilus influenzae*	**Mild:** Amoxicillin/clavulanate 45mg/kg/day PO in 2 divided doses **Systemically unwell:** Cloxacillin 200mg/kg/day (max. 2g/dose) IV in 4 divided doses **PLUS** Cefotaxime 150-200mg/kg/day (max. 2gm/dose) IV in 3 divided doses **OR** Ceftriaxone 50mg/kg/dose (max. 2gm/dose) IV q12h	Cephalexin 25-50mg/kg/day PO in 2 divided doses for 10 days	Failure to respond within 24-48 hours may indicate orbital cellulitis or underlying sinus disease. When improving & no organism identified, change to Amoxicillin/clavulanate & complete for 7 days.
Orbital cellulitis/abscess *Streptococcus pyogenes* *Streptococcus pneumoniae* *Staphylococcus aureus* *Haemophilus influenzae*	Ceftriaxone 50mg/kg/dose (max. 2gm) IV q12h for 7-14 days **PLUS** Cloxacillin 200mg/kg/day (max. 12gm) IV in 4 divided doses for 7-14 days **Inpatient:** 48-72 hours antibiotic, then oral to complete 14 days following good response (no positive culture)	**Penicillin allergy:** Clindamycin 30-40mg/kg/day PO in 3 or 4 divided doses **Also for CA-MRSA** (adjust accordingly with sensitivity)	This condition is considered surgical emergency & require immediate consultation with ENT surgeon & ophthalmologist. Urgent CT scan needed to exclude associated abscess & intracranial extension. Urgent surgical drainage of the ethmoid sinuses or of an orbital, subperiosteal or intracranial abscess may be needed. Penicillin allergy refer to Appendix 8

References:

1. Clinical Practice Guideline: Periorbital and orbital cellulitis; The Royal Children's Hospital, Melbourne. Last updated 25 August 2013.
2. Periorbital and Orbital Cellulitis: Emergency Management in Children; Queensland Health Hospital, 2017.
3. The Sanford Guide to Antimicrobial therapy 2018.
4. American Academy of Paediatrics. Commitee on Infectious Diseases. Red Book: Report of the committee on Infectious Diseases (2018).

B8. OTORHINOLARYNGOLOGY INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
Tonsillitis/Pharyngitis Group A *Streptococcus*	Phenoxymethylpenicillin (penicillin V) 25-50mg/kg/day PO in 4 divided doses (max. 2g/day) for 10 days **OR** Amoxicillin 50mg/kg/day PO in 3 divided doses (max. 1000-1200mg) for 10 days	**Penicillin allergy (non- anaphylaxis):** Cephalexin 25-50mg/kg/day PO in 2 divided doses for 10 days **OR** Erythromycin Ethylsuccinate 40-50mg/kg/day PO in 3 to 4 divided doses for 10 days	Penicillin allergy refer to Appendix 8
Rhinosinusitis *Streptococcus pneumoniae* *Haemophilus influenzae* *Moraxella catarrhalis* Group A Streptococcus	Amoxicillin 45-90 mg/kg/day in 2 divided doses PO for 10 days* **Second line:** Amoxicillin/clavulanate 45mg/kg/day PO in 2 divided doses **Failing amoxicillin/clavulanate:** Clindamycin 30-40mg/kg/day PO in 3 divided doses **AND** Cefuroxime 30mg/kg/day PO in 2 divided doses **Inpatient (sevee):** Ampicillin/sulbactam 100-200mg ampicillin/kg/day IV in 4 divided doses (max. 8g/day)	**Penicillin allergy:** Clindamycin 30-40mg/kg/day PO in 3 or 4 divided doses. Ceftriaxone 50mg/kg/dose IV daily	The most common causes are viral infections. Acute bacterial sinusitis is suspected when child with URI presents with: 1. Persistent illness (nasal discharge or daytime cough or both for ≥10 days without improvement) 2. Worsening course 3. Severe onset (concurrent fever & purulent discharge for 3 days) - For rhinosinusitis, most expert recommend using high dose amoxicillin (90mg/kg/day). Penicillin Allergy refer to Appendix 8

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Acute otitis media *Streptococcus pneumonia* *Haemophilus influenzae* *Moraxella catarrhalis*	Amoxicillin 80-90mg/kg/day in 2 divided doses <2 years old : 10 days 2-5 years old: 7 days >5years old : 5 days. For clinical failure, history of using amoxicillin in the last 30 days & has concurrent purulent conjunctivitis: Amoxicillin/clavulanate 45mg/kg/ day PO in 2 divided doses	**Penicillin allergy:** Erythromycin Ethylsuccinate 15-20mg/kg/dose PO q12h **OR** Clarithromycin 7.5mg/kg/dose PO q12h **OR** Azithromycin 10 mg/kg/dose PO on Day 1 (max. 500mg/day), followed by 5 mg/kg/dose PO q24h on Day 2-Day 5 (max. 250mg/day) **OR** Azithromycin 10 mg/kg/dose PO q24h for 3 days	Penicillin allergy refer to Appendix 8
Acute otitis externa *Pseudomonas aeruginosa* *Staphylococcus aureus*	**Mild to moderate:** Topical antibiotic with/without topical steroids. E.g. Gentamicin 0.3% ear drops: 3-4 drops 3 times/day for 7 days Polymyxin B sulphate 10,000 U, neomycin sulphate 5 mg & hydrocortisone10 g ear drops: 4 drops 3 or 4 times/day for 7 days Ofloxacin 0.3% otic solution		• Ototoxic agents like gentamicin or neomycin should not be used in the presence of tympanostomy tubes or perforated tympanic membrane. • Clinical response should be seen within 48 to 72 hours but full response may take up 6 days. • Non-response should prompt an evaluation for obstruction, presence of foreign body, non-adherence or an alternative diagnosis.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Instill 5 drops into affected ear(s) once daily for 7 days Indication: for 1-12 years old		

References:

1. Wald ER, Applegate KE, Bordley C, et al. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. Pediatrics 2013; 132: e262.
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4. The Sanford Guide to Antimicrobial therapy 2018.
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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
LOWER RESPIRATORY TRACT INFECTION			
Community-acquired Pneumonia			
Pneumonia (outpatient) **Infant (≥3 months) & children** Viral infection is more common (Influenza, RSV, human metapneumovirus (hMPV), Parainfluenza, Adenovirus) Bacteria (*S. pneumoniae,* Group A *Streptococcus, S. aureus, H. influenza*)	*High dose amoxicillin (80-90mg/kg/day) PO in 2 divided doses for 5-7 days For influenza: Oseltamivir • **<9 months old:** 3mg/kg/dose PO q12h for 5 days • **9-11 months old:** 3.5mg/kg/dose PO q12h for 5 days • **1-12 years old**: ≤15 kg: 30mg PO q12h >15-23 kg: 45mg PO q12h >23-40 kg: 60mg PO q12h >40 kg: 75mg PO q12h	Erythromycin Ethylsuccinate 15-20mg/kg/dose PO q12h	Antibiotics are not routinely recommended since viral infection is more common. For infant & children admitted to hospital, treat as presumed bacterial unless viral origin is known. Macrolide antibiotics should be used if either mycoplasma or chlamydia pneumonia is suspected. It may be started in school-going children where disease predominates. Duration: minimum 5 days & until afebrile for 2-3 days in empiric therapy with absence of an identified specific etiology & specific therapy with known pneumonia due to pneumococcus, *HI* & *Moraxella catarrhalis*. * Dosing of amoxicillin has undergone major changes in terms of dose & frequency: Standard dose: Amoxicillin 45-50mg/kg/day PO in 3 divided doses for 5-7 days. Experts recommend using high dose amoxicillin to overcome resistance conferred by cell wall changes of the bacteria (pneumococcus).

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			If a child cannot tolerate high dose, the standard amoxicillin dose can be used.
Pneumonia (inpatient, fully immunised)	Benzylpenicillin 200,000units/kg/day IV in 4-6 divided doses for 5- 7 days	**Second line/partially treated** Cefuroxime 100-150mg/kg/day IV in 3 divided doses (max. 6gm/day) **OR** Amoxicillin/clavulanate 30mg/kg/dose IV q8h (max. 1.2gm/dose)	Macrolide antibiotics should be used if either mycoplasma or *Chlamydia pneumonia* is suspected.
Severe Community-acquired Pneumonia			
Severe community-acquired pneumonia (child not fully immunised/life-threatening)	Cefotaxime150-200mg/kg/day in 3 divided doses **OR** Ceftriaxone 75-100mg/kg/day in 2 divided doses **PLUS/MINUS** Azithromycin 10mg/kg/dose (max. 500mg) IV q24h on Day 1; then 5mg/kg/dose (max. 250mg) on Day 2-5 if considering atypical organisms.	Cefuroxime 100-150mg/kg/day IV in 3 divided doses (max. 6gm/day) **PLUS/MINUS** Azithromycin 10mg/kg/dose (max. 500mg) IV q24h on Day 1; then 5mg/kg/dose (max. 250mg) on Day 2-5 if considering atypical organisms.	For the management of empyema, look at different section.

References:

1. M. Harris, J. Clark, N. Coote et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax, vol. 66, no. 2, pp. ii1– ii23.The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America Clinical Infectious Diseases 2011;53(7):e25–e76
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B10. SKIN & SOFT TISSUE INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Abscess *Staphylococcus aureus*	**Mild:** *Cloxacillin 25-50mg/kg/day PO in 4 divided doses (max. 1gm/day) for 5-7 days	Cephalexin 25-50mg/kg/day PO in 2 divided doses for 5-7days	Incision & drainage (I&D) is the MAINSTAY of therapy. Needle aspiration is inadequate, can sent pus obtained during I&D for C&S. Use parenteral route for severe infections. Consider CA-MRSA if poorly resolving, based on local epidemiology (still generally uncommon). *Doses recommended in previous columns are for children weigh less than 25kg. For children weigh more than 25kg, use adult dosage (500mg PO q6h).
	Severe: Cloxacillin 200mg/kg/day IV in 4 divided doses (max. 12gm/day) for 5-7 days		
	CA-MRSA: Clindamycin 30-40mg/kg/day PO in 3-4 divided doses for 5-7 days **OR** Trimethoprim/sulfamethoxazole 8-10mg/kg/day (TMP dose) PO in 2 divided doses for 5-7 days		
Animal bites *Pasteurella multocida, Staphylococcus* spp., *Streptococcus* spp., *Capnocytophaga* sp, anaerobes	Amoxicillin/clavulanate 45mg/kg/day PO in 2 divided doses for 5-7 days	Amoxicillin/clavulanate 30mg/kg/dose IV q8h (max. 1.2gm)	Consider rabies prophylaxis according to local epidemiology.
Cellulitis *Staphylococcus aureus* *Streptococcus pyogenes*	Cloxacillin 200mg/kg/day IV in 4 divided doses (max. 12gm/day) for 5-7 days	Amoxicillin 25-50mg/kg/day PO in 3 divided doses for 7 days **OR** Cephalexin 25-50mg/kg/day PO in 2 divided doses for 5-7days	Administer using parenteral route for extensive lesions. Total treatment until 3 days after acute inflammation disappears.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Hansen's Disease (leprosy) in children	**Paucibacillary:** **10-14 years old:** Rifampicin 450mg PO monthly **PLUS** Dapsone 50mg PO daily **<10 years old:** Rifampicin 10mg/kg PO monthly **PLUS** Dapsone 2mg/kg PO q24h		Duration of treatment: 6 months Surveillance: 5 years
	Multibacillary: **10-14 years old:** Rifampicin 450mg PO monthly **PLUS** Dapsone 50mg PO q24h **PLUS** Clofazimine 150mg PO monthly & 50mg q48h **<10 years old:** Rifampicin 10mg/kg PO monthly **PLUS** Dapsone 2mg/kg PO q24h **PLUS** Clofazimine 6mg/kg PO monthly & 1mg/kg PO q48h		Duration of treatment: 1 year for BI<4; 2 years for BI≥4 (BI: Bacteriological index) Surveillance: 15 years
Impetigo *Staphylococcus aureus* *Streptococcus pyogenes*	**Localised:** Topical 2% fusidic acid 2-3 times daily for 7 days (outpatient)		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Generalised: Cloxacillin 25-50mg/kg/day PO (max. 1gm/day) in 4 divided doses for 5-7 days	Cephalexin 25-50mg/kg/day PO in 2 divided doses for 5-7 days	
Necrotising fasciitis *Streptococcus sp.:* Group A *Streptococcus (GABHS*) Other streptococcus Staphylococcal: *Staphylococcal aureus* (MSSA & CA-MRSA)	**Streptococcal necrotising fasciitis:** Benzylpenicillin 200,000-300,000units/kg/day IV in 4-6 divided doses **PLUS** Clindamycin 20-40mg/kg/day IV in 3-4 divided doses (max. 2.7gm/day)		50% of patients have associated streptococcal toxic shock syndrome (STSS). Aggressive surgical debridement of the deep-seated infection is the mainstay of therapy. Combination therapy is needed with clindamycin to block toxin production whether or not patient manifests toxic shock syndrome. Tissues should be sent for Gram staining & C&S. IVIG can be used as an adjunct, typically at 1gm/kg on Day 1, followed by 0.5mg/kg on 1-2 subsequent days. Vancomycin is NOT RECOMMENDED for the treatment of serious MSSA infections because outcomes are INFERIOR compared with cases in which anti-staphylococcus β-lactam (cloxacillin) is used AND to minimise the emergence of vancomycin resistance. Duration of treatment: at least 2 weeks if no foci is found (no deep-seated
	Staphylococcal necrotising fasciitis: Cloxacillin 200mg/kg/day IV in 4-6 divided doses **PLUS** Clindamycin 20-40mg/kg/day IV (max. 2.7gm/day) in 3-4 divided doses	**If CA-MRSA is suspected:** Vancomycin 60mg/kg/day IV in 3-4 divided doses (max. 2gm/day)	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
			involvement plus no involvement of heart, bone, joint etc.)
Scalded skin syndrome (SSSS) *Staphylococcus aureus*	Cloxacillin 200mg/kg/day IV in 4-6 divided doses **Step down** Cloxacillin 25-50mg/kg/day PO in 4 divided doses (max. 1gm/day) Total treatment duration: 7-10 days		If no positive blood culture associated with SSSS, then intravenous therapy can be stopped following clinical improvement & switch to oral. Doses recommended in previous column are for children weigh less than 25 kg. For children weigh more than 25 kg, use adult dosage.

References:

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2. Malaysian clinical practice guideline on management of leprosy 2014.
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Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
A. GENERAL SURGERY			
Empyema thoracis (lung empyema) *Staphylococcus aureus* *Streptococcus pneumoniae* Empirical treatment needs to cover organisms mentioned above. Other bacteria implicated: *Streptococcus pyogenes,* *Haemophilus influenzae* & other Gram-negative organisms in immunocompromised individuals If patient is not responding to treatment, need to rule out TB.	Cefuroxime 100-200mg/kg/day IV in 3 divided doses **PLUS** Cloxacillin 200-300mg/kg/day IV in 4-6 divided doses Duration: 4-6 weeks	***Stapylococcus aureus*** **(methicillin-sensitive):** Cloxacillin 200-300mg/kg/day IV in 4-6 divided doses for 4-6 weeks ***Streptococcus pneumoniae*** **(penicillin-sensitive):** Benzylpenicillin 200,000-300,00units/kg/day IV in 4-6 divided doses ***Streptococcus pneumoniae*** **(penicillin-resistant, use result of C&S):** Cefotaxime 200-300mg/kg/day IV in 4 divided doses **OR** Ceftriaxone 100mg/kg/day IV in 1-2 divided doses (max. 2gm/dose; 4gm/day)	Based on C&S of pleural fluid/tissue or blood culture. All children with empyema need to receive high dose antibiotic therapy via intravenous route to ensure pleural penetration. Pneumatocoele on chest x-ray indicate *S. aureus* BUT they can also be seen in pneumococcal disease. There is NO need to routinely use a macrolide antibiotic but its use should be considered in children whom *Mycoplasma pneumonia i*s thought to be the cause (*Mycoplasma* usually cause effusion, not empyema). There is NO CONSENSUS on how long antibiotic need to be given. Most recommend 4-6 weeks of total antibiotics. For other adjunct therapy, refer MOH consensus guideline 2013.
Enterocolitis *Enterobacteriaceae , Enterococci, Bacteroides*	Ampicillin 200mg/kg/day IV in 4-6 divided doses (max. 12gm/day) **PLUS** Metronidazole 15mg/kg loading dose, followed by 7.5mg/kg/dose IV q8h	Cefotaxime 200mg/kg/day IV in 4 divided doses **PLUS** Metronidazole 15mg/kg loading dose, followed by 7.5mg/kg/dose IV q8h	Antibiotics should be adjusted with results of C&S.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
B. BONE AND JOINT INFECTIONS			
Septic arthritis (SA) & Osteomyelitis (OM) Common organisms: 0-2 months old: *S. aureus* *Streptococcus agalactiae* Gram-negative enteric organism Less than 5 years old: *Staphylococcus aureus* *Streptococcus pyogenes* *Streptococcus pneumoniae* Non-typeable *Haemophilus* spp. *Kingella kingae* Older than 5 years: *Staphylococcus aureus* *Streptococcus pyogenes*	**0-2 months old:** Cloxacillin 200mg/kg/day IV in 4-6 divided doses **PLUS** Cefotaxime 200mg/kg/day IV in 4 divided doses	Optimise antimicrobial treatment based on C&S.	Empiric antibiotics should be started based on clinical diagnosis of SA or OM. Surgical debridement often not required in OM. Urgent wash out & drainage is needed in SA in hip & other joints to reduce pressure on growth plate. *IV antibiotics can be switch to oral if no concurrent bacteremia when: Child afebrile & pain-free for at least 24 hours & CRP <20mg/L or CRP decreased by ≥2/3 of the highest value. **Duration of antibiotics:** SA: total of 3-4 weeks OM: 4-6 weeks In complex disease (multifocal, significant bone destruction, immunocompromised host & resistant/unusual pathogens), prolonged intravenous antibiotics are needed & duration might exceed 6 weeks.
	Less than 5 years old: Cefuroxime 100-200mg/kg/day IV in 3 divided doses (monotherapy)	Cefazolin 100-150mg/kg/day IV in 3 divided doses (can be use in children with suspected *S. aureus* or *S. pyogenes*. Less hypersensitivity reaction compared to cloxacillin & more convenient dosing) **Kingella kingae*: Uncommon organism causing infection in <5 years old; sensitive to β-lactam antibiotics e.g. cefuroxime or amoxicillin/clavulanate.	
	More than 5 years old: Cloxacillin 200 mg/kg/day IV in 4-6 divided doses		

References:

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B.12 TROPICAL INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Typhoid fever	Refer to Gastrointestinal Infections Section		
Cholera	Refer to Gastrointestinal Infections Section		
Scrub thyphus			
Ricketsia tsutsugamushi	Doxycycline 2-4mg/kg/day IV/PO in 1-2 divided dose for 5-7 days (max. 200mg/day)	Azithromycin 10mg/kg/dose (max. 500mg) PO q24h for 3 days	Doxycycline can be used in young children (even below 8 years old) since safety data approved its use for ricketsial diseases.
Brucellosis			
B. melitensis, B. abortus, B. suis & B. canis	Rifampicin 15-20mg/kg/day (max. 600-900mg/day) PO in 1-2 divided doses for 6 weeks **PLUS** **For children <8 years old**: Trimethoprim/sulfamethoxazole (TMP dose) 10mg/kg/day (max. 480mg TMP/day) PO in 2 divided doses for 6 weeks **OR** **For children >8 years old:** Doxycycline 4.4mg/kg/day PO (max. 200mg/day) in 2 divided doses for 6 weeks		For non-localised disease: Can use two-drug combination. Drug of choice for Brucellosis for children >8 years old: Doxycycline (plus rifampicin)
	Serious illness **PLUS** Gentamicin 5mg/kg/dose IV q24h for 7-14 days		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Leptospirosis *L. icterohaemorrhagiae, L. canicola*			
Moderate to severe disease	Benzylpenicillin 200,000units/kg/day IV in 4 divided doses (max. 12-18MU/day)	Ceftriaxone 100mg/kg/day IV q24h (max. 2gm/day) **OR** Cefotaxime 150-200mg/kg/day IV in 3-4 divided doses (max. 12gm/day)	Duration: 7 days
Mild disease	Amoxicillin 40-45 mg/kg/day PO in 3 divided doses (max. 500 mg/dose)	**For children >8 years old:** Doxycycline 2mg/kg/dose PO q12h (max. 200mg/day)	
Tetanus *Clostridium tetani*			
	Metronidazole 30mg/kg/day IV in 4 divided doses for 7-10 days **Neutralisation of toxin:** Human tetanus globulin (TIG) 500IU IM as a single dose	Benzylpenicillin 200,000units/kg/day IV in 4 divided doses (max. 12-18MU/day) for 7-10 days If TIG not available: IVIG 200-400mg/kg as a single dose	Primary tetanus infection: Clinical diagnosis to be made as negative culture is often. Steps in care: 1. Early airway protection & treatment of reflex spasm with benzodiazepam (midazolam) 2. Neutralisation of toxin: TIG single dose, administered IM (optimal dose not established) 3. Surgical debridement of infected tissues 4. Tetanus wound prophylaxis-refer table.
Melioidosis *Burkholderia pseudomallei*			
Intensive/Induction therapy:	Ceftazidime 200mg/kg/day IV in 3 divided doses	Imipenem/cilastatin 75-100mg/kg/day IV in 4 divided doses	Duration: 2-8 weeks – Uncomplicated: 2 weeks

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
		OR Meropenem 75mg/kg/day IV in 3 divided doses (neurological melioidosis: 150mg/kg/day IV in 3 divided dose)	– Complicated pneumonia, deep-seated infection, neurological melioidosis, osteomyelitis & septic arthritis: 4-8 weeks
Maintenance therapy:	Trimethoprim/sulfamethoxazole 8mg/kg/day (of TMP component) PO in 2 divided doses **PLUS** Doxycycline 4mg/kg/day PO in 2 divided doses (children above 8 years old)	**Children below 8 years old:** Amoxicillin/clavulanate 20mg/kg/dose (of amoxicillin component) PO q8h (higher relapse rate)	Duration: 20 weeks Folic acid 5mg PO q24h to be given for patients on Trimethoprim/sulfamethoxazole. Consider combination therapy of two drugs in maintenance phase if high risk of relapse.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Malaria			
Plasmodium falciparum A. Uncomplicated B. Treatment failure C. Complicated (Almost always due to *P. falciparum.* Suspect mixed infections if *P. vivax/P. knowlesi* malaria appears more severe than usual)	**Uncomplicated** Artemether/lumefantrine (Riamet®) (20mg artemether/ 120mg lumefantrine per tablet) The patient should receive an initial STAT dose, followed by second dose 8 hours later, then 1 dose q12h for the following two days – 5-14 kg : 1 tablet per dose – 15-24 kg: 2 tablet per dose – 25-35 kg: 3 tablet per dose – ≥35 kg : 4 tablet per dose	Artesunate/mefloquine FDC (ASMQ) (ASMQ is available as FDC tablet 25/55mg & 100/220mg) – 5–8 kg : 25/55mg PO q24h – 9-17 kg : 50/110mg PO q24h – 18-29 kg: 100/220mg PO q24h – >30 kg : 200/440mg PO q24h Duration: 3 days	Artesunate/mefloquine may cause seizure in children with epilepsy. Riamet® should be served with high-fat diet e.g. milk to enhance absorption. Primaquine 0.25mg base/kg to be given on Day 1 as a single dose in addition to artemisinin-based combination therapy (ACT) (G6PD testing is not required prior to administration of this dose).
	Treatment failure An alternative artemisinin-based combination therapy (ACT) regimen to be used. (If Riamet® is used as the first line regimen, use ASMQ & vice versa)	Artesunate 4mg/kg/dose PO q24h **PLUS** Clindamycin 10mg/kg/dose PO q12h for 7 days **OR** Quinine 10mg salt/kg/dose PO q8h **PLUS** Clindamycin 10mg/kg/dose PO q12h for 7 days	

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
	Complicated: Children >20 kg & adults Day 1 : IV artesunate 2.4mg/kg on admission, then repeat again at 12 & 24 hours Day 2-7: IV artesunate 2.4 mg/kg OD or switch to oral ACT Children <20 kg Day 1 : IV artesunate 3.0 mg/kg on admission, then repeat again at 12 & 24 hours Day 2-7: IV artesunate 3.0mg/kg OD or switch to oral ACT Duration: 7 days (Parenteral artesunate should be given for a minimum of 24 hours (3 doses) or until patient is able to tolerate orally & thereafter to complete treatment with a complete course of oral ACT (3 days of ASMQ or Riamet®).	Day 1: *Quinine loading dose 20mg/kg IV (dilute in 250 ml D5%) run over 4 hours; followed by maintenance dose 8 hours later; Quinine 10mg/kg IV q8h till Day 7 (max. 600mg base) **PLUS** Doxycycline 2.2mg/kg/dose (max. 100mg/dose) PO q12h **OR** Clindamycin 10mg/kg/dose PO q12h Duration: 7 days	Avoid using ASMQ (artesunate/ mefloquine) if patient presents initially with impaired consciousness as increased incidence of neuropsychiatric complications associated with mefloquine following cerebral malaria have been reported. Do not use IV artesunate as monotherapy. If IV artesunate needs to be continued indefinitely, clindamycin must be added to the regimen to complete 7 days of treatment. IM artesunate (same dose as IV) can be used in patients with difficult intravenous access. Children with severe malaria should be started on broad-spectrum antibiotic treatment immediately at the same time as antimalarial treatment. *Change to quinine PO if able to tolerate orally (max. quinine per dose = 600 mg) Reduce quinine IV dose by one third of total dose if unable to change to quinine PO after 48 hours (10 mg/kg q8h to 10 mg/kg q12h) or in renal failure or liver impairment.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	**Alternative**	
P. vivax, P. malariae, P. knowlesi (*P. malariae* & *P. knowlesi* are chloroquine-sensitive) *A.* New infection *B.* Chloroquine-resistant *(P. vivax)* or relapse *C.* Severe & complicated *P. vivax, P. knowlesi or P. malariae*	**New infection:** Total chloroquine: 25 mg base/kg divided over 3 days, as below: Day 1: 10mg base/kg PO stat then 5mg base/kg 6 hours later Day 2: 5mg base/kg PO q24h Day 3: 5mg base/kg PO q24h **PLUS** Primaquine 0.5mg base/kg PO q24h for 14 days		• Primaquine is ONLY needed for *P. vivax* for a total of 14 days. • Primaquine (0.5mg/kg) may cause haemolysis in individuals with G6PD deficiency, hence G6PD testing is required before administration of primaquine above 0.25mg/kg. • For those found to have mild to moderate G6PD deficiency, an intermittent primaquine regimen of 0.75 mg base/kg weekly for 8 weeks can be given under medical supervision. • In severe G6PD deficiency, primaquine is contraindicated & should not be used.
	Chloroquine-resistant *(P. vivax)* or relapse: (* In Sabah, considered chloroquine-resistant) ACT (Riamet® or ASMQ) (dosing as per *P. falciparum* treatment) **PLUS** Primaquine 0.5mg/kg PO q24h for 14 days	Quinine 10mg salt/kg PO q8h for 7 days **PLUS** Primaquine 0.5mg/kg PO q24h for 14 days Mefloquine 15 mg/kg single dose combined with primaquine have been found to be effective (except for *P. knowlesi*)	
	Severe & complicated *P. vivax, P. knowlesi or P. malariae* Treat as per severe *P. falciparum* malaria		• *P. knowlesi* (monkey malaria) can cause severe malaria & should be treated as severe malaria secondary to *P. falciparum*.∞
3. Mixed Infection	Treat as *P. falciparum*		

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12. Cheng AC, Chierakul W, Chaowagul W, et al. Consensus guidelines for dosing of amoxicillin-clavulanate in melioidosis. Consensus guidelines for dosing of amoxicillin-clavulanate in melioidosis. Am J Trop Med Hyg. 2008;78(2):208
13. WHO Guidelines for the treatment of malaria 2015. WHO/HTM/MAL/2015
14. The Sanford guide to antimicrobial therapy 2018.
15. American Academy of Paediatrics. Commitee on Infectious Diseases. Red Book: Report of the Committee on Infectious Diseases (2018).

History of tetanus toxoid (doses)	Clean, minor wounds		All other wounds	
	DTaP, Tdap, or Td	TIG	DTaP, Tdap, or Td	TIG
Fewer than 3 or unknown	Yes	No	Yes	Yes
3 or more	**No - if < 10 years** since last tetanus- containing vaccine dose.	No	**No if < 5 years** since last tetanus- containing vaccine dose.	No
	Yes if ≥ 10 years since last tetanus- containing vaccine dose	No	**Yes if ≥ 5 years** since last tetanus- containing vaccine dose.	No

TIG = Tetanus immune globulin
Other wounds = Such as, but not limited to, wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite

Note: DTAP is used for children <7 years of age. Tdap is preferred to Td for underimmunized children 7 years of age or older who have not received Tdap previously.

Adapted from the Red Book: 2015 report of the Committee on Infectious Diseases, p. 709:

1. First-line Anti-TB Drugs

Table 1: Recommended doses of first-line anti-TB drugs for children

Drug	Recommended daily dose	
	Dose (range) in mg/kg	Maximum dose in mg
Isoniazid (H)	10 (10 - 15)	300
Rifampicin (R)	15 (10 - 20)	600
Pyrazinamide (Z)	35 (30 - 40)	2000
Ethambutol (E)	20 (15 - 25)[c]	1000

Source: Malaysia Health Technology Assessment Section, Clinical Practice Guideline Management of Tuberculosis 3rd edition 2012.

- Pyridoxine 5 – 10 mg/day needs to be added if isoniazid is prescribed.
- The recommended daily dose of ethambutol is higher in children (20 mg/kg) than in adults (15 mg/kg, because the pharmacokinetics is different. A systematic review showed that ethambutol can be used safely in children, especially in situations where it is possible to monitor the complications (particularly optic neuritis) regularly.
- Streptomycin and amikacin should be reserved for the treatment of multi-drug resistant tuberculosis in children with known drug susceptibility to this medicines. since these drugs have auditory and vestibular toxic effects and nephtoxic effects.

2. Treatment Regimens

- Treatment have 2 phases: an initial intensive phase and a second continuation phase.
- Daily directly-observed therapy is required for treatment of active disease.
- Use of steroids:
  - Corticosteroids should be used in tuberculous meningitis, endobronchial TB or pericarditis (pericardial effusion).
  - Prednisolone: Dosage of 2 mg/kg daily or its equivalent.
    Maximum dosage of 60 mg/day for 4-6 weeks followed by tapering dose in 1-2 weeks before stopping.

Table 2: Recommended treatment regimens for children in each TB diagnostic category

TB cases	Regimen*		Remarks
	Intensive phase	Continuation phase	
New smear positive PTB*	2HRZE	4HR	Ethambutol can be stopped if the TB culture is sensitive to HRZE*
New smear negative PTB	2HRZ	4HR	
Less severe EPTB	2HRZ	4HR	
Severe concomitant HIV disease or other immunocompromised state	2HRZE	4-10HR	Depending on the site of infection
Severe form of EPTB **TB meningitis/spine/bone**	2HRZE	10HR	
Previously treated smear positive PTB including relapse & treatment after interruption	Treatment will be individualised; need to refer to paediatric infectious disease specialist		All attempts should be made to obtain C&S result
Treatment failure TB **MDR-TB**	Treatment will be individualised; need to refer to paediatric infectious disease specialist		All attempts should be made to obtain C&S result

***Direct observation of drug ingestion(DOTS) is required throughout the treatment**

PTB= pulmonary tuberculosis, EPTB= extrapulmonary tuberculosis, MDR-TB = multidrug-resistant tuberculosis

Source:
Clinical Practice Guideline Management of Tuberculosis 3rd edition 2012 (Modified from World Health Organization. Rapid advice - treatment of tuberculosis in children. Geneva: WHO; 2010. & World Health Organization. Guidance for national tuberculosis programmes on the management of tuberculosis in children. 2nd Edition. Geneva: WHO; 2010)

References:

1. Malaysia Health Technology Assessment Section, Clinical Practice Guideline Management of Tuberculosis. 3rd edition. 2012.
2. World Health Organization. Rapid advice - treatment of tuberculosis in children. Geneva: WHO; 2010.
3. World Health Organization: Guidance for national Tuberculosis programmes on the management of tuberculosis in children. 2ND Edition. Geneva: WHO; 2014.
4. Donald PR, Maher D, Maritz JS, et al. Ethambutol dosage for the treatment of children: literature review and recommendations. Int J Tuberc Lung Dis. 2006 Dec;10(12):1318-30.

B14. URINARY TRACT INFECTIONS

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Urinary Tract Infection (UTI) *Escherichia coli* Proteus spp. Klebsiella spp. Enterobacter spp.	**0-2 months old:** Ampicillin 50mg/kg/dose IV <1week of age: q12h >1week of age: q8h **PLUS** Gentamicin 5mg/kg/dose IV < 30 week of CGA: q48h > 30-34 week of CGA: q36h ≥35 week CGA:q24h **>2 months old:** Cefuroxime 100-150mg/kg/day IV in 3 divided doses (max. 6gm/day) **PLUS/MINUS** Gentamicin 5mg/kg/dose IV daily	**III young infant:** Cefotaxime 150-200mg/kg/day IV in 3 divided doses (max. 8gm/day)	Duration: 10-14days. Adjust therapy based on culture result. Duration: 7-14 days. Switch to oral therapy when improving and able to tolerate oral therapy.
Prophylaxis for UTI for infants & children with recurrent UTI	Trimethoprim 1-2mg/kg PO at night	Nitrofurantoin 1-2mg/kg at night	Antibiotic prophylaxis should not be routinely recommended in children with first-time UTI. Prophylactic antibiotics should be given for 3 days with MCUG (micturatingcystourethogram) taking place on the second day Children with Grade I-IV vesicoureteral reflux (VUR) may experience decrease in recurrent UTI by 50% following first or second febrile or symptomatic UTI with increased detection of resistant organism following antibiotic prophylaxis.

References:

1. NICE Guidelines: Urinary tract infection: diagnosis, treatment and long term management of urinary tract infection in children 2007. Last update 2017.
2. UTI Clinical Practise Guideline, Pediatrics 2011.
3. American Academy of Paediatrics. Commitee on Infectious Diseases. Red Book: Report of the Committee on Infectious Diseases (2018).
4. The Sanford guide to antimicrobial therapy 2018.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Catheter-Related Bloodstream Infection (CRBSI)			
***Coagulase-negative staphylococcus (CoNS)**			Diagnosis needs: 1. Paired blood cultures drawn from both catheters & peripheral vein. 2. If blood cultures cannot be drawn from peripheral vein, it is recommended that **two or more** blood cultures should be drawn through different catheter lumen. Long term catheters should be removed in patients with CRBSI with: Severe sepsis, suppurative thrombophlebitis, endocarditis, blood stream infections that continues despite 72 hours of antimicrobial therapy or longer to which the infecting organism is susceptible or infections due to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, fungi & mycobacterium. Attempts at catheter salvage are only recommended in uncomplicated CRBSI or CLABSI caused by bacteria that are neither too virulent nor too difficult to eradicate. Exact optimal duration of therapy has not established in children with or without catheter removal. 10-14 days after first negative blood culture is usually recommended. *For CONS, need to decide whether isolates from blood culture is coloniser or true pathogen.
Methicillin-sensitive (MSCoNS)	Cloxacillin 200mg/kg/day IV in 4-6 divided doses	Cefazolin 100mg/kg/day IV in 3 divided doses max. 6 g/day (if no endocarditis)	
Methicillin-resistant (MRCoNS)	Vancomycin 60mg/kg/day IV in 2-3 divided doses		
Coagulase-positive staphylococcus			
Methicillin-sensitive (MSSA)	Cloxacillin 200mg/kg/day IV in 4-6 divided doses	Cefazolin 100mg/kg/day IV in 3 divided doses max. 6 g/day (if no endocarditis)	
Methicillin-resistant (MRSA)	Vancomycin 60mg/kg/day in 2-3 divided doses		

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Gram-negative bacilli Enterobacteriaceae (*Escherichia coli, Klebsiella pneumoniae*, Enterobacter, Proteus sp etc.)			
ESBL –ve	*Piperacillin/tazobactam∞: 300mg of piperacillin/kg/day in 3-4 divided doses (max. 16 g/day)		*Empiric treatment with piperacillin/ tazobactam covers most of the Gram-negative organisms (Enterobacteriaceae), Gram-positive organisms & pseudomonas; follow through with C&S.
ESBL +ve	Ertapenem 30mg/kg/day IV in 2 divided doses	Imipenem 60-100mg/kg/day IV in 4 divided doses (max 4g/day) **OR** Meropenem 60-120mg/kg/day IV in 3 divided doses (max 6g/day)	
Pseudomonas aeruginosa	Piperacillin/tazobactam: 300mg of piperacillin/kg/day in 3-4 divided doses (max. 16 g/day)	Cefepime 50mg/kg/dose IV q8h	Not all pseudomonas is drug resistant. If ceftazidime remains susceptible, please use ceftazidime with anti-pseudomonas aminoglycoside to treat. De-escalation is important to preserve antibiotic for future use.
***Candida albicans* or other Candida species**			
	Fluconazole 12mg/kg IV q24h	Caspofungin loading dose 70 mg/m^2/dose IV q24hr on Day 1, followed by 50 mg/m^2/dose IV q24hr thereafter (max. 70 mg) **OR** Amphotericin B lipid complex 3-5 mg/kg/dose IV q24hr	Fungaemia: treatment without catheter removal is associated with low success rate & higher mortality.

Infection/Condition & Likely Organism	Suggested Treatment		Comments
	Preferred	Alternative	
Suppurative Thrombophlebitis *Staphylococcus aureus*			
MSSA	Cloxacillin 200mg/kg/day IV in 4-6 divided doses	Cefazolin 100mg/kg/day IV in 3 divided doses (max. 6 g/day	Diagnosis requires positive blood culture plus radiographic demonstration of thrombus. Remove catheter & a minimum antibiotic treatment of 3-4 weeks. Surgical resection of involved vein if failed conservative therapy.
MRSA	Vancomycin 60mg/kg/day in 2-3 divided doses		

References:
1. IDSA guidelines for intravascular catheter-related infection. CID 2009; 49:1-45.
2. Patricia MF. Diagnosis and management of central-venous catheter-related bloodstream infections in pediatric patients. Pediatr Infect Dis J. 2009; 28(11):1016-1017.
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5. The Sanford guide to antimicrobial therapy 2018.

SECTION C :
CLINICAL PATHWAYS IN PRIMARY CARE

Suspected pneumonia / acute bronchitis:
acute cough ± sputum

Consider differential diagnosis:
e.g. URTI, asthma, COPD, CCF, post nasal drip, ACE-I induced cough

Vital Sign Abnormalities – if any of the following:
Tachycardia (HR > 100 beats/min)
Tachypnoea (RR > 24 breaths/min)
Fever (Temperature > 38^{0}C)
Hypoxemia (SPO2 <95%)

Yes / No

Physical Examination: Abnormalities suggestive of consolidation or pleural effusion?

Yes / No

Treat as **Pneumonia**
Do CXR as baseline
(if facility available)

Do CXR, does it suggest pneumonia?

No / Yes

Physical Examination: Abnormalities suggestive of consolidation or pleural effusion?

Yes / No

Uncomplicated **Acute Bronchitis** likely:
- Symptoms suggestive of acute bronchitis: low grade fever, wheezing, chest soreness, mild SOB
- Symptomatic relief
- Bronchodilator to shorten duration of cough

Recommended dosage (mild CAP only)

Antibiotics	Dosing	Duration	Remarks
Amoxycillin	500mg PO q8h	5-7 days	Preferred
Doxycycline	100mg PO q12h	7 days	Alternative
Amoxycillin/ clavulanate	625mg PO q8h	5-7 days	Alternative

NICE guideline for Pneumonia in adults: diagnosis and management. Published: 3 December 2014.

Consider hospitalization if 2 or more:
- Confusion
- RR ≥ 30 breaths/min
- BP ≤ 90/60mmHg
- Age ≥ 65 years old

Consider **Pertussis** during outbreak:
- cough ≥ 2weeks
- paroxysms of cough
- post-tussive vomiting
- inspiratory whoop

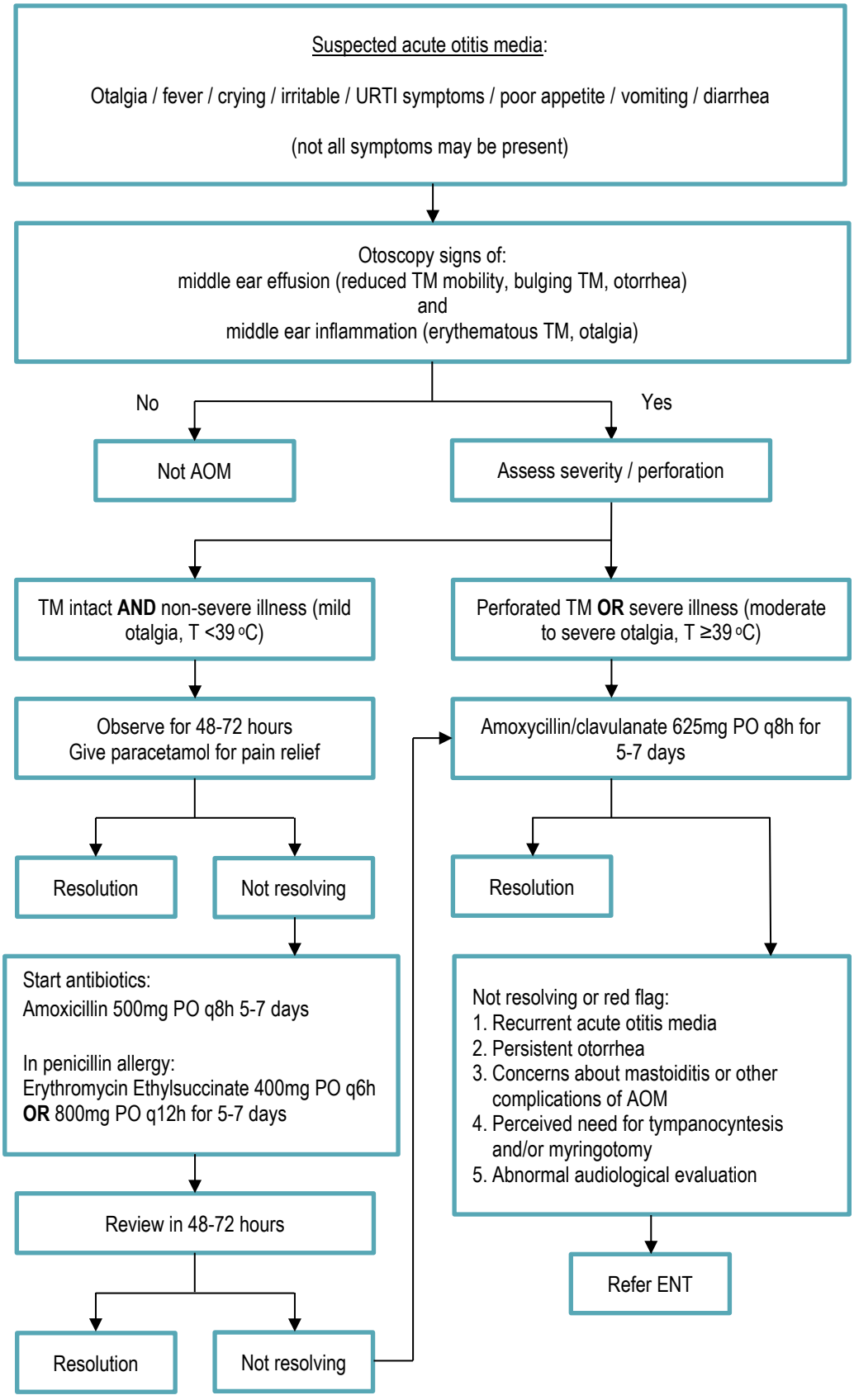
Erythromycin Ethylsuccinate 800mg PO q12h for 14 days

Consider **Influenza** during outbreak:
- acute fever and myalgia

Oseltamivir 75mg PO q12h for 5 days indicated for:
- high risk patients*
- when taken within 48 hours of onset of symptoms (for non-high risk patients)

*Patients at higher risk for influenza:
- Age < 2 years or ≥ 65 years old
- Pregnant women or immunosuppressed individuals
- Patients with chronic medical conditions e.g. CCF, IHD, chronic lung disease, asthma, CKD, DM, malignancy, chronic liver disease, etc.
- Morbid obesity (BMI≥ 40 kg/m^2)

C2. ACUTE OTITIS MEDIA



1. Consensus Guidelines on URTI, Malaysian Society of Otorhinolaryngologists Head & Neck Surgeons (MSO-HNS) 2009.
2. Otitis media (Acute): Antimicrobial prescribing. NICE Guideline March 2018.

Suspected acute pharyngitis:
e.g. sore throat

Strep score

Symptoms or signs	Points
Temperature >38ºc	+1
Absence of cough	+1
Tender anterior cervical adenopathy	+1
Tonsillar exudates or swelling	+1
Patient's age	
< 15	+1
15 to 45	0
>45	-1

Total score < 3

Symptomatic treatment:
e.g. anti-pyretic, analgesic, hydration

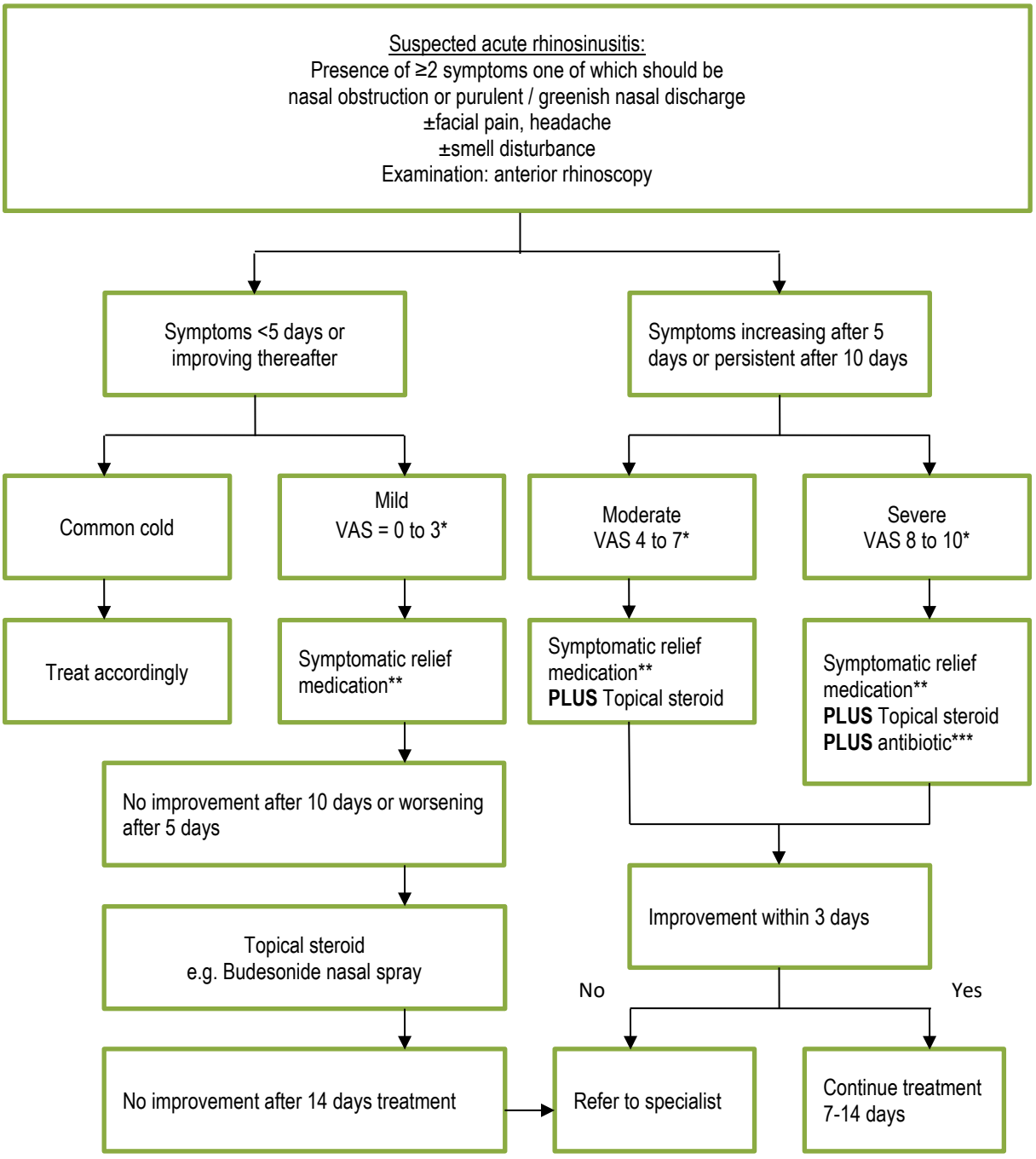
Total score ≥ 3

- Symptomatic treatment
- Anti-microbial therapy

Recommended dosage

Antibiotics	Dosing	Duration	Remarks
Phenoxymethylpenicillin (Pen V)	500mg PO q6h **OR** 1gm PO q12h	5-10 days	Preferred
Amoxicillin	500mg PO q8h	5-10 days	Alternative
Erythromycin Ethylsuccinate	800mg PO q12h	5-10 days	Alternative

1. Sore Throat (Acute): Antimicrobial Prescribing. NICE Guideline January 2018.
2. Consensus Guideline on Upper Respiratory Tract Infections, Malaysian Society of Otorhinolaryngologists Head & Neck Surgeons (MSO-HNS) 2009.



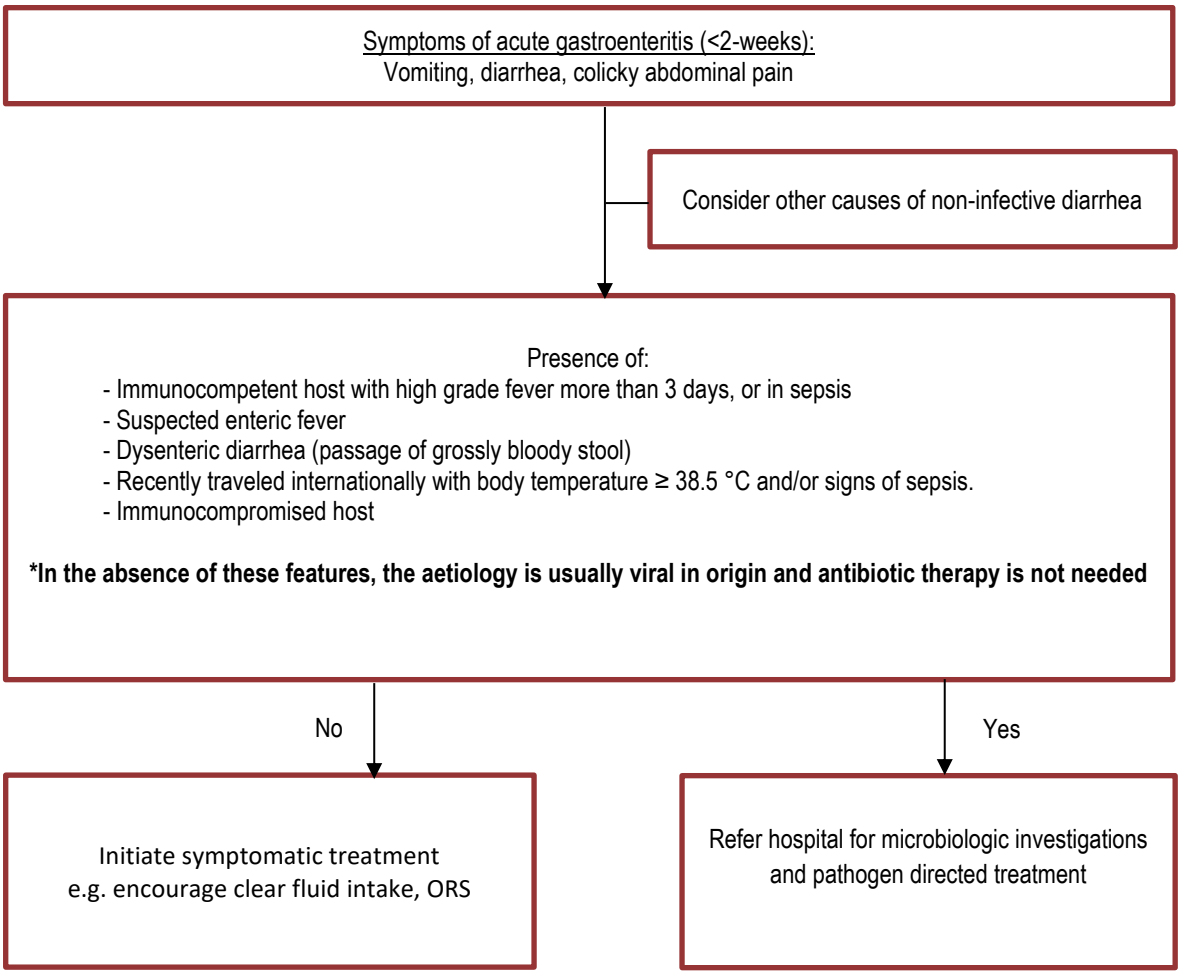
* Severity of disease can be based on Visual Analogue Score (VAS). The patient is asked: "How troublesome are your symptoms"
Not troublesome (0) to Worst thinkable troublesome (10)
** May include analgesics, nasal saline irrigation & decongestants
*** At least 3 of:
- purulent/greenish nasal discharge
- severe local pain
- fever
- elevated ESR/CRP
- double sickening (becoming worse again after initial recovery)

Recommended dosage

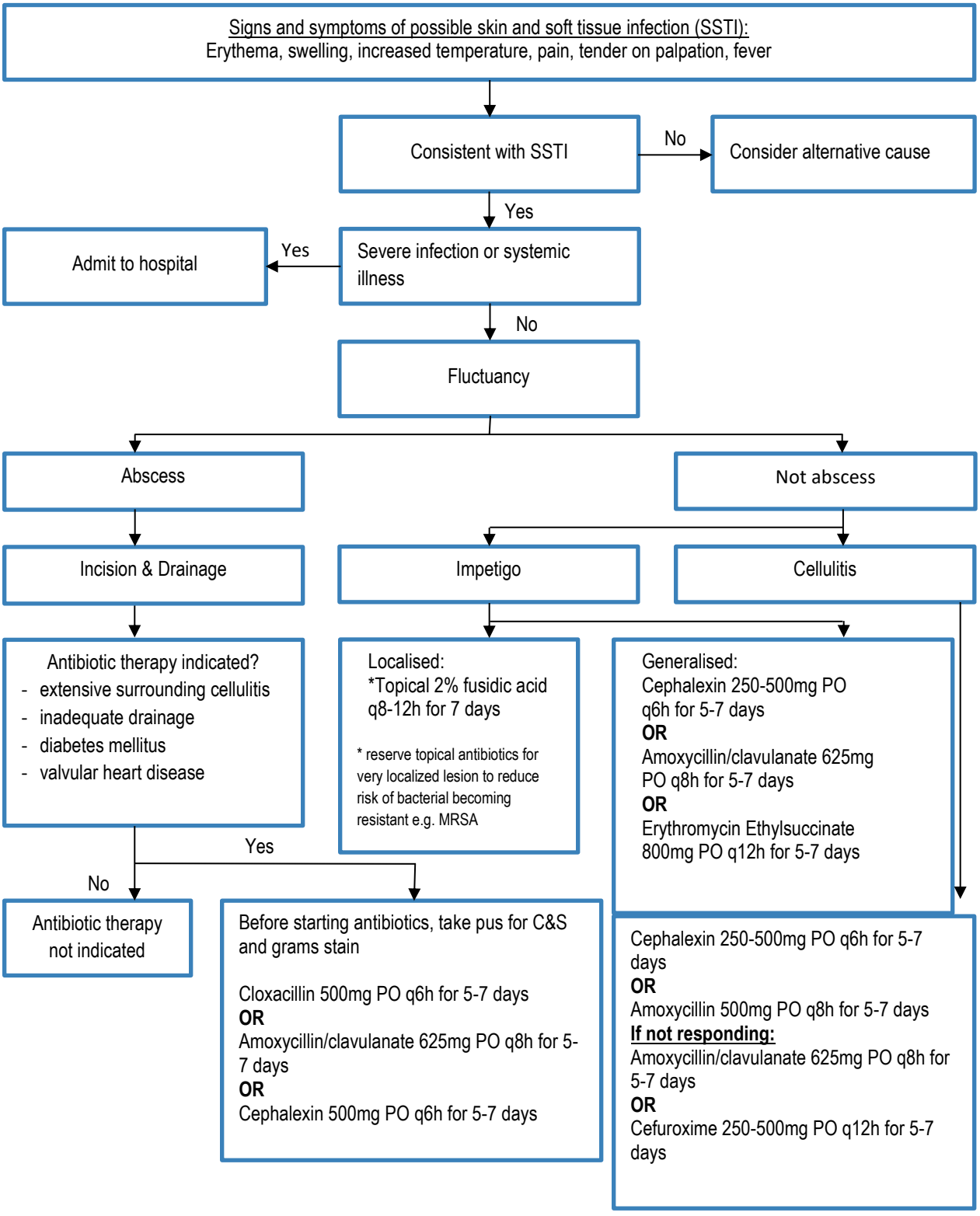
Antibiotics	Dosing	Duration	Remarks
Amoxycillin	500mg PO q8h	5-10 days	Preferred
Amoxycillin/ clavulanate	625mg PO q8h	5-7 days	Preferred
Erythromycin	800mg PO q12h	5 days	Alternative
Doxycycline	100mg PO q12h	5 days	Alternative

1. Clinical Practice Guidelines, Management of Rhinosinusitis in Adolescents and Adults 2016, MOH/P/PAK/318.16(GU).
2. IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults 2012.

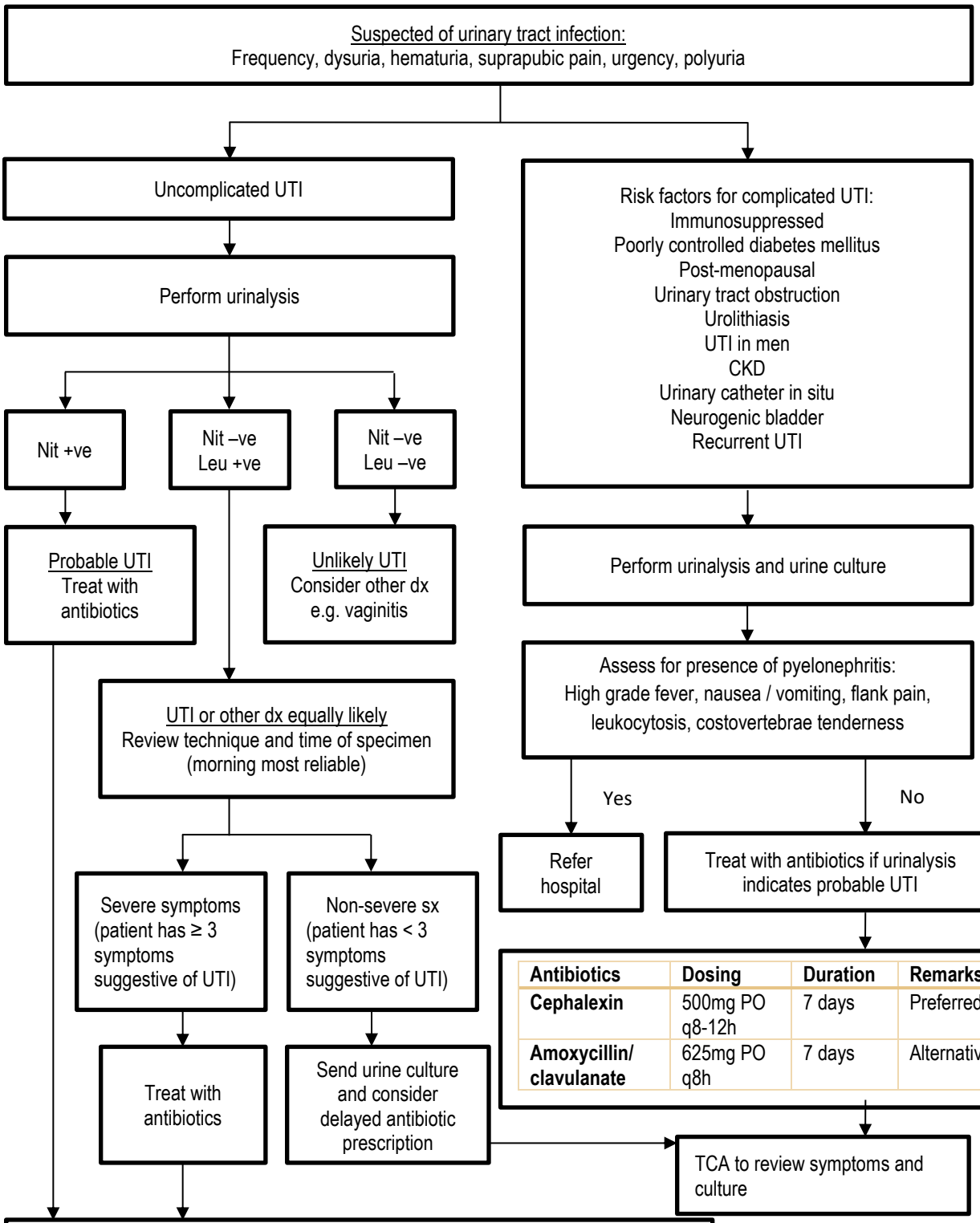
C5. ACUTE GASTROENTERITIS



C6. SKIN AND SOFT TISSUE INFECTION



1. Summary of antimicrobial prescribing guidance – managing common infection. NICE Guideline February 2019.
2. Primary Care Dermatology Society UK 2018



Antibiotics	Dosing	Duration	Remarks
Cephalexin	500mg PO q8-12h	7 days	Preferred
Amoxycillin/ clavulanate	625mg PO q8h	7 days	Alternative

Antibiotics	Dosing	Duration	Remarks
Nitrofurantoin*	50-100mg PO q6h	5 days	Preferred
Cephalexin	500mg PO q12h	3-5 days	Preferred
Amoxycillin/ clavulanate	625mg PO q8h	3-5 days	Alternative
Cefuroxime	250mg PO q12h	3-5 days	Alternative

1. European Association of Urology Guidelines on Urological Infections, 2017.
2. South Australia Clinical Guideline on Empirical treatment of Bacterial Urinary Tract Infections (adults), October 2017
3. UTI (lower): Antimicrobial Prescribing. NICE Guideline 2018.

* Nitrofurantion is contraindicated when eGFR is <30 ml/min

APPENDICES

CLINICAL PHARMACOKINETIC GUIDELINES
(UPDATED ON JUNE 2019)

AMINOGLYCOSIDE DOSING STRATEGIES

A. EXTENDED-INTERVAL THERAPY / SINGLE DAILY DOSING (EID / SDD)

EID/SDD is an approach of giving high-dose aminoglycoside over 30 minutes at an extended interval (e.g 24 hourly, 36 hourly or more).

The theoretical benefits of EID / SDD:

- Aminoglycosides display concentration-dependent bactericidal action - that is, higher dose and serum concentrations result in more rapid bacterial killing. [1]
- Optimise concentration-dependent bacterial killing by achieving a high peak (>10x MIC).[2]
- Minimize nephrotoxicity by administering larger, less frequent doses and potentially decreasing renal cortical aminoglycoside concentrations.
- Utilize the post-antibiotic effect (PAE) (2-8 hours), defined as a recovery period before organisms can resume growth after drug removal.[1]
- Minimize the development of adaptive resistance by allowing a recovery period during the dosing interval.

Exclusion criteria;

EID / SDD is reasonable in most patients, with the following exceptions:[3]

- Pregnancy
- Ascites
- Burns (>20%)
- Endocarditis
- Creatinine clearance <30ml/min
- Dialysis
- Neutropenic patients
- Patients with gram positive infections (synergistic effect).
- Heamodynamically unstable.
- History of hearing loss/vestibular dysfunction.
- Mycobacterium infection.

SDD Dosing Strategy Based On Creatinine Clearance:[4]

Creatinine Clearance (ml/min)	Dose in 24 hours	
	Gentamicin	Amikacin
> 80	5mg/kg	15mg/kg
60 - 79	4mg/kg	12mg/kg
40 – 59	3.5mg/kg	7.5mg/kg
30 – 39	2.5mg/kg	4mg/kg
< 30	Conventional dosing	Conventional dosing

EID Dosing Strategy Based On Serum Concentration:[5]

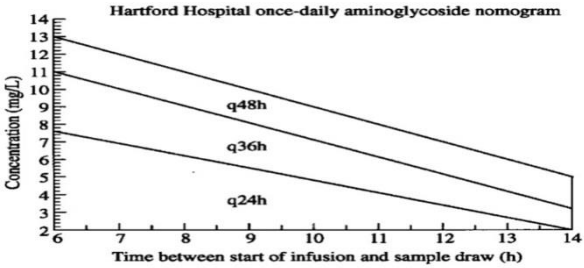
Gentamicin	Amikacin
7mg/kg per dose	15mg/kg per dose

1. Initial level monitoring*

Single level drawn 8-12 hours after the first dose (Only applicable for 7mg/kg – plotting doses lower or higher than 7mg/kg may under or overestimate clearance)

Concentration Gentamicin (7mg/kg/dose): Plot level on graph
Concentration Amikacin (15mg/kg/dose): Divide level in half, then, plot on graph

Please consult pharmacist for dosage adjustment.



2. Follow up trough level monitoring

Trough monitoring (30-60 minutes prior to dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure.

Maintenance trough levels should be monitored at least once weekly.

Sample Parameters	Gentamicin		Amikacin	
Time to sample[10]	At the 2nd dose			
Sampling time[10]	Take two samples at minimum 4 hours interval (e.g. post-2H and post-6H)			
Target levels (mcg/ml)[5,6]	TROUGH	PEAK*	TROUGH	PEAK*
	< 1	16 - 30	< 1	56 - 64

*The target reference range may be individualized based on institutional MIC value.

B. CONVENTIONAL / TRADITIONAL DOSING

Traditional dosing includes reduced doses and frequent administration of aminoglycosides using pharmacokinetic parameters to determine dose and frequency. However, in practice, dose below 7mg/kg for Gentamicin at 24 hours interval is frequently used for patients with normal renal function.

Creatinine Clearance (ml/min)	Gentamicin	Amikacin
> 60[7]	1.5 – 2mg/kg every 8 hourly	5 – 7.5mg/kg every 8 hourly
40 - 60[7]	1.5 – 2mg/kg every 12 hourly	5 – 7.5mg/kg every 12 hourly
20 - 40[7]	1.5 – 2mg/kg every 24 hourly	5 – 7.5mg/kg every 24 hourly
< 20[7]	1.5 – 2mg/kg every 48 – 72 hourly	5 – 7.5mg/kg every 48 – 72 hourly
CVVH / CVVHD / CVVHDF[8]	Loading dose 3mg/kg followed by 2mg/kg every 24 – 48 hourly	Loading dose 10mg/kg followed by 7.5mg/kg every 24 – 48 hourly
CAPD[9]	Intermittent: 0.6mg/kg in night dwell Continuous: Loading dose 8mg/L followed by 4mg/L	Intermittent: 2mg/kg in night dwell Continuous: Loading dose 25mg/L followed by 12mg/L

Sample Parameters	Gentamicin		Amikacin	
Time to sample[10]	After the 3rd dose			
Sampling time[10]	PRE: obtained just prior to the next dose OR within 30 minutes before the next dose POST: 30 minutes after completion of 30 minutes infusion OR Bolus: 1 hour after dose is given			
Sampling time for ESRF[11]	PRE dialysis			
Target levels (mcg/ml)[6,10]	TROUGH	PEAK*	TROUGH	PEAK*
	< 2	5 - 10	< 10	20 - 30

*The target reference range may be individualized based on institutional MIC value.

VANCOMYCIN DOSING STRATEGIES

Vancomycin activity is considered to be time-dependent - that is, antimicrobial activity depends on the duration that the drug level exceeds the minimum inhibitory concentration (MIC) of the target organism. Thus, peak levels have not been shown to correlate with efficacy or toxicity - indeed concentration monitoring is unnecessary in most cases.

Sample Parameters[12]	Recommendation[12]
Time to sample	Just before the 4th dose.
Optimal trough concentration – non-complicated infections	Mininum trough concentration should always be maintained above 10mg/L (10 - 20mg/L) to avoid development of resistance. For a pathogen with an MIC of 1mg/L, the minimum trough concentration would have to be at least 15mg/L to generate the target AUC:MIC of 400.
Optimal trough concentration – complicated infections (bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia caused by *Staphylococcus aureus*)	Trough concentration of 15 - 20mg/L is recommended to improve penetration, increase the probability of obtaining optimal target serum concentrations and improve clinical outcomes.

Vancomycin Dosing Strategy for Intermittent Infusion:[16,17,18]

Loading dose:

LOADING DOSE (~25mg/kg regardless of CrCl) Suggestion for 30mg/kg in seriously ill patients	
Total Body Weight (kg)	**Loading Dose (mg)**
> 75kg	2000
60 – 74	1500
50 – 59	1250
30 – 49	1000

Maintenance dose:

Renal Function	**Dose**
Normal[12]	2 – 3g/day (20 – 45mg/kg/day) in divided doses every 6 – 12h; Max 4g/day Obese: Dose based on TBW
CrCl > 50ml/min[13]	15 - 20mg/kg/dose every 12 hours (usual : 750 – 1500mg)
CrCl 20 – 49ml/min[13]	15 - 20mg/kg/dose every 24 hours (usual : 750 – 1500mg)
CrCl < 20ml/min[13]	Need longer intervals, determined by serum concentration monitoring
HD[13]	Following loading dose of 15 - 20mg/kg, given 500mg to 1000mg after each dialysis session. Pre dosing based on pre-HD level*: < 10mg/L: administer 1000mg after HD 10 - 25mg/L: administer 500 - 750mg after HD > 25mg/L: Hold Vancomycin *based on clinical judgement
CVVH[13]	Following loading dose, give 1g every 48 hours
CVVHD / CVVHDF[13]	Following loading dose, give 1g every 24 hours
CAPD[9]	Intermittent dose (once/day): 15 - 30mg/kg every 5 - 7 days Continuous dose (per/L exchange): Loading: 1000mg/L Maintenance: 25mg/L

Vancomycin dosing strategy for continuous infusion:[14,15]

Body weight	Loading Dose
< 40kg	500mg IV in 100ml 0.9% sodium chloride or 5% glucose over 1 hour
< 70 kg	1g IV in 250ml 0.9% sodium chloride or 5% glucose over 2 hours
≥ 70 kg	1.5 g IV in 250ml 0.9% sodium chloride or 5% glucose over 2.5 hours

Start the maintenance IV infusion immediately after the loading dose. The dose depends on the patient's renal function. Infusions should be administered in 250ml 0.9% sodium chloride or 5% glucose over 12 hours. The total daily dose should be split into two and the infusion rate set at 20.8ml/hr.

Creatinine Clearance* (ml/min)	Daily maintenance dose	Dose in each 250ml infusion bag for administration over 12 hours
< 20	500mg	250mg
20 - 34	750mg	375mg
35 - 59	1000mg	500mg
60 - 79	1500mg	750mg
80 - 99	2000mg	1000mg
> 100	2500mg	1250mg

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Appendix 2 : Antibiotic Dosages In Patients With Impaired Renal Function (Adult)

**Antibiotic Dosages are for IV formulation unless specified otherwise*

*** Extended infusion and continuous infusion not suitable for older age/high serum creatinine patient (Richter et al, Infection, August 2019)*

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
ANTIBACTERIAL						
Aminoglycoside						
Amikacin	7.5mg/kg q12h Trough: 5-10mg/L Peak: 15-30 mg/L	100% of normal dose q12h or 24h by levels	100% of normal dose q24-72h by levels	100% of normal dose q48h-72h by levels	IPD: 2mg/kg q24h CAPD: LD: 25mg/L MD: 12mg/L HD: 7.5mg q48h post HD	
Gentamicin	LD: 2mg/kg MD: 1.7-2mg/kg q8h Trough: 1-2mg/L Peak: 4-10mg/L	100% of normal dose q8h	100% of normal dose q12-24h	100% of normal dose q48h	IPD: 0.6mg/kg q24h CAPD: LD: 8mg/L MD: 4mg/L HD: 1.7-2mg/kg q48h post HD	
Netilmicin	1.7-2mg/kg q8h Trough: 1-2µg/mL Peak: 4-10µg/mL	100% of normal dose q8h	100% of normal dose q12-24h	100% of normal dose q48h	IPD: 0.6mg/kg q24h CAPD: 10mg/L HD: 1.7-2mg/kg q48h post HD	
Streptomycin	IM 15mg/kg q24h or IM 25-30mg/kg 2x/week or IM 25-30mg/kg 3x/week	100% of normal dose q24h	100% of normal dose q24-72h	100% of normal dose q72-96h	HD: 15mg/kg q72-96h post HD	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
Carbapenem						
Imipenem/cilastatin	500-1000mg q6h	100% of normal dose q6h	50% of normal dose q6h	25% of normal dose q6h	IPD: 500mg in alternate exchange CAPD: LD: 250mg/L MD: 50mg/L HD: 120-250mg q12h	
Meropenem	1 – 2gm q8h	100% of normal dose q8h	100% of normal dose q12h	100% of normal dose q24h	IPD: 1gm daily CAPD, HD: 500mg q24h	Can infuse rapidly over 3-5 minutes in an urgent situation.[1]
Ertapenem	IV/IM 1gm q24h	100% of normal dose q24h	<30ml/min: 50% of normal dose q24h	50% of normal dose q24h	CAPD, HD: 500mg q24h	If dosed ≤ 6 hours prior to HD, give 150mg supplement post HD. If dosed > 6hours prior to HD, no supplement required post HD.[1]
Cephalosporin: DATA ON SELECTED PARENTERAL CEPHALOSPORINS						
Cefazolin	IV/IM 1-2gm q8h (max 12gm/day)	100% of normal dose q8h	100% of normal dose q12h	50% of normal dose q24-48h	IPD: 15-20mg/kg q24h CAPD: LD: 500mg/L MD: 125mg/L HD: 1-2gm q24h	Surgical prophylaxis: IV 2gm within 60min prior to skin incision. Consider 3gm if >120kg in weight. Repeat the dose 4 hours after the first dose if still in surgery.[1]
Cefepime	1-2gm q8-12h	100% of normal dose q12h	50-100% of normal dose q24h	25-50% of normal dose q24h	IPD: 1gm q24h CAPD: LD: 250-500mg/L MD: 100-125mg/L	For continuous infusion, start with LD of IV 15mg/kg over 30 minutes and then immediately begin continuous infusion: CrCl | Dose

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
					HD: 1gm q24h (+ extra 1gm post HD)	<table><tr><td>>60</td><td>6gm q24h</td></tr><tr><td>30-60</td><td>4gm q24h</td></tr><tr><td>11-29</td><td>2gm q24h</td></tr></table>
Cefotaxime	2gm q8h	100% of normal dose q8-12h	100% of normal dose q12-24h	100% of normal dose q24h	IPD: 500-1000mg q24h HD: 2gm q24h	In life-threatening infections and meningitis, can give IV 2gm q24h.[1]
Cefoperazone	1-2gm q12h	100% of normal dose q12h	100% of normal dose q12h	100% of normal dose q12h	CAPD: LD: 500mg/L MD: 62.5-125mg/L	
Ceftazidime	2gm q8h	100% of normal dose q8-12h	100% of normal dose q12-24h	100% of normal dose q24-48h	IPD: 1-1.5gm q24h CAPD: LD: 500mg/L MD: 125mg/L HD: 2gm q24-48h	For continuous infusion, start with LD of IV 15mg/kg over 30 minutes and then immediately begin continuous infusion:[1] <table><tr><td>CrCl</td><td>Dose</td></tr><tr><td>>60</td><td>6gm q24h</td></tr><tr><td>30-60</td><td>4gm q12h</td></tr><tr><td>11-29</td><td>2gm q24h</td></tr></table>
Cefuroxime sodium	750-1500mg q8h	100% of normal dose q8h	100% of normal dose q8-12h	100% of normal dose q24h	CAPD: 750-1500mg q24h HD: 750-1500mg q24h	In more serious infection, can increase to IV 1.5gm q6h[1]
Fluoroquinolone						
Ciprofloxacin	400mg q12h	100% of normal dose q12h	100% of normal dose q24h	100% of normal dose q24h Or 50% of normal dose q12h[3]	CAPD: 50mg/L HD: 400mg IV q24h	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
Levofloxacin	750mg PO/IV q24h	100% of normal dose q24h	20-49ml/min: 100% of normal dose q48h	<20ml/min: 750mg then 500mg q48h	CAPD, HD: 750mg q24h then 500mg q48h	Preferred dose for most indications in patients with normal renal function is 750mg. For oral therapy, avoid concomitant exposure to multivalent cations (Ca, Fe, Al, Mg, Zn) in dairy products, multivitamins and antacids. Cation chelate the drug and prevent absorption.[1]
Ofloxacin	200-400mg PO q12h	100% of normal dose q12h	100% of normal dose q24h	200mg q24h	CAPD: LD: 200mg/L MD: 25mg/L HD: 200mg q24h	Avoid concomitant dairy products, multivitamins, iron supplements and antacids; they contain multivalent cations that can chelate Ofloxacin and prevent absorption.[1]
Macrolide						
Clarithromycin	500mg PO q12h	100% of normal dose q12h	50-100% of normal dose q12h	50-75% of normal dose q12h	CAPD, HD: 500mg q24h	
Erythromycin	250-500mg PO/IV q6h	100% of normal dose q6h	100% of normal dose q6h	100% of normal dose q6h	ND	
Miscellaneous Antibacterials						
Colistin[4]	IBW >75kg: 9MU IBW 61-74kg: 8MU	4.5MU q12h	30-50ml/min: 3MU q12h 10-30ml/min:	2MU q12h	IHD: On non-HD days, give baseline daily dose of 130mg (divided q12h).	IHD: Non-HD days: 2MU q12h HD day (supplement dose): 1.2MU (3 hour session),

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
	IBW 51-60kg: 7MU IBW <50kg: 6MU		2.5MU q12h		On HD days, add 30-40% (40-50mg) to baseline daily dose after 3-4 hours session. Peritonitis: LD: 300mg MD: 150-200mg q24h	1.6MU (4 hour session)[5]
Linezolid	600mg PO/IV q12h Uncomplicated skin structure infections: 400 or 600mg PO/IV q12h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	CAPD: No dosage adjustment HD : No dose adjustment, but administer one of the dose post HD	
Metronidazole[2]	250-500mg q8-12h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	CAPD, HD: 7.5mg/kg q12h	
Nitrofurantoin	Active UTI: 50-100mg PO q6h for 5-7days or for at least 3 day after sterile urine achieved. UTI prophylaxis: 50-100mg PO at night	Avoid use	Avoid use	Avoid use	Avoid use	
Trimethoprim (TMP) / Sulphamethoxazole (SMZ) TMP 80mg: SMZ 400mg	PO/IV 5-20mg/kg/day (divided q6-12h)	100% of normal dose. No changes in frequency.	10-29ml/min: 5-10mg/kg/ day (divided q12h)	5-10mg/kg q24h		
Vancomycin	15-30mg/kg q8-12h Trough: 15-20mg/L	100% of normal dose. No changes in frequency.	15mg/kg q24-96h	7.5mg/kg q48-72h	CAPD, HD: 7.5mg/kg q248-72h Trough: 15-20mg/L	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
					HD in next 24h: 15mg/kg HD in next 48h: 15mg/kg - 25mg/kg HD in next 72h: 35mg/kg Dose given at a rate of 15mg/min over last 120 minutes of HD to coincide with the end of dialysis [1]	
Penicillins						
Amoxicillin	PO 250-1000mg q8h	100% of normal dose. No changes in frequency.	100% of normal dose q8-12h	100% of normal dose q24h	CAPD: 150mg/L HD: 250-500mg q24h	IV Amoxicillin not available in FUKKM.
Ampicillin sodium	1-2gm q4-6h	100% of normal dose. No changes in frequency.	30-50ml/min: 100% of normal dose q6-8h 10-30ml/min: 100% of normal dose q8-12h	100% of normal dose q12h	CAPD: 125mg/L HD: 1-2gm q12h	
Amoxicillin/ Clavulanate	1.2gm q8h In serious infection, can increase frequency to q6h	100% of normal dose. No changes in frequency.	10-30ml/min: 1.2g first dose then 600mg q12h	1.2g first dose then 600mg q12h	CAPD: No data HD: 1.2g first dose then 600mg q12h	
Ampicillin/ Sulbactam	3gm q6h	100% of normal dose. No changes in frequency.	100% of normal dose q8-12h	100% of normal dose. q24h	CAPD: 3gm q12h IPD: 2gm q12h CAPD: LD: 750-100mg/L MD: 100mg/L	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
					HD: 3gm q24h (post HD on dialysis days)	
Piperacillin / tazobactam	3.375 – 4.5gm q6h	100% of normal dose. No changes in frequency.	20-40ml/min: 2.25-3.375gm q6h <20ml/min: 2.25-3.375gm q8h	2.25gm q8-6h	CAPD: LD: 4.5gm MD: 1.125gm HD: 2.25gm q8-12h	
ANTIFUNGAL						
Amphotericin	Amphotericin B *Test dose 1mg; starting 0.1mg/kg/day over 6 hours; increase to target dose* 0.25mg – 1mg/kg q24h (over 2-6h)	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	
	Amphotericin, colloidal dispersion 3-6mg/kg q24h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	
	Amphotericin, lipid complex 5mg/kg/day as single infusion	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	
	Amphotericin, liposomal 1-5mg/kg/day as single infusion	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	
Fluconazole	100-400mg PO/IV q24h	100% of normal dose. No changes in frequency.	50% of normal dose q24h	50% of normal dose q24h	IPD: 200mg q24-48h CAPD: 200mg then 50-100mg q24h HD:	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
					100-400mg	
Itraconazole	IV 200mg q12h for 4 doses, then 200mg q24h	100% of normal dose. No changes in frequency.	<30ml/min: Avoid	Avoid	CAPD: 100mg q12-24h (PO only) HD: 100mg q12-24h (PO only)	IV formulation is contraindicated for CrCl <30ml/min due to accumulation of cyclodextrin vehicle
	PO 100-20mg q12h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	50% of normal dose q12h		
Voriconazole	IV 6mg/kg IV q12h x 2 doses; 4mg/kg q12h	100% of normal dose. No changes in frequency.	Avoid or use PO formulation	Avoid or use PO formulation	IPD: 2.5mg/kg q24h CAPD: No data, but prefer oral route to avoid accumulation of IV cyclodextrin vehicle HD: No data, but prefer oral route to avoid accumulation of IV cyclodextrin vehicle	IV formulation is contraindicated for CrCl <30ml/min due to accumulation of cyclodextrin vehicle
	PO >40kg: 400mg PO q12h x2 doses; then 200mg PO q12h <40kg: 200mg PO q12h x2 doses; then 100mg PO q12h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.		
ANTIPARASITIC						
Pentamidine	IV/IM 4mg/kg q24h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose q24-36h	CAPD: 4mg/kg q24-36h HD: 4mg/kg q48h	
ANTIMYCOBACTERIAL						
Ethambutol	15-25mg/kg q24h	100% of normal dose. No changes in frequency.	30-50ml/min: 100% of normal dose q24-36h 15-25ml/min: 100% of normal	15mg/kg q48h	CAPD, HD: 15mg/kg q48h	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
			dose q36-48h			
Isoniazid	PO 5mg/kg q24h (max 300mg)	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	HD: 5mg/kg q24h	
Pyrazinamide	PO 25mg/kg q24h (max 2.5gm q24h)	100% of normal dose. No changes in frequency.	10-20ml/min: 100% of normal dose q48h	100% of normal dose q48h	CAPD: 25mg/kg q24h HD: 25mg/kg q48h	
Rifampin	PO 10mg/kg/day q24h (max 600mg/day)	100% of normal dose. No changes in frequency.	50-100% q24h	50-100% q24h	CAPD, HD: 300-600mg q24h	
Ethionamide	PO 15-20mg/kg/day (in 1-3 divided doses)	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	50% of normal dose. No changes in frequency.	CAPD, HD: 50% of normal dose. No changes in frequency.	
ANTIVIRAL						
Acyclovir	5-12.5mg/kg q8h	100% of normal dose. No changes in frequency.	100% of normal dose q12-24h	5-6.25mg/kg q24h	CAPD, HD: 2.5-6.25mg/kg q24h	
Adefovir	PO 10mg q24h	100% of normal dose. No changes in frequency.	100% of normal dose q48h <20ml/min: 100% of normal dose q72h	100% of normal dose q72h	HD: 10mg PO weekly post HD on dialysis days	
Ganciclovir	Induction: 5mg/kg q12h IV MD: 5mg/kg q24h OR 6mg/kg five times weekly	50-69ml/min: 50% of normal dose q12H	25-49ml/min: 50% of normal dose q24h 10-24ml/min: 25% of normal dose q24h	25% of normal dose 3x/week	CAPD, HD: 1.25mg/kg 3x/week	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min[1,2,3]			DIALYSIS DOSE[1,3]	COMMENTS
		> 50	10-50	< 10		
Valganciclovir	PO Induction (treatment): 900mg q12h MD (prophylaxis): 900mg q24h	900mg q12h	50% of normal dose q24-48h	Avoid	ND	
Lamivudine (HIV)	PO 300mg PO q24h	100% of normal dose. No changes in frequency.	300mg first dose; then 50-150mg q24h	50mg first dose; then 25-50mg q24h	CAPD, HD: 25-50mg q24h	
Stavudine	PO 30-40mg q12h	100% of normal dose. No changes in frequency.	50% of normal dose q12-24h	50% of normal dose q24h	HD: 15-20mg q24h	
Zidovudine	300mg q12h	100% of normal dose. No changes in frequency.	100% of normal dose. No changes in frequency.	100mg q8h	CAPD, HD: 100mg q8h	

HD (Hemodialysis); IPD (Intermittent peritoneal dialysis; LD (Loading Dose); MD (Maintenance Dose); CAPD (Continuous peritoneal Dialysis);
ND (No data)

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4. Guide to antimicrobial therapy in adult ICU 2017
5. International Consensus Guidelines For the Optimal Use of the Polymyxin: Endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Disease (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-Infective Pharmacology (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Disease Pharmacist (SIDP).

Appendix 3: Antibiotic Dosages in Children (age 2-10 years)

**Antibiotic Dosages are for IV formulation unless specified otherwise*

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
ANTIBACTERIAL						
Aminoglycosides						
Amikacin	LD 25mg/kg MD 18mg/kg q24h Trough: <5mg/L Max dose: 1.5gm/day for children age >10 years old	Avoid if possible. If needed, give loading dose then adjust subsequent doses according to trough level. Trough level target: <5mg/L			CAPD LD: 25mg/L MD: 12mg/L	Clearance of aminoglycosides are directly related to renal function. Hemodialysis clearance[4]: Amikacin: ~20% Gentamicin: ~50%
Gentamicin	IV or IM LD: 8mg/kg MD: 6mg/kg q24h Trough: <1.0 mg/L Max dose: 240 – 360mg for children age>10 years old	Avoid if possible. If needed, give 5mg/kg then check trough level 24 hours later and adjust subsequent doses according to trough level.			CAPD LD: 8mg/L MD: 4mg/L	
Streptomycin	IM 20 – 30 mg/kg q24h (Max: 1g)	7.5mg/kg q24h	7.5mg/kg q48h	7.5mg/kg q72-96h	HD 7.5mg/kg q72-96h	TDM monitoring is not available locally
Carbapenem						
Imipenem (+cilastatin)	15mg/kg q6h over 30 min. Severe infection: 25mg/kg over 1hr q6-8h or by constant infusion	75% of normal dose q8h	25% of normal dose q12h	15% of normal dose q24h	CAPD LD: 500mg/L MD: 200mg/L	
Meropenem	10 – 20mg/kg q8h over 5 – 30 min infusion Severe infection: 20-40mg/kg q8h IV or by continuous infusion	ND	ND	ND	ND	
Cephalosporin						
Cefazolin	IV or IM 10-15mg/kg (max 1g) q8h Severe infection:	100% of normal dose q8h	25mg/kg q12h	25mg/kg q24h	CAPD LD: 250mg/L MD: 125mg/L	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
	50mg/kg (max 2g) IV q6h or by continuous infusion Surgical prophylaxis: 50mg/kg (max 2g) at induction				IPD 15mg/kg q24h	
Cefepime	IV or IM: 25mg/kg q12h Severe infection 50mg/kg IV q8h (max 6g/day) or by continuous infusion	50mg/kg q12h	50mg/kg q24h	25mg/kg q24h	ND	
Cefotaxime	IV, IM or Continuous infusion: 50mg/kg q8 – 12h[5]	100% of normal dose q8h	100% of normal dose q8h	LD: 100% normal renal function dose MD: 50% dose with no changes in frequency	CAPD LD: 500mg/L MD: 250mg/L IPD 30mg/kg q24h	
Ceftriaxone	IV or IM: 50-75mg/kg q24h Severe infection: Increase up to 50mg/kg (max 2g) q12h Epiglottis: LD: 100mg/kg (max 2g) STAT MD: 50mg/kg (max 2g) 24 hours post LD-dose Prophylaxis of meningococcal meningitis: <12 yo: IM, 125mg single dose >12yo: IM, 250mg single dose	100% of normal dose q24h	100% of normal dose q24h	Dose should not exceed 40mg/kg/day (max 2g/day)	ND	Not dialyzable
Cefoperazone	IV or IM 25-60mg/kg (max 1g-3g) q6-12h in 1h infusion	ND	ND	ND	ND	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
Ceftazidime	IV or IM 25mg/kg q8h Severe infection/ cystic fibrosis 50mg/kg (max 2g) q6h	50-100% of normal dose q12h	15-30: 50 – 100% of normal dose q12h 5-15: 25 – 50 % of normal dose q24h	<5: 25 – 50 % of normal dose q48h	CAPD LD: 250mg/L MD: 125mg/L IPD 15mg/kg q24h	50-100% dialyzable
Cefuroxime sodium	25mg/kg q8h Severe infection: 50mg/kg (max 2g) IV q6h or by continuous infusion	100% normal dose q8h	100% of normal dose q12h	100% of normal dose q24h	CAPD LD: 200mg/L MD: 125mg/L IPD 15mg/kg q24h	
Fluoroquinolone						
Ciprofloxacin	PO 10-15 mg/kg (max 500mg) q12h IV 10mg/kg q12h Severe infection or cystic fibrosis: PO 20mg/kg (max 750mg) q12h IV 10mg/kg (max 400mg) q8h	≥40: 100% of normal dose q12h	10 – 39: 50% of normal dose q24h	<10: 33% of normal dose q24h	ND	<10% dialyzable
Levofloxacin	PO or IV (over 1 hr): 5 – 10mg/kg q12-24h	100% of normal dose q12-24h	100% of normal dose q24h	100% of normal dose q48h	ND	Not dialyzable
Ofloxacin	PO or IV (over 1 hr):	ND	ND	ND	ND	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
	5mg/kg q8-12h *or* 10mg/kg q12h					
Macrolide						
Clarithromycin	PO : 7.5-15mg/kg q12h Slow release tab (NOT/kg): 0.5 -1g q24h	100% of normal dose q12h	4mg/kg q12h	4mg/kg q24h	ND	
Erythromycin	PO or IV: 10mg/kg q6h **IV max infusion time: 5mg/kg/hr* Severe infection: 15-25mg/kg q6h Rheumatic fever (NOT/kg): PO 250mg q12h	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	ND	May cause pyloric stenosis in children <2 years old[2]. No dosage adjustment for base, salts and esters. Ethyl succinate formulation requires x1.6 higher dose (max 4g/day)[2].
Miscellaneous antibacterials						
Colistin sulphomethonate sodium **2.6mg = 1mg colistin base = 30,000iu**	IM or IV (over 5 mins): 40,000u/kg q8h *or* 1.25 – 2.5 mg/kg colistin base q12h PO or inhaled: 30,000 – 60,000 u/kg q8h	ND	ND	ND	ND	
Linezolid	PO or IV (over 1-2hr): 10mg/kg q8h (max 600mg/day) or 600mg q12h	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	ND	
Metronidazole	IV or PO: LD: 15mg/kg (max 1g) MD: 7.5mg/kg (max 1g) q8h	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	100% of normal dose q12h	ND	Extensively dialyzable, administer post dialysis

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
Nitrofurantoin	Treatment dose: PO 1.5mg/kg q6h Prophylaxis dose: PO 1-2mg/kg at night	ND	ND	ND	ND	
Trimethoprim (TMP) / Sulfamethoxazole (SMZ) **TMP 80mg: SMZ 400mg**	PO or IV (infuse over 1hr): TMP 4mg/kg q12h or 6-8mg/kg (max 300mg) q24h Renal prophylaxis: TMP PO 1-2mg/kg (max 80mg) at night	ND	ND	ND	ND	
Vancomycin	Max infusion rate: 0.3mg/kg/min LD: 25mg/kg MD: 15-20mg/kg q8-12h Trough: 10-15mg/L Severe infection: LD: 30mg/kg MD: 15-20mg/kg q8-12h Target trough level: 15-20mg/L Surgical prophylaxis: 25mg/kg over 90 min ending just before procedure *C.difficile* infection: PO 10mg/kg q6h Intraventric (NOT/kg): 10mg q48h	Give loading dose then take trough level immediately before the next dose; and take peak level 1 hour after completion of infusion. Adjust dose and interval based on trough level.			CAPD: LD: 500mg/L MD: 30mg/L IPD: 30mg/kg q5-7 days	High flux membranes and CRRT increases vancomycin clearance [4]
Penicillin						
Ampicillin	IV/ IM or PO: 25mg/kg q6h	100% normal dose q6h	100% normal dose q8-12h	100% normal dose q12h	ND	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
	Severe infection: IV 50mg/kg (max 2g) q6h or by continuous infusion					
Amoxicillin	IV/ IM or PO: 25mg/kg q8h *or* 25-40mg/kg q12h Severe infection: 50mg/kg q4-6h or by continuous infusion	100% of normal dose; no changes in frequency	100% normal dose q12h	100% normal dose q24h	CAPD: LD: 250-500mg/L MD: 50mg/L	
Amoxicillin/ Clavulanate (Augmentin)	Dose following Amoxicillin Amoxicillin 4mg: Clavulanate 1mg 15-25mg/kg q8h Amoxicillin 7mg: Clavulanate 1mg 20-30mg/kg q12h Amoxicillin 16mg: Clavulanate 1mg 30-50mg/kg q12h	100% of normal dose; no changes in frequency	100% of normal dose q12h	100% of normal dose q24h	ND	
Ampicillin/ Sulbactam (Unasyn)	Dose following Ampicillin IM or IV (infuse over 30min): 25-50mg/kg of ampicillin q6h	ND	ND	ND	CAPD: LD: 1000mg/L MD: 100mg/L	
Benzylpenicillin (C-Penicillin) **1mg= 1667u**	30mg/kg q6h Severe infection: 50mg/kg (max 2g) q4h or by continuous infusion	ND	ND	ND	ND	
Piperacillin	100mg/kg q6-8h Severe infection: To consider continuous infusion	ND	ND	ND	ND	
Piperacillin/ Tazobactam	Dose following Piperacillin (see above)	ND	ND	ND	ND	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
ANTIFUNGAL						
Amphotericin	Amphotericin B Continuous infusion: 1.5mg/kg/day (max 2mg/kg/day)	ND	ND	ND	CAPD: LD: 1mg/kg MD: 1mg/kg/day	Amphotericin B salts, liposomal, and lipid-complex products not bioequivalent; reassess dose if switching between products
	Amphotericin, colloidal dispersion 3-4mg/kg q24hr over 2-3h (max 6mg/kg for asperigillus)	ND	ND	ND	ND	
	Amphotericin, lipid complex 5mg/kg/day q24h over 1h infusion	ND	ND	ND	ND	
	Amphotericin, liposomal 3-6mg/kg (max 15mg/kg for severe infection) q24h over 1-2h infusion	ND	ND	ND	ND	
Fluconazole	12mg/kg q24h Superficial infection PO or IV: LD: 6mg/kg MD: 3mg/kg q24h	ND	ND	ND	ND	Intermittent PD: 3-6 mg/kg q24-48h (max 200 mg)
Itraconazole	Syrup: 3-5mg/kg q24h or 1.5-2.5mg/kg q12h or 5mg/kg q12h (severe infect) Capsule: 5-7.5mg/kg q24h *or* 2.5-4mg/kg q12h	100% of normal dose; no changes in frequency[3]				Food and acidic beverages may increase absorption of itraconazole capsules [5] Syrup – Take on empty stomach [5] Capsule – Take with food [5]
Voriconazole	PO <40kg 9mg/kg q12h	ND	ND	ND	ND	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
	: ≥40kg: LD 400mg q12h x 2 doses MD 200-300mg q12h IV <40kg: LD 9mg/kg q12h x 2 doses MD 8mg/kg q12h ≥40kg: LD 6mg/kg q12h MD 3-4mg/kg q12h					
ANTIPARASITIC						
Pentamidine **1mg base = 1.5mg mesylate = 1.74 isethionate**	IM or IV (over 2 hours): 3-4mg/kg (equivalent to 1.7-2.3 mg/kg base) q24h for 10-14 days	ND	ND	ND	ND	
Ethambutol	PO : 25mg/kg q24h for 8 weeks *then* 15mg/kg q24h *or* 35mg/kg for 3weeks IV: 80% of PO dose	ND	ND	ND	ND	Should be taken with food[5]
Isoniazid	PO, IM or IV 10mg/kg q24h (max 300mg) Intermittent: 15mg/kg; 3 times/week TB meningitis: 15-20mg/kg q24h (max 500mg)	ND	ND	ND	ND	PO formulation should be taken on empty stomach 1h before or 2h after meals. May be taken with meals to reduce GI discomfort [5]
Pyrazinamide	PO 35mg/kg q24h (max 2g) or 75mg/kg (max 3g)	ND	ND	ND	ND	Should be taken with food[5]
Rifampicin	PO or IV (over 3hours) 15mg/kg q24h (max 600mg)	ND	ND	ND	ND	Monitor AST levels on IV infusion[2]

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
	Staph infection: 10mg/kg (max 600mg) q12h Leprosy: 10mg/kg (max 600mg) monthly Cholestasis Itch: 10mg/kg (max 600mg) q24h					PO formulation should be taken on empty stomach 1h before or 2h after meals. May be taken with meals to reduce GI discomfort [5]
Ethionamide	Tuberculosis: PO 15-20mg/kg ON (max 1g) Leprosy : 5-8mg/kg q24h (max 375mg)	ND	ND	ND	ND	
ANTIVIRAL						
Acyclovir	EBV, herpes encephalopathy or sepsis, immunodeficiency, varicella: ≤12yo: 500mg/m^2 q8h Varicella zoster (NOT/kg): ≥2y: 800mg x 5/day for 7 days	25-50: 100% normal IV dose q12h	10-25: 100% normal IV dose q24h Or 100% normal PO dose q24h	100% normal PO dose q12h	ND	
Adefovir	PO (NOT/kg) 10mg q24h	ND	ND	ND	ND	
Ganciclovir	Induction: 5 mg/kg q12h for 2-3 weeks MD: 5 mg/kg q24h	Induction : 2.5mg/kg q24h MD: 1.25mg/kg q24h	Induction : 1.25mg/kg q24h MD: 0.625mg/kg q24h	Induction : 1.25mg/kg 3x/week MD: 0.625mg/kg 3x/week	HD, PD: Induction : 1.25mg/kg 3x/week MD: 0.625mg/kg 3x/week	
Lamivudine	PO: 4mg/kg q12h Hepatitis B: 3-4mg/kg q24h (max 100mg)	4mg/kg q12h	2mg/kg q12h	1mg/kg q24h	HD, PD: 1mg/kg q24h	

ANTIMICROBIAL	DOSE FOR NORMAL RENAL FUNCTION[1,2]	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl)[1,3] ml/min			DIALYSIS DOSE [1,3]	COMMENTS
		30-50	10-29	< 10		
Stavudine	PO <30kg: 1mg/kg q12h 30-59kg: 30mg q12h >60kg: 40mg q12h		30-50	10-29	<10	HD, PD: <30kg: 0.25mg/kg q24h 30-59kg: 7.5mg q24h post dialysis	
		<30kg	0.5 mg/kg q12h	0.25mg/kg q24h	0.25mg/kg q24h		
		30-59kg	15mg q12h	7.5mg q24h	7.5mg q24h		
Zidovudine	PO: 180 - 240 mg/m^2 q12h IV: 120 mg/m^2 q6h	100% of normal dose; no changes in frequency	100% of normal dose; no changes in frequency	50% of the normal dosage q8h	ND	
HD (Hemodialysis); IPD (Intermittent peritoneal dialysis; LD (Loading Dose); MD (Maintenance Dose); CAPD (Continuous peritoneal Dialysis); yo (years old); ND (No data)						

References:

1. Malaysian Pediatric Protocol 4th Edition 2018
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3. Drug Prescribing in Renal Failure Dosing Guidelines for Adults and Children Fifth Edition
4. Malaysian Clinical Pharmacokinetic Handbook 2015
5. Mims Malaysia Online

Appendix 4 : Antibiotic in Pregnancy and Lactation

Types of Antibiotics/ Antiviral/ Antiviral/Anti TB	FDA Pregnancy category	Lactation Considerations
Abacavir	C	Present in human milk; Not recommended
Acyclovir	B	Present in human milk; Compatible
Adefovir	C	Insufficient data; Not recommended
Amikacin	D	Present in human milk; Compatible
Amoxicillin	B	Present in human milk; Compatible
Amoxicillin / Clavulanate	B	Present in human milk; Compatible
Amphotericin B	B	Insufficient data; Not recommended
Ampicillin	B	Present in human milk; Compatible
Ampicillin / Sulbactam	B	Present in human milk; Compatible
Artesunate	Limited data for 1st trimester	Insufficient data; Caution
Azithromycin	B	Present in human milk; Caution
Bacampicillin	B	Insufficient data
Benzathine Penicillin	B	Present in human milk; Caution
Benzylpenicillin	B	Present in human milk; Caution
Caspofungin	C	Insufficient data; Caution
Cefaclor	B	Insufficient data; Caution
Cefepime	B	Present in human milk; Caution
Cefoperazone	B	Insufficient data
Cefoperazone / Sulbactam	B	Insufficient data
Cefotaxime	B	Present in human milk; Caution
Ceftazidime	B	Present in human milk; Caution
Ceftriaxone	B	Present in human milk; Caution
Cefuroxime Axetil	B	Present in human milk; Caution
Cefuroxime Sodium	B	Present in human milk; Caution
Cephalexin Monohydrate	B	Present in human milk; Caution
Chloramphenicol	C	Present in human milk; Not recommended
Ciprofloxacin	C	Present in human milk; Not recommended
Clarithromycin	C	Present in human milk; Caution
Clindamycin	B	Present in human milk; Not recommended
Clofazimine	C	Present in human milk; Not recommended
Clotrimazole	B	Insufficient data
Cloxacillin	B	Present in human milk; Caution
Cycloserine	C	Present in human milk; Not recommended
Dapsone	C	Present in human milk; Not recommended
Didanosine	B	Insufficient data; Not recommended
Doxycycline	D	Present in human milk ; Insufficient data; Compatible for short courses (eg 10 days); Long-term therapy is not recommended
Efavirenz	D	Present in human milk; Not recommended
Ertapenem	B	Present in human milk; Caution
Erythromycin	B	Present in human milk; Compatible
Ethambutol	C	Present in human milk; Compatible
Fluconazole	D	Present in human milk; Compatible
Flucytosine	C	Insufficient data
Fusidate sodium	C	Insufficient data
Ganciclovir	C	Insufficient data; Not recommended
Gentamicin	D	Present in human milk; Compatible
Griseofulvin	C	Insufficient data; Not recommended
Imipenem / Cilastatin	C	Present in human milk; Caution
Indinavir	C	Insufficient data; Not recommended

Types of Antibiotics/ Antiviral/ Antiviral/Anti TB	FDA Pregnancy category	Lactation Considerations
Isoniazid	C	Present in human milk; Compatible
Itraconazole	C	Present in human milk; Caution
Kanamycin	D	No data available
Ketoconazole	C	Present in human milk; Caution
Lamivudine	C	Insufficient data; Not recommended
Levofloxacin	C	Present in human milk; Not recommended
Linezolid	C	Present in human milk; Caution
Lopinavir / Ritonavir	C	Present in human milk; Not recommended
Meropenem	B	Present in human milk; Caution
Metronidazole	B	Present in human milk; Not recommended
Miconazole	C	Insufficient data; Caution
Minocycline	D	Present in human milk ; Insufficient data; Compatible for short courses (eg 10 days); Long-term therapy is not recommended
Netilmicin	D	Insufficient data
Nevirapine	C	Present in human milk; Not recommended
Nitrofurantoin	B	Present in human milk; Not recommended
Nystatin	C	Insufficient data; Caution
Ofloxacin	C	Present in human milk; Not recommended
Phenoxymethyl penicillin	B	Present in human milk; Compatible
Piperacillin	B	Present in human milk; Compatible
Piperacillin / Tazobactam	B	Present in human milk; Compatible
Benzylpenicillin	B	Present in human milk; Caution
Pyrazinamide	C	Present in human milk; Caution
Ribavirin	X	Insufficient data
Rifampicin	C	Compatible; may cause diarrhea in infant. Monitor infant for jaundice
Ritonavir	B	Insufficient data; Not recommended
Stavudine	C	Insufficient data; Not recommended
Streptomycin	D	Present in human milk; Not recommended
Sulphamethoxazole / Trimethoprim	D	Present in human milk; Caution; Not recommended in infants <2 months
Terbinafine HCL	B	Present in human milk; Not recommended
Tetracycline	D	Present in human milk ; Insufficient data; Compatible for short courses (eg 10 days); Long-term therapy is not recommended
Tinidazole	C	Present in human milk; Not recommended
Trimethoprim	C	Present in human milk; Caution
Vancomycin	B (oral)	Present in human milk; Caution
Voriconazole	D	Insufficient data; Not recommended
Zidovudine	C	Present in human milk; Not recommended

References

1. Anderson PO, Sauberan JB. Modeling drug passage into human milk. *Clin Pharmacol Ther*. 2016;100:42-52. Retrieved 24 Jun 2019 from https://uptodate.com/breast-feeding considerations
2. Chung AM, Reed MD, Blumer JL. "Antibiotics and Breast-Feeding: A Critical Review of the Literature". *Paediatr Drugs*. 2002;4:817-837. Retrieved 24 Jun 2019 from https://uptodate.com/breast-feeding considerations
3. Drugs.com Pregnancy / Breastfeeding

Appendix 5 : Guide To Collection & Transport Of Clinical Specimen

SPECIMEN	COLLECTION CONTAINER	TRANSPORT
Blood /Bone Marrow Aspirate	Commercial blood culture bottle (aerobe, anaerobe, paediatric, fungal, TB)	-
CSF	Sterile Bijou bottle	Immediately
Ear	Sterile swab	Amies Transport Medium
Eye	Sterile swab	Amies Transport Medium
	Corneal scrapping	Bacteriologic/Mycology culture media
Stool	Clean/Sterile container	Selenite F broth/Alkaline Peptone Water (during outbreak)
Stool for *Clostridium difficile* toxin	Sterile container	Immediately
Rectal swab (CRE/VRE screening)	Sterile swab	Amies Transport Medium
Genital	Sterile swab	Amies Transport Medium
Endocervical swab for *Chlamydia trachomatis*	Glass slide	Immediately or fixed with methanol if expected delay
Nose	Sterile swab	Amies Transport Medium
Sinus	Sterile swab	Amies Transport Medium
Bronchoalveolar lavage	Sterile container	Immediately
Sputum/Tracheal aspirate	Sterile container	-
Sterile body fluid (peritoneal/pericardial/pleural/ vitrous/synovial fluid)	Sterile container	Immediately
Throat	Sterile swab	Amies Transport Medium
Tissue	Sterile container filled with sterile normal saline (not formalin)	-
	Thioglycolate/RCMM for anaerobic infection	-
Urine	Sterile container	Within 30 minutes
Pus	Sterile swab	Amies Transport Medium
	Sterile container (aspirated from abscess)	-
	Thioglycolate/RCMM for anaerobic infection	-
Central venous catheter tip	Sterile container	Send along with peripheral blood culture
Gastric biopsy for *Helicobacter pylori*	Bullet tube filled with 0.5 ml sterile saline	Immediately
Blood film for malaria parasite (BFMP)	Thin & thick smear on glass slide	Immediately

Appendix 6 : Antimicrobial Stewardship (AMS)

The introduction of antimicrobial agents has contributed to the reduction of infectious diseases as the major cause of premature death. Treatment with antimicrobial agents seems so effective and safe that they are sometimes prescribed for dubious indications and for longer than necessary, with little concern for adverse effects and the development of resistance.

In the last 40 years, the prevalence of multidrug-resistant microorganisms have risen alarmingly. Antimicrobial resistance (AMR) occurs when microorganism that causes infection resist the effects of the medications used to treat them. There is evidence that overall rates of antimicrobial resistance correlate with the use of antimicrobials, thus the need for multiple agencies to work hand in hand to overcome AMR. Dr Margaret Chan, Former Director-General of WHO (2006-2017) in the Global Action of Plan on Antimicrobial resistance notes "Antimicrobial resistance threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases". The current Director-General of WHO, Dr Tedros Adhanom Ghebreyesus also joined in by delivering the report of the Interagency Coordination Group on Antimicrobial Resistance to the United Nations Secretary-General and had committed to implement the recommendation of that report with the Food and Agriculture Organization of the United Nations, the World Organization of Animal Health and other agencies.

According to the MyAp-AMR (2017-2021), data from National Surveillance of Antimicrobial Resistance (NSAR), the emergence of β-lactamase producers (ESBL) amongenterobacteriaceae has become a major concern in hospitals in Malaysia. Klebsiella pneumoniae, has shown an increase in resistance rate towards cefotaxime from 22% in 2008 to 35.8% in 2018. The New Delhi metallo-β-lactamase -1 (NMD-1) gene was first detected in carbapenem-resistant Klebsiella pneumoniae (CRKP) in 2010 in Malaysia. CRKP has shown a tremendous rise in the recent years, from 0.3% in 2011 to 3.5% in 2018

The emergence of AMR can cause the resistance to first-line medicines and lead to the use of second or third-line drugs which is can be less effective, more toxic, more costly and have collateral damage to the body's gut microbiota. The pace of new antimicrobial development has slowed markedly in the past 20 years. As more resistance accumulates, we are left with increasingly ineffective drug therapies. Thus AMR has a negative impact on patient outcomes, is a major threat for patient safety, increases health expenditure, renders common medical procedures more dangerous and leads to loss of options of antimicrobial therapy for common infections.

The World Health Assembly in May 2014 addressed a global consensus to combat the antimicrobial resistance. The action plan emphasized the need of an effective "one health" approach involving coordination among various sectors including human and veterinary medicine, agricultural, financial, environmental and well-informed consumers to combat the antimicrobial resistance. 5 strategic objectives had been included, and it involves:

1. Improving awareness and understanding of antimicrobial resistance through effective communication, education and training
2. Strengthening the knowledge and evidence base through surveillance and research
3. Reducing the incidence of infection through effective sanitation, hygiene and infection prevention measures
4. Optimizing the use of antimicrobial medicines in human and animal health
5. Developing the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

In line with strategy 4, antimicrobial management or stewardship programs have developed as a response. Antimicrobial Stewardship (AMS) is a coordinated systematic approach to improve the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen; right choice of antimicrobial, right route of administration, right dose, right time, right duration to optimize patients outcomes and minimize harm to present and future patients.

The development of antimicrobial resistance strains in hospitals is intensified because of the high level of antimicrobial use and concentration of patients with multiple pathogens. Ongoing monitoring and prospective audits and surveillance have been shown to improve patient care, decrease unnecessary antimicrobial use and microbial resistance and reduce pharmacy expenditures.

General AMS Policies

1. Formulation of AMS team in each hospital, Health District Office and Health Clinics

   The core members of AMS team should be multidisciplinary and appointed by Hospital Director/ District Health Officer/Medical Officer In-Charge.

2. Development and documentation of local antimicrobial policy

   Every healthcare facilities shall develop and document their local antimicrobial policy. The policy should be endorsed by the Drugs and Therapeutics Committee (JKUT) and ultimately the hospital director / District Health Officer/Medical Officer in Charge and publicized to the whole health care facility.

The antimicrobial policy shall include as below:

- Indications for antimicrobials are to be explicitly spelt out at the time of prescribing to assist with audit efforts.
- Appropriate Microbiology investigations (culture or serology) prior to antimicrobial commencement**.
- Clinicians to prescribe antimicrobials guided by the National Antibiotic Guidelines or local antibiotic guideline where applicable.
- A list of restricted antimicrobials and the procedures for obtaining approval.
- To limit the use of broad-spectrum antibiotics unless necessary.
- To review patient's antimicrobial therapy on a regular basis based on microbiology result and the patients progress.

**according to availability in primary care setting

3. Educational on AMS program via continuous medical education (CME) and antibiotic awareness campaign.

Provide regular updates on antimicrobial prescribing, practice and usage for healthcare professionals.

Specific AMS Policies

Implementation of AMS activities according to category & type of facilities.

State and Major Specialist Hospitals	Minor and without Specialist Hospitals
i. Surveillance and feedback mechanism on specific antimicrobial consumption. (Core Strategy) ii. Implementation of prospective audit and feedback according to local needs. (Core Strategy) iii. Formalize regular antimicrobial rounds by AMS team especially in State and Specialist Hospital (Core Strategy) iv. Establishment of formulary restriction and preauthorization/ approval system. (Core Strategy) v. Establishment of antimicrobial order tools for restricted antimicrobials vi. Streamlining the antibiotic usage vii. Antimicrobial selection and dose optimization of the antimicrobial viii. Initiation of intravenous (IV) to oral (PO) switch program.	i. Surveillance and feedback mechanism on specific antimicrobial consumption. (Core Strategy) ii. Implementation of prospective audit and feedback according to local needs. (Core Strategy) iii. Establishment of formulary restriction and preauthorization/ approval system. (Core Strategy) iv. Establishment of antimicrobial order tools for restricted antimicrobials v. Streamlining the antibiotic usage vi. Antimicrobial selection and dose optimization of the antimicrobial vii. Initiation of intravenous (IV) to oral (PO) switch program.

Primary care*** with Family Medicine Specialist (FMS)
i. Surveillance and feedback mechanism on specific antimicrobial consumption. (Core Strategy) ii. Implementation of process audit (clinical audit, structure audit, and Point Prevalence Survey) and feedback according to local needs. (Core Strategy) iii. Establishment of formulary restriction and preauthorization/ approval system. (Core Strategy) ***for primary care without FMS, AMS team from main clinic shall conduct a minimal AMS activity such as clinical audit

References :

1. Surat Pekeliling Ketua Pengarah Kesihatan Bil 3 / Tahun 2018, Pelaksanaan Program Antimicrobial Stewardship (AMS) di Hospital dan Klinik Kesihatan
2. Protocol on Antimicrobial Stewardship Program in Healthcare Facilities, MOH latest edition

Appendix 7 : Intravenous (IV) To Oral (PO) Antibiotics Conversion

Early intravenous-to-oral conversion (IVOC) as a key stewardship measure. This section describes the practice of converting intravenous antimicrobials therapy to an effective alternative oral formulation. Several clinical trials have been conducted that demonstrate the efficacy and safety of IV to PO antimicrobials conversion, and several studies have also addressed the economic impact of this conversion.

Cost savings are achieved through lowering direct acquisition costs, eliminating the need for ancillary supplies, reducing pharmacy and nursing time, and shortening the length of hospital stay. IV to oral antimicrobials conversion also benefits the patient by eliminating adverse events associated with IV therapy, increasing patient comfort and mobility and increasing the possibility of earlier discharge.
The optimal time to consider switching a patient to oral therapy is after 48 to 96 hours of intravenous therapy. This period of time allows the clinician to evaluate the patient's microbiology results and assess their response to treatment. A large number of clinical trials support the early switching to oral antibiotics after this period of time with equal treatment efficacy and no adverse effects on patient outcome.
All intravenous antibiotics should be reviewed after 48 hours and daily thereafter. This should be documented clearly in the medical notes.

Before switch to oral antimicrobial, a patient must meet a number of criteria:

A. Display signs of clinical improvement AND
B. Able to tolerate oral therapy AND
C. Not have a condition in which higher concentrations of antibiotic are required in the tissue or a prolonged course of IV therapy is essential

Criteria used to determine Patients for IV to PO Therapy Conversion:

A. Display signs of clinical improvement

- Afebrile (temp >36oC and <38oC for past 48 hours)
- CRP trending down
- Stable immune response (WCC > 4 and <12 x 109 cells/L or trending towards normal range) It is important to examine the patient's medication therapy for other medications that can cause an increase or sustained high WBC count such as steroids.
- No unexplained tachycardia
- No unexplained hypotension
- No tachypnoea

B. Able to tolerate oral therapy

- Patient is not nil by mouth
- Patient is tolerating oral food or enteral feeding. For *enteral feeding please consult pharmacy for advice on suitable formulation and administration method*.
- Oral absorption is not compromised (e.g. diarrhoea, vomiting, malabsorptive disorder, partial or total removal of the stomach, short bowel syndrome, unconscious, swallowing disorder)

C. Not have a condition in which higher concentrations of antibiotic are required in the tissue or a prolonged course of IV therapy is essential

- **Prolonged parenteral therapy is required for the following indications:**
  i. endocarditis
  ii. central nervous system infections (e.g.; meningitis, brain abscess, etc.)
  iii. Staphylococcus aureus bacteremia
  iv. osteomyelitis
  v. Septic arthritis
  vi. Infected implant or prostheses
  vii. Necrotising soft tissue infection
  viii. melioidosis (at least 10 to 14 days of IV therapy)
  ix. Deep-seated infection e.g. abscesses/empyema
  x. Complicated orbital cellulitis (abscess or other complication)

- **There are number of conditions in which a switch to oral therapy should be considered including:**
  a. Pneumonia
  b. Skin and soft tissue infections
  c. Urinary tract infections
  d. Uncomplicated Gram negative bacteremia
  e. Intra-abdominal infection without deep seated collections

Example of antimicrobials that can be included in IV to PO therapy conversion and bioavailability of selected antimicrobials available in both IV and PO formulations

Common oral antimicrobial options

Current parenteral regimen		Oral Regimen (Adult dose)	Oral Bioavailability
Ampicillin/Sulbactam 1.5gm IV q6h	>	Amoxicillin/Clavulanate 625mg PO q12H	Amoxicillin: 80% Clavulanate: 30-98%
Ampicillin/Sulbactam 3gm IV q6H	>	Amoxicillin/Clavulanate 625mg PO Q8H	Amoxicillin: 80% Clavulanate: 30-98%
Azithromycin 500mg IV once daily	≈	Azithromycin 500mg PO once daily	Azithromycin: 34-52%
Cefazolin 1g IV q8H	>	Cephalexin 500mg PO Q6H	Cephalexin: 90%
Cefepime 2g IV q8-12H	>	Amoxicillin/Clavulanate 625mg PO Q8H Pseudomonas: Seek advice from Infectious disease specialist or Clinical microbiology	Amoxicillin: 80% Clavulanate: 30-98%
Cefazolin 2g IV q8H	>	Cephalexin 1000mg PO Q6H	Cephalexin: 90%
Ceftazidime 1-2g IV q8H	>	Amoxicillin/Clavulanate 625mg PO Q8H Pseudomonas: Seek advice from Infectious disease specialist or Clinical microbiology	Amoxicillin: 80% Clavulanate: 30-98%
Ceftriaxone 1-2g IV once daily	>	Amoxicillin/Clavulanate 625mg PO Q8H 0r Cefuroxime axetil 500mg PO Q12H	Amoxicillin: 80% Clavulanate: 30-98% Cefuroxime axetil: 37-52%
Cefuroxime 750mg-1.5g IV q8H	≥	Cefuroxime axetil 500mg PO Q12H	Cefuroxime axetil: 37-52%
Ciprofloxacin 400mg IV q12H	≥	Ciprofloxacin 500mg PO Q12H	Ciprofloxacin: 50-85%
Ciprofloxacin 400mg IV q8H	≥	Ciprofloxacin 750mg PO Q12H	Ciprofloxacin: 50-85%
Clindamycin 300mg IV q6-8H	≥	Clindamycin 150mg PO Q6-8H	Clindamycin: ~90%
Clindamycin 300mg IV q6-8H	≥	Clindamycin 300mg PO Q6-8H	Clindamycin: ~90%
Cloxacillin 1-2g IV q6H	≥	Cloxacillin 500mg-1g PO Q 6H	Cloxacillin: ~50% (1H before meal)
Erythromycin lactobionate 500-1000mg IV q6H	≈	Erythromycin base: 500-1000mg PO Q6H Erythromycin Ethylsuccinate: 800mg PO Q12H	Erythromycin: 18-45% (ethylsuccinate maybe better absorbed with food)
Fluconazole 200mg-400mg IV once daily	≈	Fluconazole 200mg-400mg PO once daily	Fluconazole: >90%
Levofloxacin 500mg-750mg IV once daily	≈	Levofloxacin 500mg-750mg PO once daily	Levofloxacin: ~99%
Linezolid 600mg IV q12H	≈	Linezolid 600mg PO Q12H	Linezolid: ~100%
Metronidazole 500mg IV q8-12H	≈	Metronidazole 400mg-500mg PO Q8-12H	Metronidazole: 100%
Moxifloxacin 400mg IV once daily	≈	Moxifloxacin 400mg PO once daily	Moxifoxacin: ~90%
Penicillin G 1-4 mega units IV Q4-6H	>	Penicillin VK 500mg Q6H	Penicillin VK: 60-73%
Piperacillin/Tazobactam 4.5g IV Q6-8H	>	Amoxicillin/Clavulanate 625mg PO Q8H Pseudomonas: Seek advice from Infectious disease specialist or Clinical microbiology	Amoxicillin: 80% Clavulanate: 30-98%
Trimethoprin/sulfamethoxazole IV 10mg/kg/day-20mg/kg/day (TMP)	≈	Trimethoprin/sulfamethoxazole PO 10mg/kg/day-20mg/kg/day (TMP)	Trimethoprin/sulfamethoxazole: 90-100%

≈ =Sequential therapy with direct conversion (same medication with the same IV to oral dose)
≥ =Sequential therapy without direct conversion (same medication but different IV to oral dose)
> =Switch or step down therapy (same or different class of medication with same/similar spectrum of activity)

Reference :

1. Protocol on Antimicrobial Stewardship Program in Healthcare Facilities, MOH latest edition

Appendix 8 : Antibiotics Allergy Evaluation Protocol

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Key points

Background

- Adverse drug reactions (ADR) are mainly grouped into two broad categories namely type A reactions and type B reactions. Type A reactions are predictable reactions which are related to the pharmacological actions of the drug while type B reactions are unpredictable reactions which are usually not related to the pharmacological actions of the drug.
- Type B ADR corresponds to drug hypersensitivity reactions which can be immune-mediated (allergic) or non-immune mediated (non-allergic)
- The estimated true incidence of penicillin hypersensitivity worldwide is low
- Cross-reactivity between truly penicillin allergic patients with third and fourth generation cephalosporins and/or carbapenem is very low (Figure 1 and Table 1)
- Careful evaluation of antibiotic allergy and prior tolerance history is essential to providing optimal treatment
- Alterations in antibiotic prescribing due to reported penicillins allergy has been shown to result in poorer clinical outcomes, increased incidence of serious antibiotic-resistant infections, prolonged hospitalisation, and increased healthcare burden
- Careful drug allergy evaluation with or without drug testing may lead to more judicious use of narrow spectrum beta-lactam (BL) antibiotics when clinically indicated. This will improve patient safety.

Evaluation of Penicillins Allergy

- Obtain a detailed history of the drug allergic reaction
- Send bloods for in vitro tests; refer for skin and provocation testing to centers specialized in drug allergy testing for high risk patients

Algorithm for patients suspected of Penicillins and Cephalosporins Allergy
See Figure 3 and 4

Follow up Documentation

- If provocation is not tolerated, document the BL(s) intolerance in the patient record
- If provocation is tolerated, delabel and/or document BL(s) tolerance in the patient records
- An allergy card/passport/medic alert should be issued for future avoidance of the allergic BL(s)

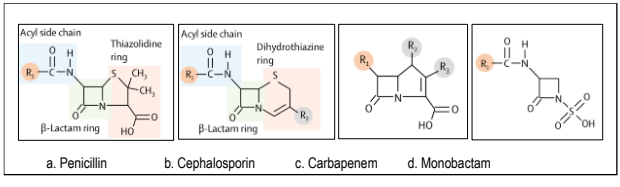

Figure 1: β-lactams antibiotics structure (adapted from Blumenthal KG et.al, 2019)

Table 1. β-lactam cross reactivity in penicillins allergic patients.

Drug Class and Available Formulary agents	Estimated Cross-Reactivity‡,‡
1st Generation Cephalosporins (e.g. cefazolin, cephalexin)	1.9 – 7.9%
2nd Generation Cephalosporins (e.g. cefaclor, cefuroxime, cefoxitin)	1.9%
3rd Generation Cephalosporins (e.g. ceftriaxone, cefotaxime, ceftazidime)	0.7%
4th/5th Generation Cephalosporins (e.g. cefepime, ceftaroline)	Not available
Carbapenem (e.g. imipenem, meropenem, ertapenem)	≤ 1%
Monobactam (Aztreonam)	Negligible (except with ceftazidime which shares identical side chains)

‡Pichichero ME and Zagursky R, 2104; ‡Romano et al, 2016

EVALUATION

Patient history

Obtain a detailed assessment of the allergic reaction. Information collected should include the following:

1. Source of the allergy history (i.e. from patient, family member, healthcare professional, etc)
2. The specific antibiotic that was prescribed and type of infection treated
3. Antibiotic dose and route of administration
4. Signs and symptoms experienced together with the time of onset (Table 2) of the reaction in relationship to the initiation of the antibiotic.
5. Medical evaluation conducted, if any.
6. Treatment given for the reaction and response.
7. The medication(s) taken since the occurrence of the reactions (before and/or after) and possibly provide the brand & generic names.
8. Recurrent signs and symptoms occurring with subsequent drug exposure.
9. Concurrent medications at the time that the reaction occurred and, if any of these were newly started.
10. Prior tolerance of BL antibiotics and other antimicrobials.

Table 2. Clinical history of suspected allergy (basic prerequisite of a full history – temporal association and nature of symptoms)

Likely type I hypersensitivity reaction to penicillin	Likely type IV hypersensitivity reaction to penicillin	Unlikely Hypersensitivity reaction to penicillin	Indeterminate
One or more of the following symptoms ≤ 1 h of administration of first dose: • Cutaneous symptoms: urticaria, pruritus, flushing • Angioedema • Rhinitis or rhinoconjuctivitis • Bronchospasm (chest tightness, SOB, wheezing, cough, cough, desaturation, cyanosis) • Haemodynamic instability (presyncope, syncope, loss of consciousness,	One or more of the following symptoms > 1 h after exposure to penicillin (regardless of the number of doses): • Delayed onset cutaneous manifestations such as maculopapular eruptions, urticaria/angioedema,nonspecific rash, pruritus, flushing • Other systemic responses eg. FDE, DRESS, SJS/TEN, AGEP • Other rare systemic hypersensitivity reactions: haemolysis, acute interstitial nephritis, vasculitis, etc.	• No temporal association between symptoms and exposure • Subsequent exposure to the same drug without a reaction • Symptoms not suggestive of an immune-mediated reaction (eg. headache, blurred vision, isolated GI symptoms, etc)	• The temporal association between drug administration and onset of symptoms is vague/unknown • Vague history with no details (eg. childhood label of penicillin allergy) • Patient is uncertain whether onset of symptoms happened after the first dose or after more than one dose • Adverse reaction after administration of > 1 medications simultaneously

Likely type I hypersensitivity reaction to penicillin	Likely type IV hypersensitivity reaction to penicillin	Unlikely Hypersensitivity reaction to penicillin	Indeterminate
arrythmia, seizures, cardiac arrest)			

AGEP, acute generalized exanthematous pustulosis; DRESS, drug rash with eosinophilia and systemic symptoms syndrome; FDE, fixed drug eruptions; GI, gastrointestinal; SJS, Stevens Johnson syndrome; SOB, shortness of breath; TEN, toxic epidermal necrolysis

Referral for skin testing

Consider referring a ***patient labeled with penicillin allergy*** for skin testing if any one of the following criteria are met:

- The patient requires frequent antibiotics use.
- The patient is in an immunosuppressed state who may require narrow-spectrum antibiotics treatment.
- The patient is planned for an elective surgery.
- The patient was reported/documented with multiple non-chemically related antibiotics allergy (underlying disease such as chronic spontaneous urticaria, thyroid disease, autoimmune diseases and/or mastocytosis should be sought in such cases).
- The patient has suffered anaphylaxis when a BL agent was administered concurrently with multiple other agents.

***There is NO MERIT in drug skin testing referrals for SCREENING purposes**

Box A: *The current reference standard ('gold standard') test to confirm drug tolerance oceeding provocation test in patients with high risk histories*.

Patients with histories of severe non-IgE-mediated reactions such as Stevens-Johnson syndrome/toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS) or organ-specific nonimmediate non-IgE-mediated reactions (e.g. interstitial nephritis, hemolytic anemia etc) are ABSOLUTELY CONTRAINDICATED to undergo skin testing (skin prick and/or intradermal testing) or provocation test. Therefore, they should avoid penicillins indefinitely.

In vitro tests

- Bloods should be sent for mast cell tryptase level during (up to 6 hours) a suspected acute anaphylaxis
- This should be repeated 24 hours later for baseline measurements
- In vitro quantification may be sent for specific IgE to penicilloyl G and penicilloyl V to the Allergy lab, Institute for Medical Research (IMR)

Skin testing

- Skin testing are performed for high risk patients at centers specialised in drug allergy evaluation and testing.
- It should be performed ONLY by medical practitioners trained in drug allergy testing
- Stratification of high risk and low risk patients are detailed in Table 3.

Provocation/ challenge test

- Provocation/challenge test for high risk patients is performed at centers specialised in drug allergy evaluation and testing.
- It should be performed ONLY by medical practitioners trained in drug allergy testing (please refer to the detailed protocol for further details).
- Stratification of high risk and low risk patients are detailed in table 3.
- Low risk patients may undergo a test dose challenge procedure performed by any medical specialists with knowledge of the procedure (please refer to the detailed protocol for further details).
- Test dose procedure is a short, graded challenge for those with a low calculated risk of being allergic to the BL being tested (e.g. low risk history OR BL being tested have a low risk of cross reactivity [i.e. dissimilar side chain – Figure 2]).

Table 3. Risk stratification into low and high risks based on structured clinical history and associated comorbidities

Low risk	High risk
• GIT symptoms only • 'Benign' rash only (urticaria, exanthematous rash, angioedema) > 1 hour after the first dose or during a course of therapy • Poorly described symptoms but not deemed serious (no systemic involvement, no hospitalization* ± history of mild/moderate well-controlled asthma ± mild/moderate well-controlled COPD ± stable cardiac comorbidities • Presyncope only (after oral dose) • A BL with identical/similar side chains has been represcribed and tolerated since the index episode	• Upper and/or lower airway symptoms • 'Benign' rash only (urticaria, exanthematous rash, angioedema) ≤ 1 hour after the first dose • Poorly described symptoms but not deemed serious (no systemic involvement, no hospitalization* but there is history of severe or brittle or unstable asthma (mild, moderate or severe) ± unstable COPD ± unstable cardiac comorbidities) • Anaphylaxis (defined as any of the following): ➢ Upper and/or lower airway symptoms and rash ➢ Upper and/or lower airway symptoms and syncope or presyncope ± rash ➢ Collapse (severe hypotension) ➢ Upper and/or lower airway symptoms and GIT symptoms ➢ Rash ± GIT symptoms ± upper and/or lower airway symptoms ± collapse or presyncope or syncope

COPD, chronic obstructive pulmonary disease; GIT, gastrointestinal tract

*Treated and managed at the emergency department

BL allergy evaluation algorithm

Please see Figures 3 and 4 for details

Follow up Documentation

- If provocation is not tolerated, document the BL(s) intolerance in the patient records
- If provocation is tolerated, delabel and/or document the BL(s) tolerance in the patient records
- An allergy card/passport/medic alert should be issued for future avoidance of the allergic BL(s)

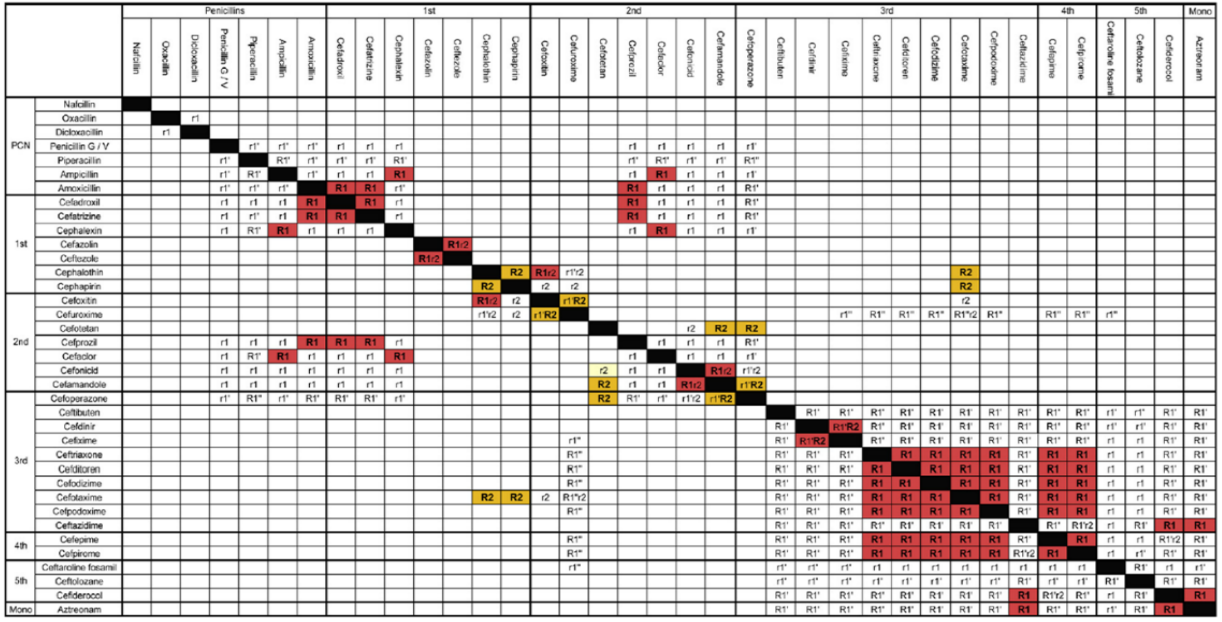

Figure 2. Comparison of R1 & R2 structural similarities between B-lactams drugs. Drugs that have identical R1 or R2 are listed as R1 (red cell) or R2 (gold cell). If ONLY the ring or branch chain moiety of the R1 structure is identical, it is listed as R1' or R'', respectively. Drugs that have similar R1 or R2 structures are listed as r1 or r2. If ONLY the ring or branch chain moiety of R1 structure is similar, it is listed as r1' or r1'', respectively. Blank cells imply NO R1 or R2 structural similarities. (Zagursky&Pichichero, 2018)

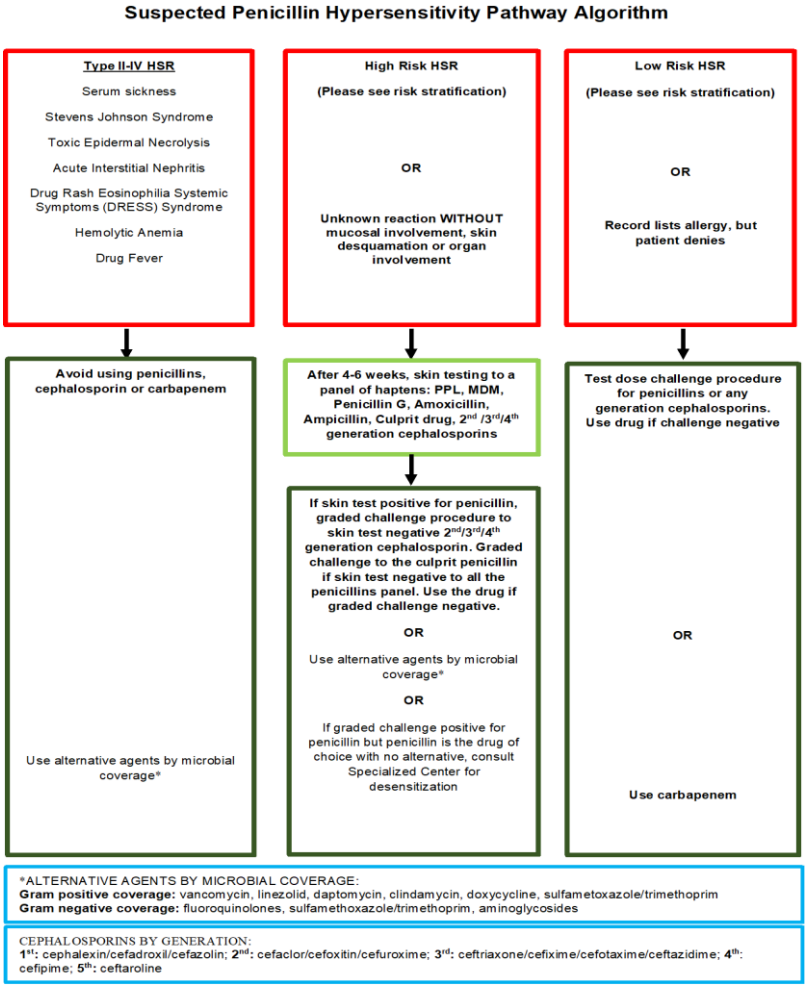

Figure 3. Penicillins Allergy Evaluation Algorithm

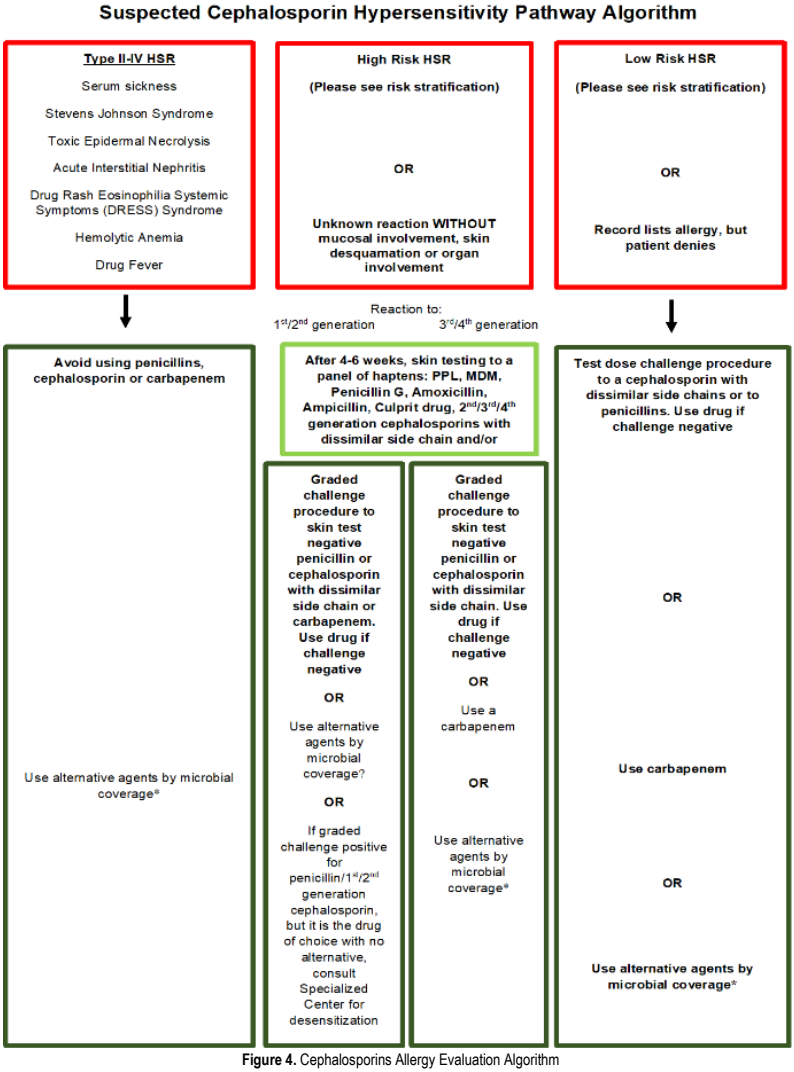

Figure 4. Cephalosporins Allergy Evaluation Algorithm

Appendix 9 : Outpatient Parenteral Antibiotic Therapy (OPAT)

Prepared by Afra Nahdia Marizan Nor, Pharmacist, Hospital Sungai Buloh
Reviewed by Dr Benedict Sim Lim Heng, Infectious Disease Consultant, Hospital Sungai Buloh

Introduction

Outpatient Parenteral Antimicrobial Therapy (OPAT) as defined by the IDSA is 'the provision of parenteral antimicrobial therapy in at least two doses on different days without intervening hospitalisation'.

OPAT is useful for patients who require parenteral therapy for moderate to severe infections but are otherwise well enough to initiate or continue therapy without an overnight stay in hospital. It involves a comprehensive and systematized service in providing specific medical services, nursing expertise and an antibiotic formulary.

Over the 40 years that OPAT has been used worldwide, a wealth of evidence has accumulated supporting its clinical justification; safety and effectiveness, and cost-effectiveness. The benefits of OPAT include admission avoidance and reduced length of stay in hospital, with resulting increases in inpatient capacity, significant cost savings compared with inpatient care, reduction in risk of healthcare-associated infection and improved patient choice and satisfaction.

OPAT Team and service structure

The OPAT multidisciplinary team should include

1. A physician specialist (e.g. An infectious diseases physician, internal medicine specialist or a surgeon with an infection interest)
2. A nurse with expertise in parenteral drug administration and intravascular access device
3. A pharmacist knowledgeable in OPAT

A management plan should be agreed between the OPAT team and the referring team for each patient and this should be documented. There should also be a system in place for rapid communication between team members and patient.

Patient selection

Initiation of OPAT requires that a physician determine that such therapy is needed to treat a defined infection, that hospitalization is not needed to control the infection, and that alternate routes of drug delivery are not feasible or appropriate. The inclusion and exclusion criteria should incorporate specific infection severity criteria where appropriate and physical, social and logistic criteria. Initial assessment for OPAT should be performed by a competent member of the OPAT team. Patients and carers should be fully informed about the nature of OPAT and should be given the opportunity to decline or accept this mode of therapy.

Antimicrobial management and drug delivery

The infection treatment plan should be agreed between the OPAT team and the referring clinician before commencement of OPAT. The OPAT team may suggest a suitable intravascular access for each patient. The selection of antimicrobial agent for OPAT will be depend on various aspect which has to be looked into carefully. They are as follows:

- Type of infection
- Availability of antimicrobial agent
- Method of administration
    - Slow Infusion
    - Elastomeric Infuser

The choice of antimicrobial must comply with the local antimicrobial stewardship in ensuring judicious use of antibiotics in the management of an infection. It is also strongly recommended that the first dose a new antimicrobial should be administered in a supervised setting to minimize the risk associated with the development of a serious drug allergy including anaphylaxis.

The use of elastomeric infuser

The development of elastomeric infuser is most beneficial for OPAT. It improves the method of delivery, hence allowing flexibility of care for patients who requires multiple frequency antimicrobial agent. With the use of elastomeric infuser, antimicrobial agents will be administered continuously over a specified time period, usually over 24hours. It should be highlighted that the pharmacokinetics/pharmacodynamics (PKPD) of an antimicrobial agent changes when using continuous infusion. Therefore, the use of continuous infusion in OPAT requires detailed consideration:

- The antimicrobial agent
- Type/model of infuser
- Antimicrobial stability / Elastomeric shelf-life
- Suitability

Monitoring of the patient during OPAT

OPAT is inherently associated with increased risk compared with treating in the inpatient setting, since patients are under less-close clinical observation. Overall, at least 25% of patients receiving OPAT will develop adverse reactions, which range from mild antibiotic-associated

diarrhoea to life-threatening line infections. Therefore, it is important that physicians and nurses managing OPAT patients are familiar with potential complications so that these can be detected early. It has been recommended that a regular multidisciplinary meeting/virtual ward round to discuss progress (including safety monitoring and outcome) of patients receiving OPAT. Patients should be regularly reviewed by the OPAT nurse and physician. The frequency should be agreed by the team members. Patients should have blood tests performed which includes:

- full blood count
- renal and liver function
- C-reactive protein (CRP)
- therapeutic drug monitoring (if required)

Other tests may be required for specific indications or therapies. The OPAT team is responsible for monitoring clinical response to antimicrobial management and blood investigations, and for reviewing the treatment plan. A mechanism should be in place for urgent discussion and review of emergent clinical problems during OPAT. There should also be a clear pathway for 24-hour immediate access to advice/review/admission for OPAT.

Outcome monitoring and clinical governance

It is critical that OPAT services have a robust clinical governance structure and are subjected to the same rigour of inspection and risk assessment. Standard outcome criteria should be used on completion of intravenous therapy. In monitoring treatment outcome. it is recommended, as a minimum, that clinical outcome of the OPAT episode and the response of the infection to the antimicrobial therapy is recorded at the end of intravenous therapy. OPAT outcome should also take into account adverse events, need for change in antimicrobial therapy and readmission.

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“The Secretariat would like to thank all those who have contributed directly or indirectly for this guideline”