

INFECTIOUS DISEASES

Cellulitis
Neonatal sepsis (GBS)
Pneumonia
URTI - pharynx, tonsil
Infective endo

Meningitis
Meningococcal
disease

Urethritis /
cervicitis
Disseminated
disease

Hosp. acquired
line infections,
VAP

UTI
Cholangitis
diverticulitis

GRAM POSITIVE										GRAM NEGATIVE									
MSSA	MSSA	Strep ABCG	Pneumococcus	Enterococcus faecalis	Enterococcus faecium	VRE	Listeria	Respiratory	C.DIFF	Neisseria meningitidis	Haemophilus	Moraxella	E.coli	Kleb	Proteus	Pseud	ESCAPPs	Chlamydia	Legionella
Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav	Amox/clav
Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin	Clindamycin
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Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline	Doxycycline
Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin	Azithromycin
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Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem	Meropenem
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Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin	Daptomycin

*Dependent on sensitivities

BACTERIA

Atypical pneumonia (Mycoplasma)
Atypical + chlamydia
A/E = prolonged QT
+ C. difficile

Avoid

- Co, Fe + antacid
- child + pregnant
- (↓ bone + tooth dev)
- YELLOW STAIN

MACROLIDE

- Azithro - (gram -)
- Erythro -
- Clarithro -

TETRACYCLIN

- doxy

AMINO GLYCOSIDES

- Gentamicin, Neomycin, Amikacin, Tobramycin, Streptomycin
- OTO + NEPHROTOXIC VESTIBULAR

CHLORAMPHENICOL

(block transpeptidase) at 50S

A/E: BMF - aplastic anaemia

PBP

• Meropenem B-Lactams

PENICILLIN

• Cephalosporins

1st, 2nd, 3rd, 4th, 5th

- fa - pen - am - ceft - ceftaz - ceftio - ceftaz - ceftio

• Co-amoxiclav / Tazocin

QUINOLONE = CIPROFLOXACIN

- DNA GYRASE (Topoisomerase 2 inhibitor)
- GI distress / Achilles tendon rupture
- Avoid: MMR + antacid + EPILEPSY (↓ threshold)

GLYCOPETIDE = VANCOMYCIN

- Inhibit X-link cell wall
- Gram +ve ONLY

MYCOBACTERIA

- TB - RIPE (rifampin, isoniazid, pyrazinamide, ethambutol)
- Leprosy - Dapsone (folic acid synthase inhibitor)
- Clofazimine (DNA binder)
- Rifampin
- Ulcerans - rifampin
- Moxifloxacin

VIRUS

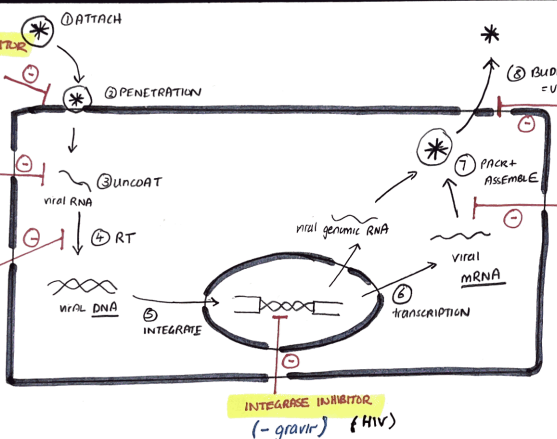
FUSION INHIBITORS

(enfuvirtide - HIV)

AMANTADINE

(rimantadine - influenza)

- 1 NRTI or NNRTI (Hep B)
- 2 NRTI (HIV)
- 3 NRTI (Hep C)
- 3 Viral DNA pol inhibitor (Hep C)
- CMV (ciclovir)



INTEGRASE INHIBITOR (-gravir) (HIV)

Antibiotics with excellent oral bioavailability

- Azithromycin
- Clindamycin
- Fluoroquinolones (ciprofloxacin, moxifloxacin)
- Trimethoprim-sulfamethoxazole (Bactrim)
- Linezolid
- Metronidazole
- Azole antifungals (fluconazole, posaconazole, voriconazole)
- Anti-tuberculous drugs (isoniazid, rifampicin)

Clinical Pearls:

- Avoid alcohol + metronidazole → when used to treat anaerobes
- Abx allergies (20-30%) have intolerance
- Nitrofurantoin (not used in 3rd trimester)
- avoid TETRACYCLINE in children - permanent teeth staining and AKI

Adverse reactions:

- Anaphylaxis
- SJS + epidermal necrolysis
- DRESS syndrome (drug reaction with eosinophilia and systemic symptoms)
- AIN
- Is it an allergy or side-effect? - e.g. nausea, vomit, diarrhoea?
- Long QTc interval = clarithromycin, quinolones, fluconazole, voriconazole

FUNGAL

DISSEMINATED SYSTEMIC INFECTION → RIGOR, FEVER, CHILL, AKI, Hep K (LACUTE TOXICITY)

"Tinea Pedis" → RASH, ITCH, BUBLES, CRACKS, FISSURES

ATHLETE FOOT → JOCK ITCH

• GI, rash, itch, headache (- FINE)

• RINGWORM, NAIL (dermatophytes) / INFECTION

• LICHEN PLANUS

• ST syndrome

• Hepatitis

• AVOID use w/ amphotericin (6 effect)

• ECHINOLANDIN (CANDIDA)

• N/D

• Rash

CELL WALL 1,3-β-glucan

ERGOSTEROL-RICH FUNGAL MEMBRANE

ERGOSTEROL

ERGOSTEROL

ERGOSTEROL

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ANAPHYLAXIS

Practice points:

- 1) Document allergy list on myhealth record
- 2) **Stop offending drug** immediately
- 3) **Classic S+S** = urticaria, angioedema, SOB
- 4) **Educate + prepare anaphylaxis care plan** + prescribe epiPen (educate on administration)
- 5) **Hx questions** = timeline of reaction, trigger (food, drug, chemical)

Allergic reactions can be **amplified** by:

- 1) ++ quantity of food
- 2) Exercise
- 3) Alcohol
- 4) Sleep deprivation
- 5) Cooking time (roasting vs reheating)
- 6) Spice, chill and capsicum spices
- 7) NSAIDs – nurofen, aspirin, Mobic within 24 hrs
- 8) Falling ill (increased immune response)
- 9) Pre-menstrual

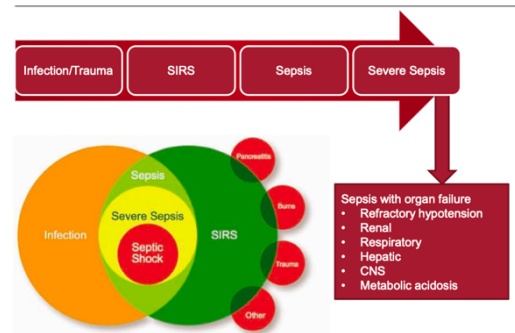
	#1: Myelodysplastic syndrome + red itchy rash	#2: recurrent allergic reactions requiring adrenaline	#3 latex allergy BUT needs IDC in general practice	#4: radiocontrast media reactions (RCM)	#4.5: Rapid onset tongue swelling after switching ARB w/ CaB
Px	- Hx of URTi 2 wks prior - Postural HypoTN → Rx w/ IVF + antihistamine	- Unresponsive to antihistamine (10mg loratadine) - weaning dosage regimen of oral CS	Recurrent exposure to latex in childhood	Hx of iodine rash and urticaria after RCM	- Normal C1 inhibitor level - IM 0.5mg unhelpful
Dx	Post viral urticaria (self-limiting)	Post viral urticaria and angioedema	: latex allergy	RCM allergy	CCB reaction
Rx:	Check C1 inhibitor level and function required	Antihistamine + Add nizatidine 3000mg bd and montelukast 10mg daily	Latex free glove and silicone catheter	- Oral 50mg pred given 13h and 1h before contrast media +/- oral non-sedating antihistamines	- Stop CCB - Alert ICU - I+V (if needed)

	#5 Drug allergy	#6: mushroom allergy	#7: Rash and pain periorally	#8: Vomiting and swollen throat w/ underlying asthma
Px	Newborn or child 1st time given ABx (or could be med chart error)	- New restaurant and takes ibuprofen before starting meal for headache severe streaky red rash	- Called hairdresser to use new herbal product - OR black henna tattoo in Bali	- Recent ingestion of thai food ++ WoB (wheeze + SOB, dysphagia and drooling) - HypoTN, tachycardic, warm
Dx	Drug-induced anaphylaxis	Shiitake mushroom flagellate dermatitis	PPD contact dermatitis (paraphenylenediamine)	IgE mediated Allergic anaphylaxis to peanuts
Rx:	- Call 000 - Stop offending agent 200mg HC IV and ranitidine - Medical brace alert - Entry into myhealth record	Cook shiitake mushrooms well 	Stop herbal product 	- IM 1mg adrenaline - neb adrenaline 5mg 100mg HC 50mg ranitidine 5mg neb SAB - ImmunoCAP peanut rAra h2 = 43.5 kU/L

	#9: Vomiting and later diarrhoea	#10 gardener w/ generalise urticaria and pruritis + iWoB	#11 Intractable vomiting or food allergy
Px	- HypoTN, tachycardic, COLD NIL allergen specific-IgE	- Coughing - HypoTN - Nil sig. Hx - Known tick bite 3/52 ago (no local reaction)	- Persistent N/V (>3x episodes) improved w/ hot shower - Ate outside previous night - Nil systemic signs or focal signs of infection - Nil PR mucus or bleed - Heavy marijuana Hx
Dx	FPIES (food protein induced enterocolitis syndrome)	Mammalian meat allergy after tick bite (specific IgE directed against tick salivary protein)	Cannabinoid hyperemesis syndrome
Rx:	2x IM 500mcg adrenaline - ImmunoCAP NEGATIVE for all foods - T-cell mediated (NOT IgE mediated)	2x IM 500mcg adrenaline - IV 200mg HC - PO loratadine 10mg	- Hot shower → stimulated TRP1 to induce desensitization - Counsel on marijuana usage

Sepsis, Antibiotic Usage & Resistance

	(at least 2 of these to meet criteria)	Pathophysiology:
SIRS	- Body temp >38°C or <36°C, - HR > 90/min - RR > 20/min or PaCO₂<32mmHg - WCC >12.0 x 10⁹/L or <4.0 x 10⁹/L	- Raised pro-inflammatory mediators (IL-1.6 and TNF-α from macrophages activates neutrophils, platelets and endothelial cells) → DIC + increased vascular permeability - Raised acute phase proteins (buy time) - HypoTN, hypoperfusion, hypoxia
Sepsis	Life-threatening organ dysfunction caused by a dysregulated host response to infection	
Severe Sepsis	Sepsis + evidence of organ dysfunction (e.g. hypoxia, oliguria, AKI, Coag dysfn, hypoTN, raised lactate > 2mM, thrombocytopenia)	
Septic Shock	- Sepsis + arterial BP drop causing organ hypo-perfusion - Systolic BP < 90 (DESPITE adequate fluid resus) - Raised lactate > 4mM	
Septicaemia	Bacteria enters bloodstream triggering sepsis (e.g. meningococemia)	
Bacteraemia	Bacteria in the bloodstream. May or may not cause SIRS or sepsis.	
Risk factors	- Extremes of age (<1 yo or > 75 yo) - Chronic conditions (e.g. COPD and diabetes) - Chemo, immunosuppressants and steroids - Recent surgery, trauma or burns - Pregnancy or peripartum - Indwelling devices (e.g. catheters and central lines)	



qSOFA score

IF SCORE > 1 THEN INVESTIGATE FOR PRESENCE OF ORGAN DYSFUNCTION AND INCREASE FREQUENCY OF MONITORING

Sequential Organ Failure Assessment → measure mortality in ICU

- Quick **SOFA** (≥ 2 of the following = **HIGH** Mortality)
- GCS < 15, RR ≥ 22, sBP < 100
- Febrile
- Reduced UO- cloudy urine

Types of shock + Mx

Shock type	Hypovolaemic	Cardiogenic	Distributive			Obstructive
Cause	Haemorrhagic (big 5 → chest, abdo, external, long bone, pelvis) Electrolyte imbalance (V + D, Dehydration) Non-haemorrhagic (burn)	↓ contractility (MI, CHF, valvular) ↓ HR (Arrhythmia) ↓ preload ↑ afterload Aortic dissection - Meds (BB, CaB)	<i>paraplegia</i>, <i>acute SCI</i> <i>spinal anaesthesia</i> SNS inactive – no signals sent to brain	- Gram +ve/-ve - Fungi - Virus - Protozoa - Causes pain (if attacks nerves)	- Injection (penicillin) - Anaesthetics - Stings - shellfish	- Tension pneumothorax - PE - Pericardial effusion/tamponade - Air embolism
CR	Long + Cool/dry		Short + Warm/dry (due to vasodilation)			Long + Cool/dry
HR	↑↑↑	↓↓↓	↓↓↓	↑↑↑	↑↑↑	↑↑↑
BP	↓↓↓	↓↓↓	↓↓↓	↓↓↓	↓↓↓	↓↓↓
Ix	- FBC (blood loss) - EUC - CXR - Pelvic XR (pelvic #) - eFAST (abdo)	Examination - murmurs ECG signs: - AMI signs, LVH, SVT CXR = Acute pulmonary oedema ECHO – determine need for fluids vs inotropes	- Sphincter dysfn - Paraesthesia - Weakness Signs opposite to typical shock	3 tests: - Blood lactate (VBG) 2x sets Blood cultures - Urine output 3 treatments: - O₂ (maintain 94-98%) - Empirical broad spectrum Abx - IVF	Rash (urticaria) Wheeze Gut pain, Oedema, Angioedema – IgE released → mast cell degranulate → histamine → vasodilation -	Tension Pneumothorax - Distended neck veins - Dev. trachea Beck's Δ (tamponade) - HypoTN - Muffled heart sounds - Distended veins
Rx/Mx	Acute Mx: IV bolus NS (500-1000mL) – lower if elderly Surgical Mx: - Surgical/radiological / endoscopic surgery → trauma, blood loss, intra-abdominal issue - Embolise bleeding vessel - Endoscopic clipping (variceal bleeds)	Inotropes (e.g. dobutamine) Vasopressor (adrenaline if hypoTN is dominant feature) * Fluid challenge rarely useful To improve diastolic filling of coronary arteries and reduce afterload Mild hypothermia can improve neuro outcome of STEMI - Angiography - PCI - Thrombolysis *intra-aortic balloon - TOO HIGH = block L SCA - TOO LOW = block renal flow (pre-renal)	Check for bleeding 1st (? spinal trauma) e.g. may be bleeding out but is on a BB ↓ (1) Rule OUT hypovolaemic shock ↓ (2) Rule OUT drugs and poisons (e.g. opioid, nitrate, BB)	Hemodynamic resus (SEPSIS 6) Treat within 1 hour IV fluids crystalloids 20mL/kg - NS = elevated Cl - Hartman = elevated lactate Vasopressors = Rx refractory shock if NA fails or if profound hypoTN 1st line: NORAD (potent a1 vasoconstrictor w/ mod. B1 induced HR, contractility) adrenaline (arrhythmias or splanchic ischaemia) vasopressin to taper adrenaline Target MAP >65 + normalise lactate + CVP monitoring Inotropes (dobutamine – pure B) Early Abx (within 1 hr after cultures) - Local guidelines – vancomycin, tazocin → narrow spectrum (after culture result) Source control = debride, remove, drain septic source, repair perforation Maximizing oxygen delivery → maintain tissue perfusion - Intubation, ventilator (if ≤30 cmH₂O) - Transfusion (esp. if Hb < 70, plt < 20) - High vol. hemofiltration in severe met acidosis or renal failure	IM adrenaline - High flow FIO₂ - Monitor IV fluid (if hypoTN) – 0.5mg (1:1000) = flat = avoid hypoTN crisis (observe ≥ 4hrs)	Bedside - ECG - Right heart strain (for massive PE) - CXR = Pneumothorax

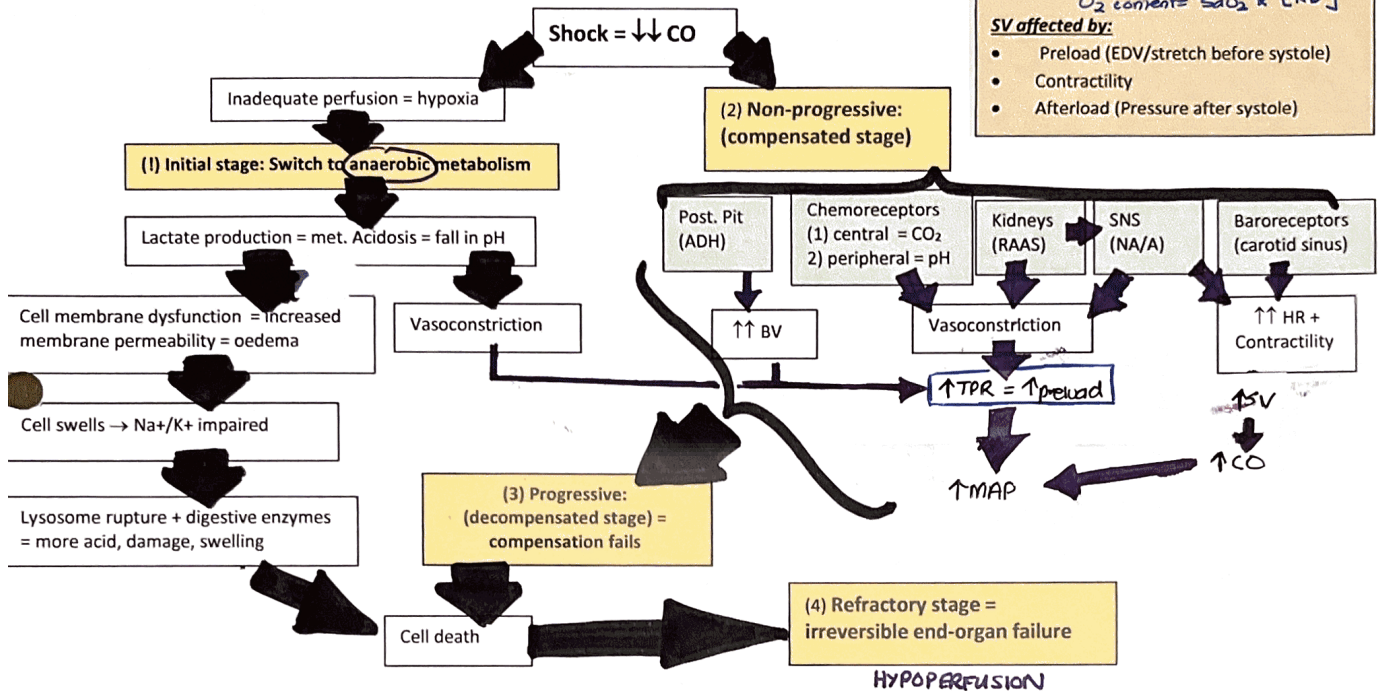
- For children CPR:**
- 1-hand (≤ 8)
 - 2-hand (> 9)
 - Chest compress (100-120bpm)
 - 15 comp/2 breaths for all children

L2.1 Shock & Sepsis

Define shock

- Physiologic state characterized by **inadequate delivery of oxygen** and nutrients to **meet metabolic demands of vital organs** → anaerobic metabolism + cannot remove wastes
- Nb: imbalance may be due to increased demands!

Review basic physiologic aspects of shock



Understand monitoring of patients – Vitals are vital

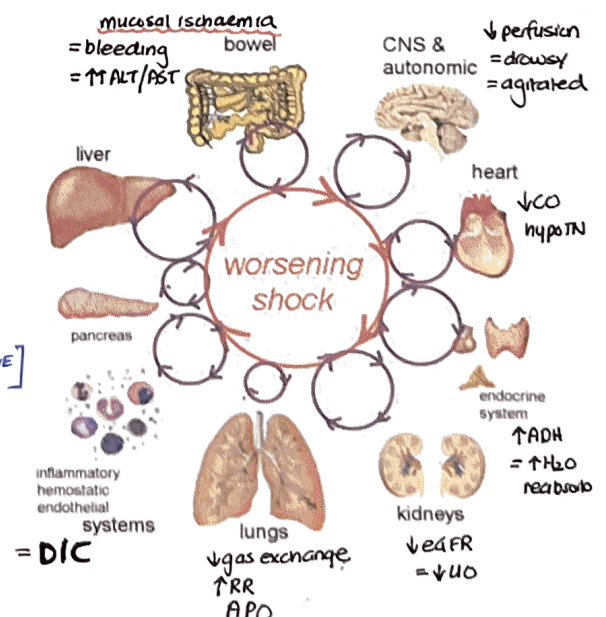
	Early signs of shock (ANY)	Early Deterioration	No intervention	Last line
Clinical signs	- Cool/pale periphery due to vasoconstriction → *(warm in distributive shock)* - Sweating, Polydipsia - delayed cap refill time + STERNUM (CENTRAL)	- Drowsy - confused	- Drowsy, - decreased LOC - agitation = hypoperfusion to brain	- Unconscious - Gaspig respiration
UO	Normal (0.5ml/kg/hr)	Oliguria (< 400ml)	Oliguria (worse)	Anuric
HR/Pulse	Normal	Increased	Increased	Bradycardia
BP	Normal	Normal	Hypotension	Profound HypoTN
RR	Normal	Increased	Increased	Decreased

+ Focal signs – PNEUMONIA, PIV INFECTION, CELLULITIS
+ ACUTE ABDOMEN

Key points:

- Shock = patient looks like crap!** → Early recognition critical to prevent irreversible organ damage
 - Different patients have different normal vital ranges! → Ask what is normal (relative to individual) and observe trends
 - Shock Index = PR / SBP (normal 0.5-0.7)
- Hypotension = late sign**
- Delayed cap refill time = always check centrally = sternum press** → early sign of shock
- Meningococcal** = well-looking adult/child with ↑ RR and ↑ HR with [DISTRIBUTIVE] unexplained fever
- MI = R-sided chest pain radiating down right arm = MOST specific**
 - Since many causes of L-sided chest pain (e.g. MSK, PE)

6. **LACTATE ≥ 4mm (treated as sepsis)**



Principles of Sepsis Control

General Hx:

1. Hx: **Source (Resp, GU -UTI, Abdo), cellulitis**
2. Recent procedures, foreign bodies
3. PHx – immune status, co-morbidities, prior infections, antibiotic use, travel, exposures, lines, ports, catheters
4. Medications & allergies
5. Check for prior **ANTIBIOTIC USE → affect blood culture, allergy and hide severity of sepsis**

EXAM:

1. Vitals + check trends – BP, PR, RR, temp (high or low)
2. **Systemic manifestations** → Altered mental status, hypoperfusion, oliguria
3. Peripheries warm, → become cold in latter stages
4. Head to toe check – look for source (**PULL PANTS!!**)
5. E.g. **fournier's gangrene** (necrotising fasciitis in perineum, scrotum, penis),

General work-up for

- **FBC** – check Hb – low? = high risk of rapid deterioration
- **EUC** – renal function, electrolytes
- **LFT** – cause of sepsis
- **COAGs** – DIC?
- **CRP** – monitor progress
- **Cardiac serum markers** (troponin)
- **BSL**
- **VBGs** (Lactate, met. Acid/alkalosis)
- **Blood cultures** – peripheral and from lines to check for bacteremia
- **Urine dipstick + MSU M/C/S**

Imaging:

- **USS** → MRI (no radiation)
- **CXR**
- **CT** brain, abdomen (radiation)

Special:

- **LP** – ?meningitis, encephalitis

Important considerations:

- **For any trauma** = check for bleeding **BEFORE** diagnosing neurogenic shock
- **5th shock type = Metabolic/resp**
→ Disturbance in oxygen diffusion
- **COLLOIDS** replace circulating volume more efficiently than crystalloids but NO benefits (actually more harm) → Not useful for cardiogenic
- **High-output state** = ↑HR, ↑BP ↑RR, Febrile
 - **Thyroid storm**
 - **BERI-BERI (WET)**

Outline common sources of hospital acquired infection (HAI) in ICU with reference to ventilator associated pneumonia and catheter associated infections

Hand hygiene = remove transient microbes from hands to

- Reduce hospital acquired infection
- Reduce hospital stay time
- Reduce patient morbidity and mortality
- Decrease spread + rise of Abx-resistant microbes (stewardship)

Factors to consider:

- Immunocompromised
- Local prevalence of pathogen in hospital
- Infection control practices (e.g. HH)
- "Complacency" w/ cohorting
- Antimicrobial stewardship (reduced Abx resistance)



Isolation Precautions



	Mode of Transmission	Personal Protective Equipment (PPE)	Room Type
Contact	Prevent transmission of infections spread by direct or indirect contact with the patient or patient's environment	Gown and Gloves	Single-Patient Room
Droplet	Prevent transmission of infections spread via air droplets by coughing, sneezing, talking, or close contact with respiratory secretions/mucous membranes	Surgical Mask	Single-Patient Room
Airborne	Prevent transmission of infections that remain infectious over long distances when suspended in the air	N95 or Higher Level Respirators	Airborne Infection Isolation Room (AIIR) Negative Pressure, Special Ventilation

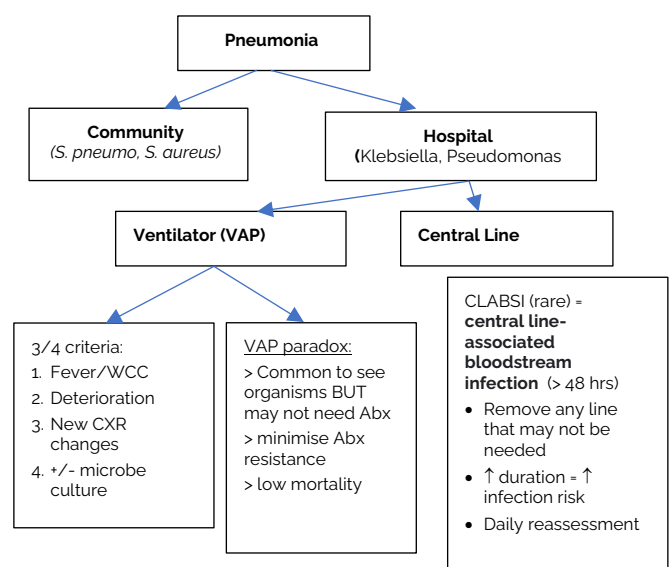
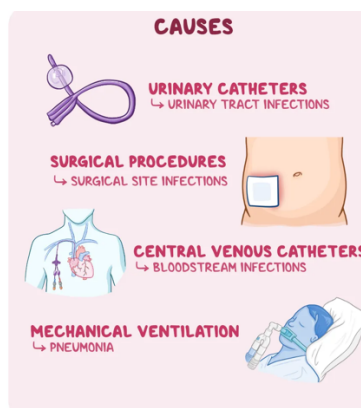
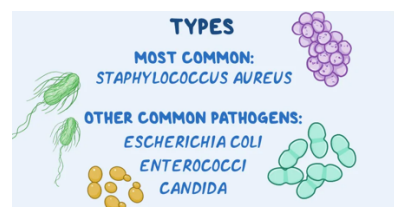
Causative organism

MRO colonisation, enteric (norovirus), scabies, impetigo, abscess, HSV, Hep A

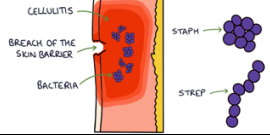
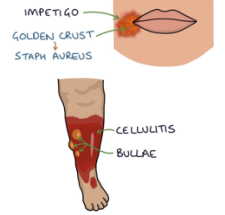
N. meningitis, influenzas, MMR, GAS, Varicella, Virus (adeno, rhino, parvo)
Mycoplasma pneumoniae

Measles, Ebola, TB, varicella, COVID

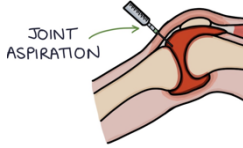
*All precautions above need "**Standard precautions**" = HH, clean equipment, PPE, aseptic technique



COMMON INFECTIONS

	MENINGITIS	URTI (ear, nose, throat)	LRTi	INFLUENZA	Skin infection
Cause	Bacterial - Neisseria meningitis → gram -ve diplococci Viral - HSV, enterovirus, varicella zoster virus Main complications Hearing loss (main comp.) - Seizure /epilepsy - Cognitive impairment - Memory loss - FND (limb weakness or spasticity)	VIRAL (Adenovirus, rhinovirus, coronavirus, RSV) - Incubation period = 7-10 days Bacterial Strep. Pneumo → pharyngitis Strep. Pyogenes (GAS) → sinusitis, tonsillitis, otitis media Bordetella pertussis → whooping cough (post-cough vomit) → public health notification?	Viral bronchitis (most common) DDx: Epstein-barr = tonsil exudate Bacterial Strep. Pneumo (50%), HIB (20%) Moraxella Catarrhalis (immunocomp. Or lung disease) Pseudomonas (CF, Bronchiect) S. aureus (CF) Atypical (Legionella, C. psittaci, mycoplasma, chlamy. Pneumo, Q fever (Coxiella burnetii))	RNA virus: - Type A - Type B - Type C Risk factors: - Age extremes (>65 or child) - Pregnant - Chronic co-morbidities (e.g. Asthma, COPD, HD, T2DM) - HCW	Staphylococcus aureus (MSSA vs MRSA) (CELLULITIS) Group A Streptococcus (streptococcus pyogenes – ERYSEPELIAS, tonsillitis) Group C Streptococcus (Streptococcus dysgalactiae) 
S+S	Typical symptoms - Fever, neck stiffness - Photophobia - Non-blanching purpuric rash - Altered LOC and seizures Non-specific Sx for neonates and babies: - Hypotonia, - Poor feeding, lethargy, - Bulging fontanelle	Centor Criteria for tonsillitis (is it bacterial?) Sore throat Fever > 38 - Tender enlarged anterior cervical LN - Tonsillar swelling + Exudate NO cough Other = otalgia, ear d/c, coryza,odynophagia	- Productive cough, fever + SOB - INSPIRATORY CRACKLES + Jair entry Legionella = SIADH = HypoNa Mycoplasma = erythema multiforme (target lesions) Coxiella = farmer w/ flu PCP (fungal) = low CD4 (HIV)	Fever + coryzal symptoms - Sore throat - Myalgia / muscle aches - Fatigue - Headache - Dry cough - LoA	Warm, hot, swollen painful area Thickened and oedematous area (+/- bullae – fluid filled blisters) Golden crust = impetigo = S. aureus
Ix	Exam: Kernig's sign – SUPINE patient straighten knee while hip flexed caused reproducible spinal pain and reduced ROM Brudzinski's sign – SUPINE patient uses hands to life head and neck off bed and flex chin to chest → involuntary flexing of hips + knees SEPSIS Screen LP + CSF analysis (M/C/S + viral PCR) Indications for LP: - Under 1 /12 presenting w/ fever 1-3/12 w/ fever and unwell < 1Yo /w unexplained fever	PCR resp. swab (nasal/throat) General exam: vitals, ENT, LN, Chest aus. Antibiotics ONLY if: - Symptomatic > 7 days + purulent nasal discharge, sinus tenderness - Persistent Fever ≥ 39°C (for 3 days) Double sickening (get well then worse) Consider Scarlet fever (GAS): - Complications = IE, PSGN - Post-infective Ix = ECHO, UA	PCR resp. swab (nasal/throat) FBC, EUC, CRP, CXR, sputum culture, serology, urinary antigen C – Confusion (new disorientated in person, place or time) U – Urea > 7 R – Respiratory rate ≥ 30 B – BP < 90 /60 65 – Age ≥ 65 - Score 0/1: Rx at home - Score ≥ 2: Rx hospital admission - Score ≥ 3: Rx ICU assessment	PCR resp. swab (nasal/throat)	Clinical diagnosis Skin swab M/C/S + PCR 
Comp.	Meningococcal septicaemia (non-blanching purpuric rash) DIC + subcutaneous haemorrhages - Meningococcal meningitis	Retropharyngeal abscess - sepsis	- Sepsis → death - Pleural effusion → lung abscess → empyema → ARDS	- Otitis media, sinusitis, bronchitis - Pneumonia - Febrile convulsions (child) - Encephalitis - Worsening HF, COPD	Septicemia – bacteria enters bloodstream
Rx	Acute Mx: - Urgent admission IM/IV STAT empirical ABx < 3/12 old = cefotaxime + Amoxil (listeria coverage) > 3/12 – ceftriaxone - If allergy = transfer is priority NOT antibiotics Acyclovir (if suspected or confirmed HSV meningitis) Long-term Mx: Dexamethasone PO qid to children > 3/12 if bacterial meningitis confirmed → reduce frequency and severity of hearing loss Notify public health Post-exposure prophylaxis w/ single dose of ciprofloxacin to close contacts esp. those with prolonged contact in past 7 days	Viral = Supportive Mx (fluids, analgesia, rest) NSAID w/ food ***** Refer to local ABx guidelines Bacterial Pharyngitis = Penicillin V aka phenoxymethylpenicillin for 10 days Bacterial rhinosinusitis = amoxicillin Bacterial otitis media = amoxicillin ONLY if symptoms don't resolve after 3-7 days Bacterial sinusitis < 10 days = no ABx > 10 days = 2 wks high-dose nasal steroid spray OR 5-day Penicillin V (if bacteria suspected) Any allergy: - Use augmentin (co-amoxiclav), doxy - Use erythromycin (if pregnant)	Supportive Mx (fluids, analgesia) FLU and COVID-19 vaccine – cover antigenic shift in influenza A - Pneumococcal vaccine ***** Refer to local ABx guidelines Mild CAP = 500mg Amoxil PO tds or macrolide for 5 days Mod-severe CAP = IV ABx then switch to oral for 7-10 day Atypical CAP = macrolides, quinolones, tetracyclines ○ AVOID tetracyclines in children (permanent teeth staining and AKI)	Rx given based on hx, exam If healthy, - No anti-virals meds If symptomatic – must start antivirals within 48hrs to be effective - Osetamivir 75mg bd PO for 5 days - Zanamivir 10mg bd inhaled for 5 days *Provide post-exposure prophylaxis in close contacts using above for 10 days	Generally community managed: 500mg flucloxacillin PO Alternatives - Clarithromycin - Clindamycin - Co-amoxiclav Admit ONLY if signs of sepsis IF MRSA consider the use of: BACTRIM VANCOMYCIN MEROPENEM

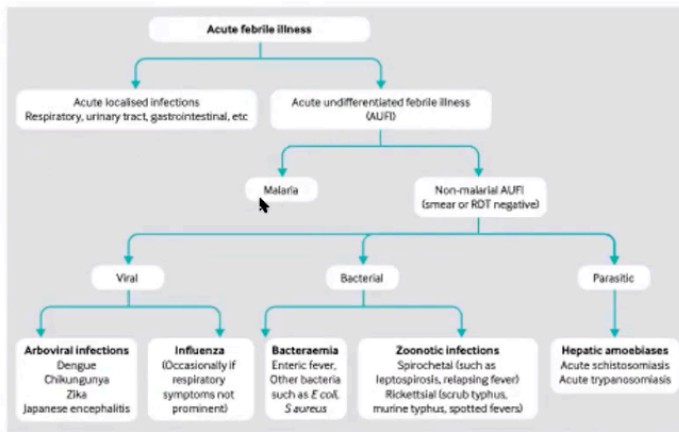
COMMON INFECTIONS

	SEPTIC ARTHRITIS	INTRA-ABDO INFECTIONS	Gastroenteritis	UTI
Cause	- Infection within a joint Risk factors: - Open wound - Joint replacement surgery - Revision surgery Bacterial causes: <i>S. aureus</i> (most common cause) <i>N. gonorrhoea</i> (sexually active) – gram-ve diplococci - GAS (usu <i>S. pyogenes</i>) - HiB <i>E. coli</i>	Long list of causes: - Acute diverticulitis, cholecystitis, cholangitis, appendicitis . SBP, abscess Common organism - Anaerobes (bacteroides, clostridium) <i>E. coli</i> <i>Klebsiella</i> <i>Enterococcus</i> <i>Streptococcus</i>	Inflammation of intestines (enteritis) and stomach (gastritis) Viral causes - Rotavirus - Norovirus - Adenovirus is a less common cause and presents with a more subacute diarrhoea Bacterial causes: <i>E. coli esp. 0157</i> (shiga toxin) <i>Campylobacter</i> (traveller's diarrhoea) – raw milk, undercooked chicken, untreated water <i>Salmonella</i> (raw eggs, poultry) <i>Bacillus cereus</i> (fried rice, IVDU) Giardiasis (parasite) = stool of infected animal	Females (short urethra), sexually active Poor hygiene (wiping back to front) Instrumentation (IDC, IVDU, TATTOO) Mainly Bacterial <i>E. coli</i> (gram -ve rod) > 35 yo C+G < 35 YO <i>Klebsiella</i> + <i>Proteus</i> (gram -ve anaerobe) <i>Enterococcus</i> <i>Pseudomonas</i> <i>S. saprophyticus</i> <i>Candida albicans</i>
S+S	Hot red swollen painful joint - Reduced ROM - Stiff - Fever, lethargy		2-5 days incubation → 3-6 days resolve Sx - Abdo cramps - Diarrhoea (often with blood) - Vomiting - Fever - Lymphadenopathy → ?Yersinia, mesenteric adenitis	Dysuria + FUN WISE (LUTS) Confusion (in frail or elderly) Pyelo = Fever, loin/back pain, haematuria, renal angle tenderness Consider → bladder scan, PV check, DRE
Ix	- FBC, EUC - CRP Joint aspirate (?pus-filled) → gram stain, M/C/S + polarized microscopy Nasopharyngeal swab (?gonorrhoea) DDx - Gout - Pseudogout - Reactive arthritis (2° urethritis or gastroenteritis) - Hemarthrosis 	FBC, EUC, LFT CRP, AXR - ?SBO/LBO Abdo USS – gallstones, appendicitis, Stool M/C/S + O/C/P	FBC, EUC, LFT CRP, AXR - ?SBO/LBO Abdo USS – gallstones, appendicitis, Stool M/C/S Stool O/C/P (?giardiasis)	FBC, EUC, CRP B-HCG – exclude ectopic Urine dipstick MSU + M/C/S +/- STI swab +ve nitrites (specific) +ve WCC (sensitive) USS KUB – renal stones CT KUB – Anatomical abnormalities Refer to ID or Hospital Protocol of early empirical Abx if sepsis is suspected
Comp.	Sepsis	Sepsis	<i>E. coli</i> and <i>Shigella</i> → HUS <i>Campylobacter jejuni</i> – GBS, reactive arthritis ALL = lactose intolerance, IBS	Cystitis Pyelonephritis → urosepsis → refer to hospital
Rx	Refer to local ABx guidelines EMPIRICAL ABx IV 3-6 weeks in total 1st line = Flucloxacillin plus rifampicin 2nd line (penicillin allergy, MRSA or prosthetic joint) → Vancomycin plus rifampicin - Clindamycin is an alternative	Common regimes: <i>Co-amoxiclav</i> alone <i>Amoxicillin</i> + <i>gentamicin</i> + <i>metronidazole</i> <i>Ciprofloxacin</i> + <i>metronidazole</i> (penicillin allergy) <i>Vancomycin</i> + <i>gentamicin</i> + <i>metronidazole</i> (penicillin allergy) *Nb: ABx should be given orally unless serious infections **STAT gentamicin dose given to severely septic pt to provide initial strong bactericidal gram negative action Regime for SBP: - Tazocin - Cephalosporin (cefotazime) - Levoflox + metro (if penicillin allergy)	Improve hand hygiene Fluid challenge (rehydration w/ gastrolyte) Avoid Abx if shiga toxin bacteria Avoid antidiarrhoea (loperamide) and anti-emetics (metoclopramide) Refer to local ABx guidelines <i>Shigella</i> = azithromycin + ciprofloxacin <i>Salmonella</i> = supportive + ABx (only if severe) <i>Bacillus cereus</i> (fried rice, IVDU) - RECOVERS within 24h Giardiasis = metronidazole	Uncomplicated cystitis, LUTS 300mg Trimethoprim PO once daily for 3 days (avoid in 1st trimester – anti-folate effect) 100mg Nitrofurantoin PO qid (not if AKI, eGFR < 45 and 3rd trimester – haemolytic anaemia and pulm. fibrosis) 500mg Cefalexin PO bd 5 days (if allergy or pregnant) Uncomplicated PYELO. Augmentin (875 +125mg) PO bd for 14 days OR Cipro 500mg bd 7 days Add ceftriaxone (for gram -ve) if complicated How long? 3 days for simple UTI in women 5-10 days in immunosuppressed, abnormal anatomy or impaired kidney function 7 days for men, pregnant, or catheter related UTI

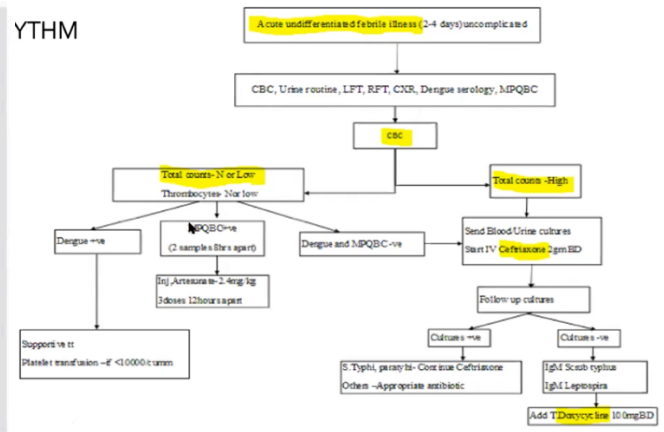
HIV, TB, Traveller's Diarrhoea and Malaria

	HIV	TB	Traveller's Diarrhoea	Malaria															
Epi	- HIV = human immunodeficiency virus - AIDS (late stage-HIV) = acquired immunodeficiency syndrome	1 in 4 people infected w/ TB worldwide Active TB = ACTIVE INFECTION in various parts of body Latent TB = when immune system encapsulates sites of infection and stop progression Reactivated /secondary TB = reactivation of latent TB Miliary TB = when TB disseminates	80% bacterial (E.coli usu. ETEC, EAEC) 20% - viral, giardia, cryptosporidium	Transmitted by mosquitoes – Plasmodium falciparum Infects liver first → sporozoites infect hepatocytes and multiple asexually → released as merozoites int blood → fever Merozoites infects RBC (sickle cell protective) to form schizont → haemolysis → release merozoites to repeat 7-30 day incubation period															
Causes	HIV-1 = most common type (RNA retrovirus) Destroys CD4 T helper cells	➤ <u>Mycobacterium TB bacteria – rod shaped bacillus</u>	ETEC = most common (Travellers) EAEC = Enteroaggregative E. coli	<u>2X MAIN sporocyte types:</u> Plasmodium Falciparum (in 6 wks) = MOST SEVERE FORM o 50-90% = longer if on mefloquine prophylaxis) Plasmodium Vivax (mths later) 10-50%															
Tx	Exchange of Bodily fluids (semen, saliva, MSM) Vertical transmission (pregnancy, birth, BF) Open wounds, sharing needles, blood splash in eye	Known or close contact with active TB (via droplets) Immigrants from endemic areas Immunosuppressed (HIV, steroids, IVDU, old, EtOH)	Faecal-oral	Mosquito bites															
S+S	AIDS defining illness: <table><tr><th>CD4 > 500</th><th>CD4 > 200</th><th>CD4 < 200</th></tr><tr><td> - Gullian-barre - Reactive arthritis ↓ plt </td><td> - TB - HZV - HSV - Candida - Bell's </td><td> - Kaposi's (HHV8) - CMV retinitis - NHL - PJP </td></tr></table>	CD4 > 500	CD4 > 200	CD4 < 200	- Gullian-barre - Reactive arthritis ↓ plt	- TB - HZV - HSV - Candida - Bell's	- Kaposi's (HHV8) - CMV retinitis - NHL - PJP	Pulmonary ➤ SOB, chest pain ➤ Haemoptysis ➤ Systemic signs – UWL, fever, NS, LoA Extra-pulmonary ➤ Erythema nodosum ➤ Spinal pain (Pott's disease of spine) ➤ Confusion (meningitis, encephalitis)	60% Abd cramps 15% bloody stools 10% fever If prolonged diarrhoea (> 14 days) ddx: Parasitic cause (e.g cylosopra) → Rx: bactrim Lactose intolerance IBD (UC, Crohn's) + iBS	Pallor (anaemia) Jaundice (bilirubin released from ruptured RBC) +HSM, Diaphoresis GI issue → N/V abdo pain Complications of falciparum: ➤ Cerebral malaria ➤ Haemolytic anaemia → SOB, chest pian, lightheaded ➤ Seizures ➤ Reduced LOC ➤ AKI ➤ APO ➤ MOF + DIC									
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- Gullian-barre - Reactive arthritis ↓ plt	- TB - HZV - HSV - Candida - Bell's	- Kaposi's (HHV8) - CMV retinitis - NHL - PJP																	
Ix	SCREENING - o Testing for any patient w/ RF - o Requires formal verbal consent Antibody blood test - o Can be negative for 3 mths post exposure so repeat testing is needed P24 antigen – provide earlier result PCR testing for HIV RNA → gives viral load - o "undetectable" = 50-100 copies/mL Monitor CD4 count - o 500-1200 (normal) ART is offered to everyone with a diagnosis of HIV irrespective of viral load or CD4 count	FBC (anaemia) Sputum M/C/S – acid fast bacilli (Zeihl-Neelsan stain) → bright red against blue background Mantoux test -previous immune response to TB (> 5mm induration = positive result – may be active) IFN-γ assay -positive = active TB CXR +/- Bronchoalveolar lavage Primary TB = patchy consolidation, pleural effusions and hilar lymphadenopathy Reactivated TB =w patchy or nodular consolidation with cavitation (gas filled spaces in the lungs) typically in upper zones Disseminated Miliary TB = "millet seeds" uniformly distributed throughout lung fields LN aspiration or biopsy	FBC - Leucopenia - Thrombocytopenia Colonoscopy if OCP (ova, cysts, parasites) negative for prolonged diarrhoea	FBC = severe anaemia (haemolysis) + low plts (DIC) EUC = elevated Cr BSL = Hypoglycaemia ABG = Metabolic acidosis Malaria blood film (EDTA bottle or cassettes) - 3x samples taken over 3 consec. Days to exclude malaria (since 48 hr cycle of malaria released into blood) 2nd = Giemsa stained- Thick & thin Malaria films - o Thick = identify parasite - o Thin = species identification (e.g. ring-form trophozoites for P. F.)															
Mx	- Protease Inhibitors (PIs) -navirs - Integrase Inhibitors (IIs) - <i>gravirs</i> 2x NRTI/NNRTI drug + potent 3rd agent (NNRT,INSTI or PI) Additional Mx: Prophylactic ABx → co-trimoxazole (Septrin) – protect against PJP Statins = reduce risk of CVD Yearly pap smears (HIV increased risk of cervical cancer) +check partner HIV status IUTD (avoid live vaccines) LCSC and BF offered to HIV +ve women (unless underectable viral load) Post-exposure prophylaxis = reduce risk of transmission (BUT must start within 72 hrs) - o Truvada (emtricitabine / tenofovir) and raltegravir for 28 days - o HIV test initial + 3/12 after exposure to confirm negative status	ACUTE Mx: - 4 drug therapy - MDT involvement R – Rifampicin for 6 months – red urine/tears I – Isoniazid for 6 months - PN P – Pyrazinamide for 2 months – gout E – Ethambutol for 2 months – Colour blindness, reduced visual acuity Mx of Latent TB: ➤ Isoniazid + Rifampicin for 3 months ➤ Isoniazid for 6 months Further/Long-term Mx: ➤ Ensure patients take all 4 ABx ➤ Test contacts for TB + other BBV (HIV, hep B/C) ➤ Notify Public Health authority ➤ Corticosteroids for extrapulmonary disease	General Mx: <i>Hand hygiene</i> <i>Safe drinking and eating (e.g "boil, cook, peel everything)</i> <i>Self-treatment = education esp. to high-risk (e.g. pregnant, young children, elderly)</i> Pre-exposure prophylaxis: Cholera vaccine (>90% efficacy against Vibrio cholera) Fluroquinolones = highly effective 80-95% Nb: rifaximin = highly effective (not used in Aus.) Post-exposure prophylaxis Oral rehydration salts, Antimotility (4mg loperamide 2x tablets STAT – opioid agonist) When to seek extra help? ➤ Unremitting fevers (>38.5oC for 48 hrs) OR bloody diarrhoea OR cannot tolerate oral fluids ➤ 3x stool OCP samples (at least one) ➤ Start empirical Abx (azithro, cipro) – 1g IM stat azithromycin (one-off) Long-term surveillance TD sufferers = 4x risk of developing IBD	Conservative Mx: Dusk to dawn care (minimise night life) → indoors, mosquito nets Mosquito repellents (adequate amounts of > 50% DEET spray), Light long-sleeve shirts → Permethrin on clothing Air-conditioned accommodation Beware of high-risk groups (e.g. friends/relatives → reduce likelihood of seeking medical attention) Medical Mx: (before and after trip) <table><tr><th>Doxycycline</th><th>Atovaquone-proguanil</th><th>Mefloquine (quinine)</th></tr><tr><td>Cheap, widely used (covers atypicals), short and long term</td><td>Short-terman (acute given IV)</td><td>Long-term usage</td></tr><tr><td>100mg/day (2days before exposure and continue for next 4 weeks)</td><td>One tablet (day before exposure and continue for 1 wk)</td><td>250mg once weekly (2-4 wks before exposure and continue for next 4 weeks)</td></tr><tr><td>Pregnancy, BF, child (<8yo), tetracycline allergy</td><td>Pregnancy, LBW (< 5kg), history of epilepsy, A+D (psych issue)</td><td>Pregnancy, BF (clindamycin can be used as last resort in pregnancy)</td></tr><tr><td>Photosensitivity, vaginal candida, nausea, indigestion</td><td>Headache, nausea, insomnia, vivid dreams</td><td>Headache and nausea Expensive</td></tr></table>	Doxycycline	Atovaquone-proguanil	Mefloquine (quinine)	Cheap, widely used (covers atypicals), short and long term	Short-terman (acute given IV)	Long-term usage	100mg/day (2days before exposure and continue for next 4 weeks)	One tablet (day before exposure and continue for 1 wk)	250mg once weekly (2-4 wks before exposure and continue for next 4 weeks)	Pregnancy, BF, child (<8yo), tetracycline allergy	Pregnancy, LBW (< 5kg), history of epilepsy, A+D (psych issue)	Pregnancy, BF (clindamycin can be used as last resort in pregnancy)	Photosensitivity, vaginal candida, nausea, indigestion	Headache, nausea, insomnia, vivid dreams	Headache and nausea Expensive
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Approach to Fever in India & returned traveller:

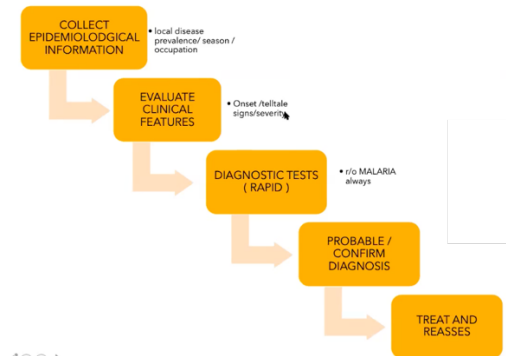


YTHM



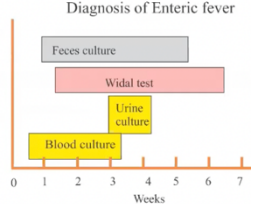
Management – empirical approaches with fever:

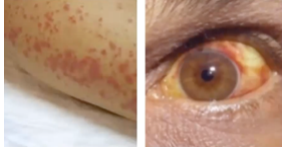
Fever w/	General Mx	Specific Mx	Causes
Low platelets		- Plt transfusion NO steroids	dengue, - leptospirosis, measles, rubella, - meningococcal, malaria
Jaundice	- Antipyretics - IV fluids - IV ceftriaxone - Monitor for signs of shock + bleeding, seizures	- Doxycycline tablet - Monitor UO, - seizures, Enceph - FFP/CryoPPT for bleeding	bacterial sepsis, malaria, scrub typhus leptospirosis
Encephal		- IV acyclovir - IV mannitol (for ICP)	- HSV, Jap B, enterovirus - Scrub typhus, malaria
Renal failure		- Doxycycline tablet - Renal replacement therapy	bacterial sepsis, malaria, scrub typhus leptospirosis
ARDS		- Venturi mask - IV azithromycin - Tablet oseltamivir (H1N1)	scrub typhus, - influenza (H1N1), - falciparum malaria

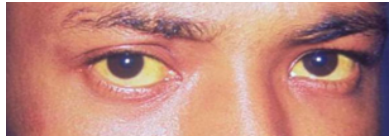


Incubation period:

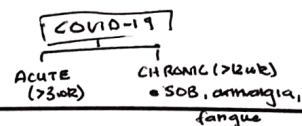
- < 10 days** = dengue, para/typhoid, influenza, Rickettsia, Yellow fever (flavus = yellow jaundice)
- 10-21 days** = malaria, typhoid, Q fever – Coxiella Burnetii (inhale dust in area of contaminated animals – cattle, sheep), African trypanosomiasis, Lyme (borrelia bacteria → spread via tick bites in summer)
- > 3 wks/mths** = viral hep E, amoebic liver abscess, leishmania, schistosomiasis, TB

	Typhoid "Enteric" fevers	Rickettsia	Rabies
Location	- Mekong, India, Pakistan - Young pts	black eschar + mosq. Borne + walking barefoot in contaminated water – paddy fields, flooding	<i>Acute, progressive encephalomyelitis caused by neurotropic lyssaviruses of the Rhabdoviridae family</i> - Avoid animal exposure (bats, rabbits) - Beware in India, Nepal, Sri Lanka, Vietnam, Peru, Columbia
Causes	Gram -ve bacilli - Salmonella Typhi S. paratyphi [7-14 incubation days]	Gram -ve coccobacilli - Australian tick typhus (scrub) - Mediterranean spotted fever < 10 incubation days	- Avoid animal exposure (bats, rabbits) - Beware in India, Nepal, Sri Lanka, Vietnam, Peru, Columbia
Tx	consumed contaminated food and water	Tick bite	
S+S	Week 1: fever + GI + cough - Slow rising FEVER - Headache, COUGH, abdo pain, N/V Constipation > diarrhoea Week 2: - High grade fever + bradycardia - Hepatosplenomegaly - Rose spots (day 7) = salmon coloured blanching maculopapular Week 3 – complication week: Bowel perforation → altered mental state	Remittent Fever (fluctuates >2°C) w/ Black eschar on site Maculopapular rashes (1st week) Neurological, hepatic + renal involvement   Maculopapular rashes	Non-specific Sx e.g. - fever, anorexia, fatigue - headache, myalgia, - cough sore throat, - agitation and apprehension Specific Sx - Paresthesia and fasciculations in proximity of the wound
Ix	FBC - Normal WBC - Eosinophilia - Normal ESR 1st week: Culture – bloods, faeces BEFORE Urine  Diagnosis of Enteric fever	FBC - Leucopenia - Thrombocytopenia - EUC & LFT normal Serology (IgM + PCR) - For later diagnosis but cross-reactions with other strains → high false +ve	Pre-exposure prophylaxis: Human diploid cells rabies vaccine (HDCV) = inactivated virus vaccine (IM injection to deltoid ONLY) Train adaptive immune system to necessary antibodies to better fight possible rabies virus infection Post-exposure prophylaxis - Give vaccine immediately after bite - Add rabies Ig if Lick on broken skin or any Bites and saliva contamination from any bat
Rx	Ceftriaxone (1 st line due to ciprofloxacin resistance) IV fluid resuscitation.	Empiric doxycycline [children = permanent teeth staining and AKI]	*Only stop Rx if animal remains healthy though 1- day observation period. ** exposure to bat blood, urine or faeces = not indication for PEP

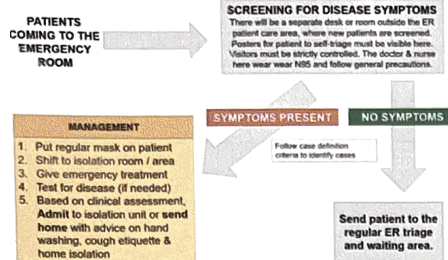
	Amoebic liver abscess	Leptospirosis	Eosinophilia (e.g. Schistosomiasis)
Epi	- Tropical areas + crowded conditions with poor sanitation - India, Asia, South America, Mexico, North Africa	- agriculture bare-foot → contaminated water and soil spread into skin abrasions or conjunctiva DDx: rickettsia, adenovirus	Eosinophilia = 5% of returning traveller [usually worms!] Egypt, Asia, S. America, Middle East
Causes	Parasite = Entamoeba histolytica → forms infective cyst in liver incubation = > 3 wks	Spiral shaped gram -ve spirocheate	Helminths = parasitic flatworms called schistosomes from snails through damaged skin
Tx	Feecal-oral	Fishing + swimming contaminated water	Freshwater exposure (e.g. swimming, water rafting)
S+S	80-90% of infections asymptomatic Fever & RUQ pain (2-5/12 after travel) Diarrhoea (30-40%) 	SEPTIC PHASE (5-14 days) - Fever, headache, myalgia (calf tenderness) - Conjunctival suffusion (Redness w/o exudate) Immune phase (4-30 days) - Aseptic meningitis - Pulm. Haem - ARDS - Shock + MOD (hepatic + renal dysfn)	Fever [katayama] Rash + itchy skin = "swimmer's itch" Stomach pain Cough Headache Myalgia Specific species = location - Bladder = S. haematobium (SCC) - Bowel = S. mansoni (S. typhi)
Ix	FBC - No eosinophilia Amoebic Serology: Liver US and CT scan DDx: Giardiasis: ➢ Ingested cyst ➢ Explosive diarrhoea + mucus ➢ Stool O/C/P ➢ Rx: metronidazole	 LFTS: Abnormal creatinine, ALT PCR - IgM Dark field microscopy MAT IgM	Test asymptomatic (esp. 3 mths exposure) - Urine dipstick (haematuria, proteinuria) - FBC (eosinophilia) - Serology 3x terminal urine (look for cysts in S. haem - best during NOON as most active) 3x stools OCP - other species
Rx	Metronidazole → then paromomycin to kill enteric carriage	Empiric doxycycline	Anti-helminths = Praziquantel (Biltricide) x2 days Check co-travellers (50-80%)

	Dengue "breakbone" Fever	Chikungunya	Hepatitis A/E
Epi	Urban disease (Along equator) - Sometimes Aus. = northern Qld - Leading cause of child mortality (SE Asia)	Tropical areas + crowded conditions with poor sanitation	- India, Asia, Middle East, Mexico, North Africa 10-40% Asian indigenous pop. immune
Causes	Dengue ssRNA virus → 4 serotype → Infection only protects against ONE strain	Chikungunya virus	Viral hepatitis A/E
Tx	Mosquito daytime bites	Mosquitoes	Waterborne contaminated food/water!: Hep B (main) /C = beware of IDVU or tattoos
S+S	The Course of Dengue Illness 	DENGUE "Break-bone fever" ★ Fever (5-7 days) ★ Anorexia ★ Sore throat ★ Rash ★ Nausea ★ Emesis ★ Myalgia & arthralgia (large joints) ↓ Hct ↓ Platelets ↓ WBC ↑ Hematocrit CHIKUNGUNYA "That which bends up" ★ Fever (2-3 days) ★ Headache ★ Retro-orbital pain ★ Rash ★ Nausea ★ Chronic arthralgia (small joints) ★ Severe myalgia ↓ Platelets, ↓ WBC = Hematocrit ↑ ESR, ↑ CRP	- GI issues (N+V, bowel changes) - Jaundice - Hepatomegaly - Mild fever, diaphoresis  Mostly Hep A (4 wk incubation) - Check Previous home Also Hep E: incubation = 4-6 wks - NO chronic state - Higher fatality in pregnant women
Ix	Vitals – check for signs of shock - Narrow PP + hypoTN - Tachycardia + clammy + cold extremities - Always thirsty + vomiting FBC - Very low WCC, plts - High HCT Serology (NS1 + IgM) - NS1 antigen virus +VE in blood +ve IgM (after 4-day fever) +ve IgG (after 7-10 days) - Cannot tell what strain Other flaviviruses cross-react (e.g. yellow fever, Jap encephalitis)	FBC - Leucopenia - Normal HCT EUC/LFT: - Normal albumin + electrolytes ESR/CRP - Elevated Chikungunya titres: - PCR chick antigen - Anti-IgM and anti-IgG	- Albumin & INR levels [test for liver Fn] - LFTs – ALT/AST [any liver damage] - Hep Serology
Rx	Mosquito repellents + supportive care	Supportive – hydrate + anti-pyretics (avoid NSAIDs)	Vaccine ONLY available for Hep B/ C Hep A = usu self limiting but vaccine available

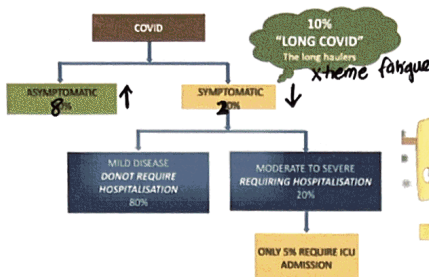
COVID-19 ICU beyond the boundaries:



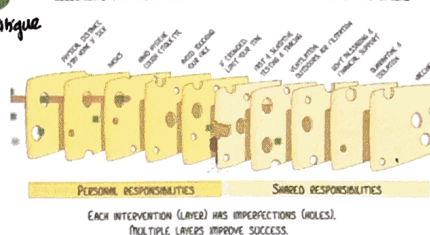
SCREENING FOR EPIDEMIC



Why are we discussing??

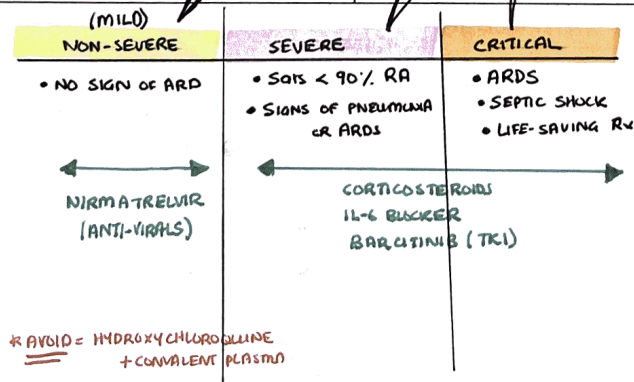


THE SWISS CHEESE RESPIRATORY VIRUS PANDEMIC DEFENCE



"long COVID" = cannot undergo further surgery (as high risk VTE)

	Case 1	Case 2	Complications of COVID-19
PS	37 yo male with 6 day fever, 5 day cough, 3 day SOB	45 yo male w/ 4 day fever + 3 day dry cough SOB grade III-IV	
Sx	91% sats even with FIO2 = 10L		
Rx	AWAKE • Prone w/ HFNC (best to improve sats) • Cannot prone w/ NIPPV (worsening SOB)	• Tachypnoea, hypotensive, low vol. pulse • Bilateral air entry into lungs • WARM PERIPHERY CRT 2/5	MULTI-SYSTEM INFLAMMATORY SYNDROME!! • Cytokine storm → Coagulopathy = MI, PE, DIC • High incidence of PE in COVID-19 • DVT PROPHYLAXIS FOR ALL (even w/ no coag issues) • CTPA for unexplained hypoxia • CNS affected (e.g. ICH, SDH, strokes, cavernous sinus venous thrombosis) – beware of use of anti-coags, status epilepticus • HEART - MYOCARDITIS - ACS - ARRHYTHMIA • AKI (complicated by DM) +++ proteinuria (albuminuria) +++ haematuria • SKIN RASH • LYMPHADENOPATHIES • BULBAR CONJUNCTIVITIS
Ix	THROMBOINFLAMMATION MARKERS • FBC • Elevated Acute phase biomarkers: CRP, ferritin, LDH, procalcitonin, IL-6 (cytokine storm), d-dimer • Neutrophil:lymphocyte (N:L ratio) = high = strong indicator for good prognosis • D-dimer - coagulopathy • ABG = severe respiratory acidosis w/ no compensation (T2 RF) • USS = ?pleural effusion, oedema ECHO = ↓LVEF (1/3rd may be normal) • CT = PERIPHERAL ground glass opacities + septal thickening → fibrosis (late sign) • Pleural effusion less common		
Rx	• Remdesivir 100mg (3 days) • Solumedrol (methylprednisone) 40mg bd → improved mortality • Enoxaparin 40mg bd SC • Abx coverage → to manage co-infections - DOXY - ATYPICAL COVERAGE (COMMON) - BACTRIM	• Critically ill → Need intubation → ICU • Prone ventilation LINE DISPLACEMENT • Comp. (pressure sores, facial oedema) • CI: Unstable spine, open abdomen, haem unstable • ECMO ← IF STILL HAEM UNSTABLE • CXR	
	ESCALATION OF RESPIRATORY SUPPORT 1. NC @ 6 LPM 2. Venturi mask 24-55% 3. NC + Non-rebreather 4. HFNC 45-60% O2 6L/min 5. NIPPV: CPAP 6. Intubation Core Principles of Managing this Epidemic Identification Separation Infection Control Isolation Treatment Beware	Rx: 1) PREDNISONE 2) IL-6 receptor blocker (Baricitinib)	After recovery from COVID-19 • Discharged with high flow O2 • Pulmonary fibrosis (severe) → anti-fibrotic therapy (e.g. nintedanib) • Main symptoms: Fatigue, muscle aches, SOB • May need lung transplants • Pulm rehab is needed • FU = CT, CXR ↓ • PERIPHERAL LESIONS USU. SEEN • NO Consolidation • LONG-TERM HF - HTN, CAD, STROKE



Common Poisonings & Overdoses in India

Poisons	Symptoms		Investigation	Treatment
Organophosphates "Farmer" - pesticide/insecticide - Inhibit ACHE at NMJ = prolonged depolarisation	- Salivate - Lacrimate - Urinate - Defecate - GI effects - Emesis (N/V)	- Early LOC - Miosis ↑ WOB - Hx of quarrelling - Fasciculations / twitch	- Vitals – Orthostatic HypoTN, bradycardia - ECG (prolonged QT) - ABG (hypoxia) - ACHE Levels < 3000 (=exposure)	- PPE (respirator + thick gloves) + decontaminate patient (remove clothes) - ABCD - IV bolus 1-2mg atropine + activate charcoal (50-100mg) for excretion - IV 30mg/kg bolus Pralidoxime (within 24 hrs) – reactivate ACHE - Supportive care (oxygen, ventilation, fluids) Beware of: - IMS – intermediate syndrome (24-96 hrs) = weak ocular muscles, neck +resp. muscle - OPIDN – Organophosphate delayed polyneuropathy (2-3 wks) = cramp, numb, parasthesia distally, gait apraxia, foot/wrist drop
Serotonin syndrome DDX: (1) sepsis w/ delirium, (2) thyroid storm, (3) mania from undiagnosed bipolar	- ANS (sweat, agitation) - SNS (tremor, clonus, hyperreflexia) - Altered mental state - Hx of depression (recent use of new drugs, SSRI)		- Vitals - ECG (tachycardia) - FBC (WCC), EUC - TSH, T3/T4 - Urine for amphetamines	Withdraw new meds Paralyse = Cyproheptadine (5-HT3 antag) - Anti-psychotic (e.g. olanzapine) Sedate = Diazepam (muscle relaxant) Cool via evaporation INTUBATE (if needed)
Anti-cholinergic OD <i>(e.g. TCA, amitriptyline)</i>	- Dry mouth - Urinary / faecal retention	- Mydriasis - Drowsy	- Vitals = tachycardia, hypoTN, febrile = shock - ECG = VT/VF - ABG (met acidosis)	- Gastric lavage + activated charcoal - NaHCO₃ (Rx: for met. Acidosis)
Benzodiazepine (GABA)	- Miosis + ATAXIA - Sedation, drowsy, low grade coma		- HypoTN - Dose-dependent resp. depression (RR < 8)	- Gastric lavage to remove tablets – supportive care (O2, ventilation, fluids) 0.2mg IV Flumazenil (Short-acting GABA-A → only to confirm – pt wakes up suddenly)
Digoxin	- N/V + confusion - Xanthopsia (yellow vision) - Gynecomastia			Digibind (↓K+) – reduce acute AKI/Gastro
CO poisoning	- Cherry red lips + red peripheries - Headache, light-headed - Facial plethora - Drowsiness		100% O2 sats - Polycythaemia - Check carboxyHb levels	- Hyperbaric O2 chamber - Anaesthetic referral
Aluminium phosphate "quick-phos tablets" - Rat poison	- Abdo pain + vomiting - Cough + SOB - Anxious + confused Rotten-fish-like odour - Cool peripheries - NO fasciculations + clear chest	Al phosphide + water → phosphine gas → inhibit mitochondria + cellular hypoxia → ARDS, GI	Vitals (hypotension, Shock) - ABG (hypoxia, met. Acid) - FBC, EUC - ECG (sinus tachy, vent. Ectopics) Phosphine detection (filter paper with AgNO₃) – hold close to mouth or dip in vomit = changed to black	- PPE (respirator + thick gloves) + decontaminate patient (remove clothes) - ABCD - Gastric lavage + potassium permanganate + activated charcoal MgSO₄ = Rx arrhythmia (protect heart) Assisted ventilation = ARDS Supportive care = oxygen, ventilation, fluids, vasopressors
Warfarin (Rat poison) Inhibit Vit K dependent clotting factors	- Symptoms take time to develop – appear normal XS bleed = epistaxis, haemorrhage, ICH		- HypoTN - Hypothermia - COAGS = Prolonged PT and raised INR	decontaminate patient (remove clothes) - ABCD - Gastric lavage - Inject Vit K + FFP Supportive care = oxygen, ventilation, fluids

Paracetamol “suicidal pregnant mother”	> 150mg/kg = OD - RUQ pain + N/V - Hepatotoxic - Crosses placental barrier (affects fetus)	- Asymptomatic - Liver damage in 24-36 hrs = check PT/INR - Normogram (4 hrs after ingestion) - VBG = screen for met acidosis + plasma venous HCO₃	- IV N-acetyl-cysteine (will also Rx baby) 150mg/kg → 50 → 100 mg/kg (15mins) (4hrs) (16 hrs) - Check for reaction = flush + wheeze (stop infusion + give anti-histamine → 30 mins) - Give cyclizine for nausea to prevent harm to baby) - Psych evaluation
Narcotic “opiates, heroin”	- LOC + confused/sedated + seizures - Miosis Resp. depression (main ddx against benzo) - CNS depression (feeling high)	- Irregular RR, low Sats - hypoTN - Bradycardia - Hypothermia	- Gastric lavage 0.5mg IV Naloxone (For diagnosis + treatment) - If withdrawal = sweat, agitated, lacrimation, rhinorrhoea, yawn, goosebumps
Ethylene glycol + methanol	- Mimic alcohol intoxication - Blurred vision + drowsy + SOB - N/V + abdo pain	- After 12-24 hrs → ABG (met. Acid) = ↑RR - High-anion gap	Orally administered ethanol (50mL of 100% ethanol) e.g. whisky 10mg/kg IV Fomepizole (4-methylpyrazole)
Salicylates (aspirin)	- GI irritation → N/V + abdo pain - Tinnitus (ototoxic + nephrotoxic)	↑RR, anion gap (met acid) ↓BSL - Normal PaO₂, hypocapnic, normal A-a gradient	- IV NaHCO₃ (Rx: for met. Acidosis) - activated charcoal
Scorpion bite India = red scorpion = black Na channel (ANS storm)	- Restless agitated - Mydriasis - Drenching sweat - Vomit + priapism Pancreatitis	↑ HR, HTN, ↑ RR, low Sats - Widespread crepitation → APO (CXR) - ABG (lactic acidosis due to hypoxia)	- Anti-venin + ICU Ax (BUT anapylaxis risk) - Prazosin = for APO (due to myocardial toxicity → LVF, vasoconstrict) - BB (metoprolol) - Loop diuretic)
Snake bite	- Krait = “unknown bite” + abdo pain + paralysis - Cobra = sudden severe pain + ecchymoses - Viper = uncontrolled bleeding at bite + gangrene - Echis = slow swelling at bite site (S+S after 1 wk)	Krait clinical features: - Bilateral ptosis+ Mydriasis - Broken neck sign - Intact reflex - HTN + resp. paralysis	- Resp support (ETT) - Anti-snake venom - Atropine BEFORE neostigmine (as Krait venom ↑ Ach release) - Nitroglycerine to control HTN
Oduvanthalai Inhibit Na/K ATPase 	- Consumed leaves/fruits of plant - Brady-tachy arrhythmias (Heart block, VF) - SOB, tremor - Visual disturbance, altered sensation	- Severe Hypokalaemia (<1.5mM) - Acidosis - Detect cliestantin A in blood + urine	- Gastric lavage + charcoal - Correct hypoK + acidosis - Supportive care (O₂, fluid, bicarb)
Datura “Devil’s weed” 	2-3 seeds cause anti-cholinergic symptoms - Bitter taste = burning in epigastrium - Delirium + hallucinations + confused - Dry mouth + skin, mydriasis - Urinary retention	- Anti-CHOL = ANTI-SLUDGE - Tachycardia, hyperthermia	- Gastric lavage + charcoal - Correct hyperthermia – IV fluids + convection cooling (STRIP BODY – ICE PACKS) - Supportive care (O₂, fluid, IDC, sedation)
Pheno/ acids/ corrosives	- Burns = redness, muscoal white patches, ulceration - Abdo pain + vomit - GI ulceration + bleed - Seizure + coma	- HypoTN + shock - ECG: arryhtmia	- Patient decontaminated - Supportive care (oxygen, ventilation, fluids, HCO₃, diazepam, blood products) - Avoid gastric lavage = damages/perforates oesophagus



Hookworm

- When walking barefoot
- Isolated within subcutaneous layer and moves



- Maggot of Tumbu fly** causes myiasis = skin infestation (due to flies laying eggs near open wound)
- Rx involves excision

Infection & inflammation: Mechanisms of Autoimmunity = self-antigen confirmed + immune reactivity proven

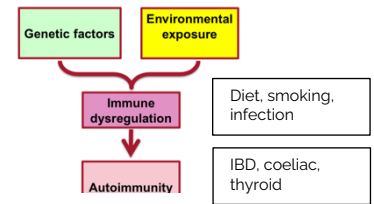
	Autoinflammatory (INNATE)	Autoimmune (ADAPTIVE RESPONSE)	Classical Recurrent Fevers
Cells	Neutrophils, macrophages	T and B cells	
Proteins	PAMP, DAMP (E.g. TLR)	Antibodies, Immune complexes	FMF: familial Mediterranean fever CAPS: cryopyrin-associated periodic fever syndrome (AKA NLRP3-AID) MKD: mevalonate kinase deficiency TRAPS: TNFRSF1A-receptor associated periodic fever syndrome
Cytokines	IL-1 family, IL-6, TNFα	IFNγ, IL-4/5/13, IL-17	
Mechanism	Inflammasome (E.g. NLRP3 produces IL-1)	<i>Innate mechanisms</i> : NETosis & Complement	

***NB: Both can have elements of each other**

***Rx = IL-1 OR TNF-α inhibitors, colchicine**

Explain how genetic and environmental factors contribute to autoimmunity

- strong genetic component** (e.g. FHx, monozygote twins, Gene polymorphisms e.g. CTLA4, HLA, PTPN22 etc.)
 - Immune regulatory genes (CTLA-4): changes in immune regulation → induce autoimmunity
 - HLA-A, -B, -C (**CD8 T CELLS**);
 - HLA-DR, -DP, -DQ (**CD4 T CELLS**) e.g. **HLA-II polymorphic assoc. with AIDS**
- Environmental factors** (e.g. infection, smoking, diet, antibiotic use) → can trigger immune dysregulation in those genetically predisposed
- Dysbiosis** (diet, antibiotic use) can predispose to autoimmune diseases (e.g. IBD)
- Autoimmune disease can follow **acute infection** (mostly due to **cross-reactivity with self-antigen – molecular mimicry**), such as:
 - acute rheumatic fever** after ← streptococcal infection [EXOTOXIN]
 - reactive arthritis** following ← bacterial infection [UTI- chlamydia]



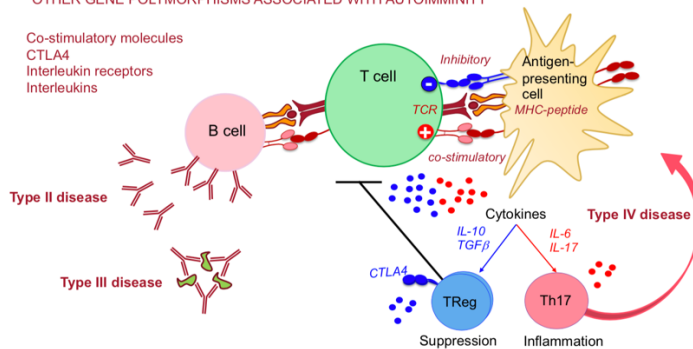
Potential mechanisms:

- cross-reactivity between the infectious pathogen and self antigens (molecular mimicry)
- release of sequestered antigens from damaged tissue
- production of inflammatory cytokines
- immune recognition of drug-self molecule complex

Describe the immune mechanisms involved in the development of type II, III, IV autoimmune diseases

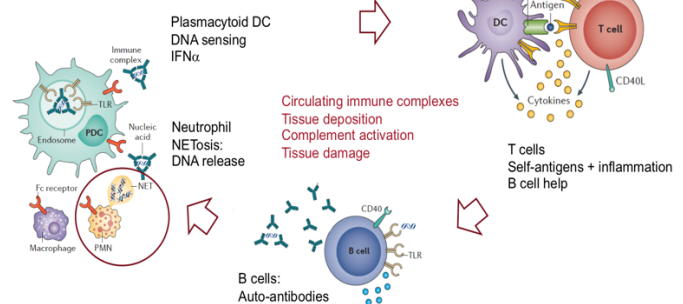
T cell activation and regulation of the response

OTHER GENE POLYMORPHISMS ASSOCIATED WITH AUTOIMMUNITY



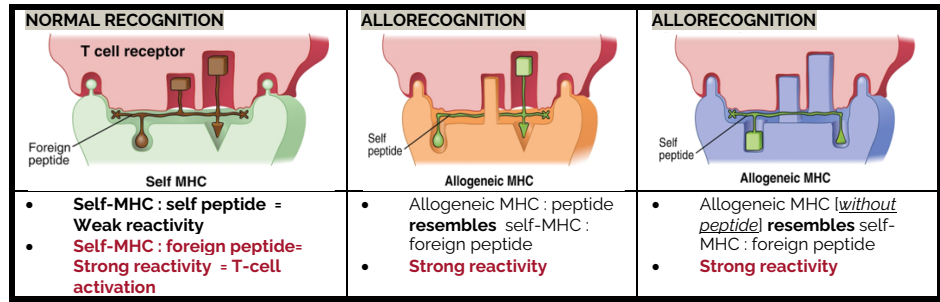
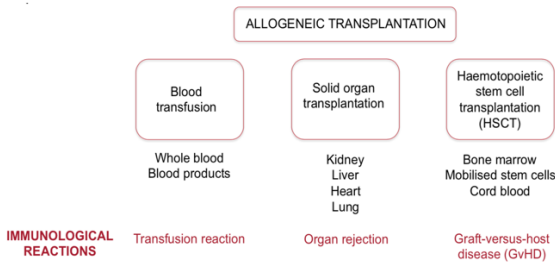
Neutrophils and NETosis (SLE)

NEUTROPHIL EXTRACELLULAR TRAPS (NETs) TRIGGER AUTOIMMUNE RESPONSE



Type I Immediate hypersensitivity	Type II Ab-mediated (high IgM = high complement activation)	Type III Immune-complex	Type IV Cell-mediated (delayed hypersensitivity)
IgE-mediated IL-4 = switch B cell class to IgE	Autoantibodies react with self-antigens present on cell surfaces or in ECM to induce: - Phagocytosis or complemented mediated lysis - Inflammation - Inhibit cell function	- Antigen combines with antibody (IgG1: IgM) to create small immune <u>complexes</u> that deposit in <u>endothelial vessel walls</u> + <u>ACTIVATE</u> complement - Leads to: - Cytolysis - Anaphylatoxin - Chemotaxis - Opsonisation	CD8 T cell-mediated → direct killing of cells expressing self-antigen → tissue damage (sustained by immune cells, complement and cytokines) CD4 T cell-mediated → damage mediated by cytokines (esp. IL-17, -22 secreted by Th17 cells = important) which sustain local inflammation - Cytokines involved in CD4 T cell differentiation (IL-10, IL-17)
- Allergic reactions - Asthma	ABO incompatibility AHA → Antibodies/complement opsonise RBCs (e.g. via Rh Factor) or platelets for phagocytosis Pernicious Anaemia (parietal cells) Vasculitis → ANCA (anti-neutrophil cytoplasmic Abs) Goodpasture's [Anti-GBM against kidney glomeruli and lung alveoli → release complement byproducts (C5a, C3a) for neutrophil recruitment + tissue damage] Myasthenia gravis [Self-reactive B cells produce autoantibodies to eliminate AChR → progressive muscle weakness] Graves' disease [B cells produce stimulating anti-TSHR antibodies]	SLE (HLA DR2/3) - Neutrophils in SLE prone to netosis to form NETs → releases DNA PDC (plasmacytoid dendritic cell) release IFNα → drive inflammation - complement activation → tissue damage RA PSGN Subacute IE IgA nephropathy Hypersensitivity pneumonitis CLASSICAL PATHWAY Antigen: Antibody complexes ↓ COMPLEMENT ACTIVATION	T1DM (CD8 against pancreatic islet B-cells) RA (CD4 against antigens localised in joint synovium) (HLA DR1/4) Citrullinated peptides (a.k.a. neo-antigenic peptides e.g. rheumatoid factor - RF) become self-antigens → inflammation and damaged synovium → RA MS (CD4 against myelin sheath + can enter brain via BBB for CNS demyelination) IBD (CD4 against intestinal floral antigens – dysfunctional epithelial barrier → inflammation w/ relapsing flares) Hashimoto's thyroiditis [CD4 & CD8] - Psoriasis - Graft rejection – acute on chronic organ rejection - Contact dermatitis - Poison Ivy - Steven-Johnson Syndrome - TB - Scabies pruritus
Generally treat with: - Immunosuppressant (steroids) - Anti-TNFα (infliximab)			

Explain role of blood group antigens, histocompatibility antigens, and pre-existing antibodies in immune reactions against the graft



3 fundamental problems in transplantation:

1. Introduced transplant performs its normal function
2. Maintain health of both recipient and transplant during and after surgery
3. Prevent the recipient's immune system from responding to transplant

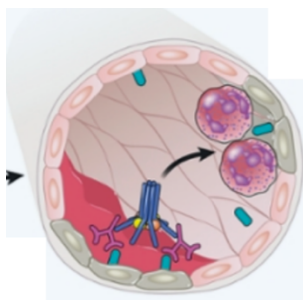
Transplantation:

- Autologous
 - Syngeneic
 - **Allogeneic**
- Histocompatibility**
- Immune-mediated rejection**

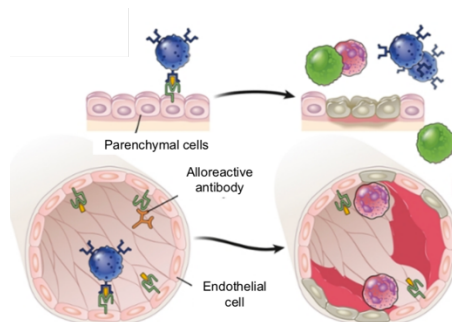
CHALLENGES	OVERCOMING THE CHALLENGE
Ischemia (cadaveric)	Organ preservation
Time to transplantation	Logistics (transport networks)
Histocompatibility	Donor selection, matching, immunosuppression
Pre-existing immune response to the graft [i.e. autoimmune responses]	Recipient preparation
Graft survival	Immunosuppression to prevent rejection
Stress to donor organ (trauma; death; ischemia)	Improved organ preservation
Stress to recipient (underlying disease often immune-mediated; surgery)	Careful selection criteria

MAIN CAUSES FOR REJECTION IN TRANSPLANTATION

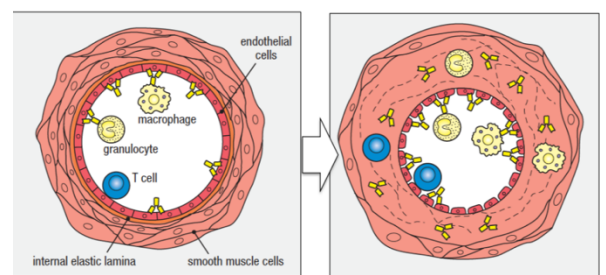
Type of reaction	Underlying mechanisms	Reaction directed against	Effect
Hyperacute rejection (solid organs); Type II reaction [hypersensitivity]	Pre-existing donor-specific Antibodies due to <i>previous blood transfusion, organ transplant, multiparous women</i>	Blood ABO & HLA-A,B,C on graft vasculature	1. Antibodies bind to vascular endothelium of graft → 2. Complement activation → endothelial damage → 3. inflammation → thrombosis (vessel occlusion) 4. Rejected graft due to ischaemia
Acute rejection (solid organs); Type IV reaction [cell-mediated]	By recipient CD8, CD4 T cells (Antibodies)	Adaptive immune response to graft alloantigens (HLA class I & II)	Acute cellular and/or vascular rejection 1. Parenchymal cell damage → Interstitial inflammation 2. Endotheliatis [<i>vascular rejection</i>] 2 types – where do DCs come from? 1. Direct alloreognition [from graft] = allogenic MHC molecules present on graft DCs [short-window] 2. Indirect alloreognition [from host] = Graft antigens presented to recipient dendritic cell
Chronic rejection (solid organs); complex	By recipient CD8, CD4 T cells (Antibodies)	Adaptive immune response to graft alloantigens (HLA, non-HLA)	Immune reaction + HTN + chronic drug toxicity 1. Chronic inflammatory reaction in vessel wall 2. Intimal SMC proliferation 3. Vessel occlusion
Acute GvHD (HSCT)	Effector T cells in graft attack recipient tissues	Effector T cells on the graft	Donor organs attacks recipient cells
Chronic GvHD (HSCT)	Adaptive immune response of graft against recipient tissues	Adaptive immune response to recipient alloantigens (HLA, non-HLA, minor histocompatibility antigens)	Newly developed immune cells created by graft • 2 forms: acute and chronic • Affect skin, liver, GIT, lung



Type II Reaction



Type IV reaction



Chronic rejection

Do all transplants require HLA matching and immunosuppression?

Which organ is transplanted? (anatomy; function; vasculature):

- **Cornea of eye** can be transplanted without HLA matching with minimal immunosuppression (since active tolerance maintained in the anterior chamber)
- **Liver transplantation** (*good outcomes across HLA-I and II mismatch*): ONLY ABO blood groups need to be assessed → Liver creates its own tolerogenic environment?; hepatocytes express low HLA class I and no HLA class II CsA/tacrolimus improve outcomes
- **Bone marrow** – most sensitive to HLA mismatch → **IS for prophylaxis** and **treatment of GvHD** (acute; chronic – affect skin, liver, GIT)

What organs/tissues can be given?

Organs	Deceased donor	Living donor
Kidney, liver, lung		
Heart, small intestine		
pancreas		Islet cells only
Tissues		
Blood & bone marrow		
Cornea & skin		

Histocompatibility

Pre-transplant testing:

1. **HLA typing** (Donor-recipient matching) via PCR, DNA sequencing
 - o HLA-A2, B2 and DR2 = main HLA alleles from Chr 6 cross matched and tested
2. **Recipient:** identify broadly reactive anti-HLA antibodies (% panel reactive antibody)
 - o Higher % = higher risk of hyperacute and acute rejection (preformed antibodies)
3. **Donor-recipient cross-matching** (functional assay):
 - o recipient serum mixed with donor lymphocytes prior to transplantation;
 - o **Positive cross-match** = high risk of hyperacute rejection

Immunosuppression

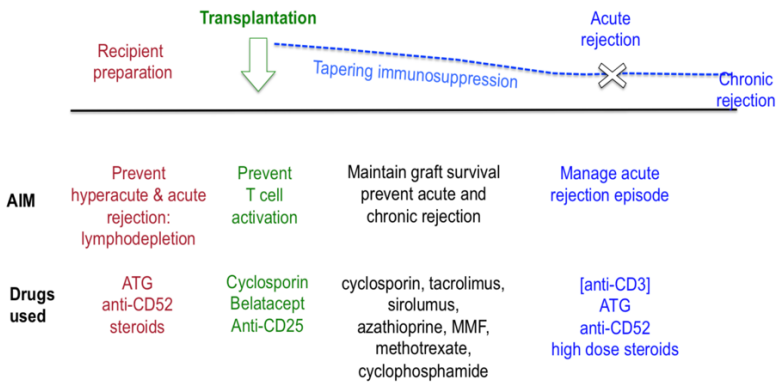
- Large Patients numbers → often some HLA mismatch (some potential for rejection) → managed with Immunosuppressive drugs that block T cell activation/differentiation in different ways
- Have to minimise side effects
- **Immunosuppression is not antigen-specific but broad suppressions of entire immune system** (unlike vaccinations)
 - o **Susceptibility to infection** → CMV infection (most common atypical pneumonia post-transplant)
 - o **long term** = increased risk of certain cancers – lymphomas, osteosarcomas

RED BLOOD CELL COMPATIBILITY TABLE

Recipient	O-	O+	A-	A+	B-	B+	AB-	AB+
Donor								
O-	✓	✗	✗	✗	✗	✗	✗	✗
O+	✓	✓	✗	✗	✗	✗	✗	✗
A-	✓	✓	✓	✗	✗	✗	✗	✗
A+	✓	✓	✓	✓	✗	✗	✗	✗
B-	✓	✗	✗	✗	✓	✗	✗	✗
B+	✓	✓	✗	✗	✓	✓	✗	✗
AB-	✓	✗	✓	✗	✓	✗	✓	✗
AB+	✓	✓	✓	✓	✓	✓	✓	✓

O = universal donor
AB = universal receiver

Explain the rationale behind the use of specific drugs at different stages of transplantation



Pre-transplant /acute reaction drugs

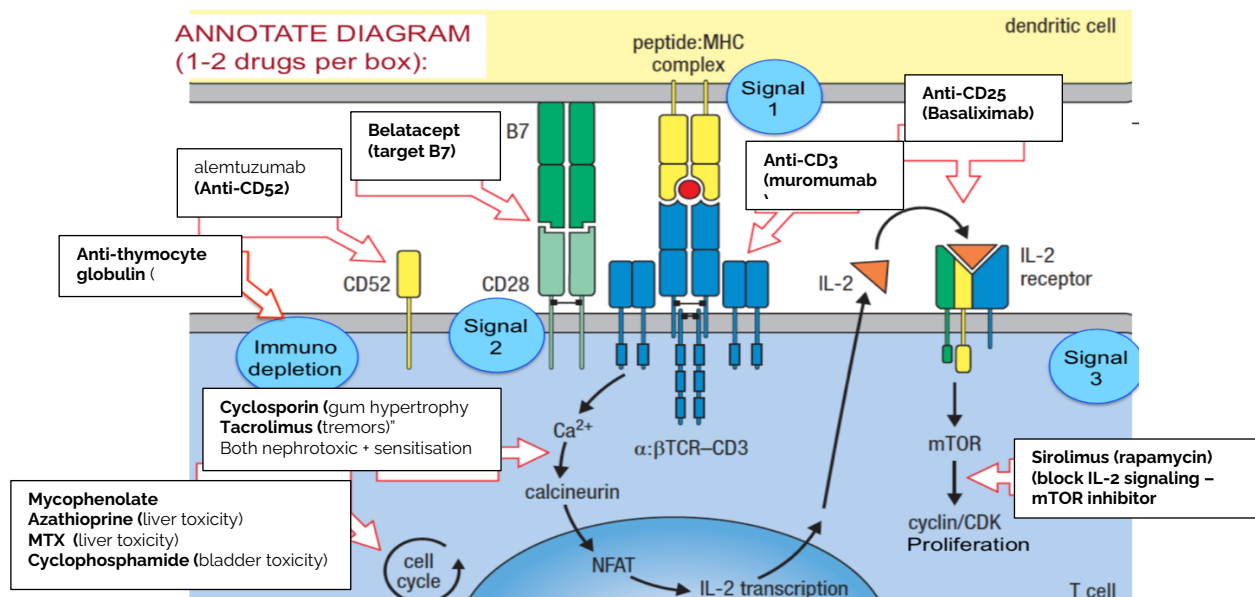
- **Steroids (prednisolone)** – prodrug for short-term usage → acts by preventing activation of NFκB – reduce inflammatory cascade
- **Anti-CD52** (alemtuzumab) – binds and blocks CD52 expressed on inflammatory cells
- **Anti-thymocyte globulin** (Atg) – binds to and depletes T cells

Targetting strategy:

1. **Block TCR signal (stop IL-2 transcription)** – tacrolimus, cyclosporin, muromumab
2. **Block co-stimulation** – belatacept, ,
3. **Block IL-2 stimulation** – sirolimus, basiliximab

Post-transplant drugs:

- **azathioprine (prodrug)** – blocks lymphocyte proliferation by inhibiting purine synthesis
- **Mycophenolate Mofetil (prodrug)** – blocks lymphocyte proliferation by inhibits guanine nucleotide synthesis
- **Cyclophosphamide (prodrug)** – alkylating agent – stops DNA cross-linking
- **MTX** – inhibits folate synthesis – prevents DNA replication



Vaccination in Australia

Describe the population level health impact of vaccination

Key points:

- Vaccination is active immunity that is synthetically acquired → essential to protect populations from infectious diseases
- Coverage in **children** in Australia is **high**.
- Adult** vaccination coverage rates are **sub-optimal** (esp. 18-65) → esp. flu and pneumococcal (*only free for certain patient groups*)
- Ongoing surveillance is important.
- Factors affecting the uptake of vaccine are context specific and differ between adults and children / diff. countries etc.

Vaccine benefits	Disadvantages	Live vaccines	Common childhood diseases:
- Simple + safe Health economics: Cost-effective + safe Reduces morbidity and mortality + economic + social costs Aim for herd immunity → sufficient pop. Immunized to minimise spread even among unvaccinated Aim to eradicate disease	> 1 dose may be required - Given via injection Common side effects: - pain, redness and/or swelling at injection site Serious side effects: anaphylaxis, sepsis	- MMR - Zostavax - Rotavirus (PO) - Varicella Vaccine preventable Most → least common - Influenza - Whooping cough - Meningococcal - Measles (most contagious) - Rotavirus (Highly contagious → N/V/D + fever) - HPV (Gardasil) = Increasing HPV coverage in adolescence	Diphtheria [corynebacterium]: grey-white membranes over tonsils (like Scarlet Fever), barking cough, swollen LN (submental) Mumps [RNA paramyxovirus]: 2° to parotidomegaly, fever, myalgia, headache, fatigue Measles [airborne]: triad of 'c' [cough, conjunc, coryza] + rash, fever, Koplik's spots in mouth Watch for those born in 70 and 80s & unvaccinated children travelling overseas to endemic countries (e.g. Israel) Rubella: rash across trunk and limbs + fever and generalised LN (occipital, cervical) + forchheimer spots (petechiae on uvula/soft palette) Patent ductus arteriosus Scarlet fever: red bumpy tongue, sandpaper rash, fever, sore throat, headache, LN

Beware if splenectomy performed → **MUST**

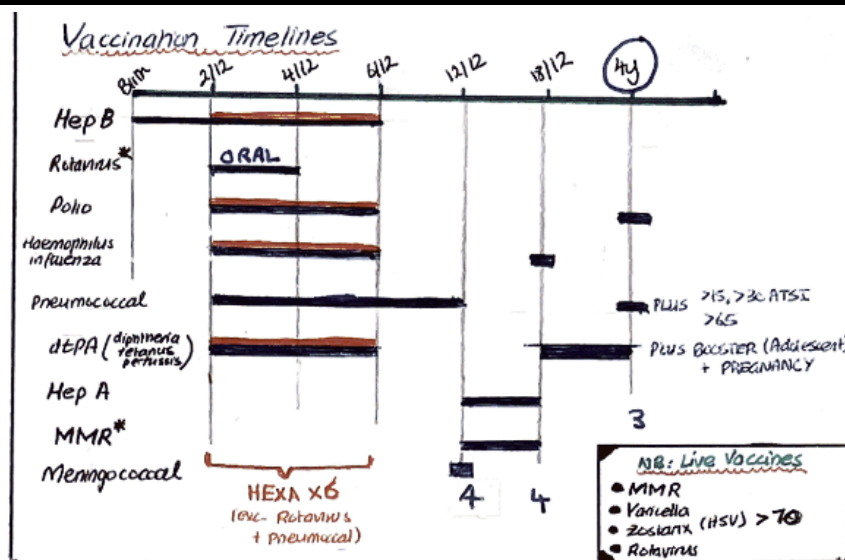
vaccinate against capsulated organisms:

- Strep pneumoniae
- Neisseria meningitidis

Evaluate the implementation of vaccination policy in key populations

Vaccine term	Definition
Vaccine efficacy (RCT)	reduction in incidence of disease in vaccinated group compared to unvaccinated under optimal conditions (%).
Vaccine effectiveness	How well a vaccine prevents negative outcomes in "real world" settings
Vaccination coverage	Important measure of program success in adults → managed by Australian Immunisation Register (AIR) - Inc. vaccines given via National Immunisation Program, through school programs and privately

	Children	Adults
National Immunisation Program (NIP)	vaccines against 17 diseases, including measles, mumps and whooping cough	Pneumococcal (> 65, ATSI >50 OR those with specific med. Conditions) Herpes Zoster (live → 70-79 y.o.) Influenza (>65 or < 65 w/ comorbidities, ATSI >15y.o.)
Factors impacting vax	- Safety & Awareness - Accessibility - Perceived risk & susceptibility Attitudes and Beliefs [Parent acceptability of HPV vaccine driven by attitudes and beliefs regarding the vaccine's effectiveness and safety]	- Safety - Awareness - Access (location) - Perceived risk & susceptibility - Attitudes and Beliefs Prioritisation (what is important them?) GP recommendation
Coverage	Coverage in children in Australia is high	- Influenza & pneumococcal vaccination coverage highest in Remote and Very remote areas (57%) → likely due to special clinics targeting remote areas [increased ACCESS] 51% of >65 years immunised against pneumococcal and influenza



NSW Immunisation Schedule

Funded October 2021



Childhood vaccines			
Age	Disease	Vaccine	Information
Birth	Hepatitis B	H-B-VAX II OR ENGERIX B (IM)	Within 7 days of birth (ideally within 24 hours)
6 weeks	Diphtheria, tetanus, pertussis, <i>Haemophilus influenzae</i> type b, hepatitis B, polio	INFANRIX HEXA (IM)	ROTARIX: Dose 1 limited to 6-14 weeks of age BEXSERO: Prophylactic paracetamol recommended. Catch up available for Aboriginal children <2 until 30/06/2023
	Pneumococcal	PREVENAR 13 (IM)	
	Rotavirus	ROTARIX (Oral)	
	Meningococcal B (Aboriginal# children only)	BEXSERO (IM)	
4 months	Diphtheria, tetanus, pertussis, <i>Haemophilus influenzae</i> type b, hepatitis B, polio	INFANRIX HEXA (IM)	ROTARIX: Dose 2 limited to 10-24 weeks BEXSERO: Prophylactic paracetamol recommended. Catch up available for Aboriginal children <2 until 30/06/2023
	Pneumococcal	PREVENAR 13 (IM)	
	Rotavirus	ROTARIX (Oral)	
	Meningococcal B (Aboriginal children only)	BEXSERO (IM)	
6 months	Diphtheria, tetanus, pertussis, <i>Haemophilus influenzae</i> type b, hepatitis B, polio	INFANRIX HEXA (IM)	Children ≥6 months with at risk conditions for IPD‡ are recommended to receive an additional dose of PREVENAR 13 – see AIH* Aboriginal children ≥6 months with certain at risk conditions may require an additional dose of Bexsero – see AIH*
12 months	Meningococcal ACWY	NIMENRIX (IM)	Bexsero: Prophylactic paracetamol recommended. Catch up available for Aboriginal children <2 until 30/06/2023
	Pneumococcal	PREVENAR 13 (IM)	
	Measles, mumps, rubella	MMR II OR PRIORIX (IM or SC)	
	Meningococcal B (Aboriginal children only)	BEXSERO (IM)	
18 months	Diphtheria, tetanus, pertussis	INFANRIX OR TRIPACEL (IM)	
	Measles, mumps, rubella, varicella	PRIORIX TETRA OR PROQUAD (IM or SC)	
	<i>Haemophilus influenzae</i> type b	ACT-HIB (IM OR SC)	
4 years	Diphtheria, tetanus, pertussis, polio	INFANRIX-IPV OR QUADRACEL (IM)	Children with at risk conditions for IPD‡ are recommended to receive an additional dose of PNEUMOVAX 23 – see AIH*

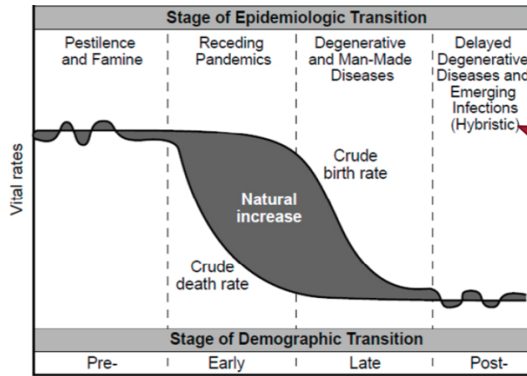
At risk groups, adolescents and adults			
Age/group	Disease	Vaccine	Information
All people with asplenia, hyposplenia, complement deficiency and treatment with eculizumab	Meningococcal ACWY	NIMENRIX (IM)	See AIH* for required doses and timing Additional groups are recommended to receive these vaccines but these are not funded
	Meningococcal B	BEXSERO (IM)	
>5 years with asplenia or hyposplenia	<i>Haemophilus influenzae</i> type b	ACT-HIB (IM or SC)	If incompletely vaccinated or not vaccinated in childhood
Year 7	Diphtheria, tetanus, pertussis	BOOSTRIX OR ADACEL (IM)	
	Human papillomavirus	GARDASIL 9 (IM)	
Year 10	Meningococcal ACWY	NIMENRIX (IM)	
Pregnant	Influenza	INFLUENZA	Influenza: Any trimester
	Pertussis	BOOSTRIX OR ADACEL (IM)	Pertussis: each pregnancy between 20-32 weeks
Aboriginal people ≥50 years	Pneumococcal	PREVENAR 13 (IM) then PNEUMOVAX 23 (IM)	Prevenar 13: ≥50 years Pneumovax 23: 2-12 months later Pneumovax 23: at least 5 years later
70 years	Pneumococcal	PREVENAR 13 (IM)	Pneumococcal funded for people ≥70 Zoster: Catch up available for 71-79 year olds until 31/10/2023
	Zoster	ZOSTAVAX (SC)	
People with at risk conditions for IPD‡	See the online AIH* for conditions recommended to receive PREVENAR 13 and PNEUMOVAX 23		

Influenza		
Age/at risk condition	Recommendation	Information
All children 6 months <5 years	ANNUAL INFLUENZA VACCINATION	For vaccine brands and eligibility see: www.health.nsw.gov.au/immunisation/Pages/flu.aspx
Aboriginal people ≥ 6 months		
People with at risk conditions ≥6 months		
≥65 years		
Pregnant women		

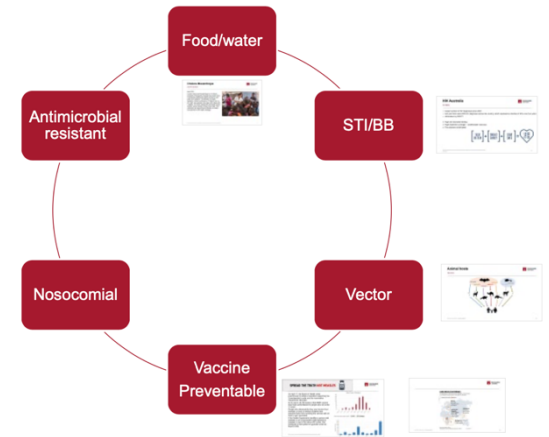
The term Aboriginal is inclusive of Aboriginal and Torres Strait Islander people.
‡ IPD: Invasive pneumococcal disease. *AIH: Online Australian Immunisation Handbook.

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Current status of infectious (communicable) diseases



*COVID-19, alzheimer's = **post phase** of demographic transition



Key measures	Significance
Individual case counts	For statistics to measure level of infection to assess effectiveness of control
Prevalence rate (compare Pop.)	# of cases at point (period) / Population at time during which cases were ascertained
Incidence rate (compare Pop.)	# of new cases/ Population at risk × time during which cases were ascertained & the population group (e.g. # of women aged 15-44, total births, total live births etc.)
Case fatality ratio (rate)	# of deaths/number with condition of interest (i.e. symptomatic or infected?)
Years life lost (YLL)	gap in years from disease free life expectancy
Disability adjusted life years (DALY)	quantifies burden of disease – combines quality (health) and years of life lost

Terminology	Significance	Continued intervention	Disease example
Control	Reduce disease incidence, prevalence, morbidity or mortality to a locally acceptable level	Required (e.g. social distancing)	
Elimination of disease	Reduce to zero incidence of a specified disease	Required	Polio, smallpox, rubella (german measles), malaria (if in Australia), neonatal tetanus
Elimination of infections	Reduce to zero incidence of infection caused by a specific agent (regardless of getting disease or not)	Required to prevent re-establishment of transmission	Measles (if there is documented surveillance system w/ no cases in 12 mths) HIV mother to child transmission
Eradication	Permanent reduction to zero of worldwide incidence of infection	NOT needed	Smallpox
Endemic	Disease always present in a region		HIV, TB, chicken pox (varicella) Malaria
Epidemic	Affects a greater number than expected		Gonorrhoea, measles, Ebola, smallpox
Pandemic	Epidemic that spreads across a region		COVID-19, SARS
Cluster	≥2 cases (not in same household) but common source not yet established		
Outbreak	≥2 cases (not in same household) from specific group or time period associated with common source known		Cholera, COVID-19 = single case of contagious disease may be considered an outbreak

Apply concepts of infectious disease surveillance to describe outbreaks

Surveillance

Systematic collection of data on the occurrence of communicable diseases

Objective of surveillance

- Monitor disease trends
- Detect outbreaks (e.g. COVID-19, influenza)
- Assess effectiveness of prevention & control measures
- Identifying disease risk factors
- Formulating prevention strategies

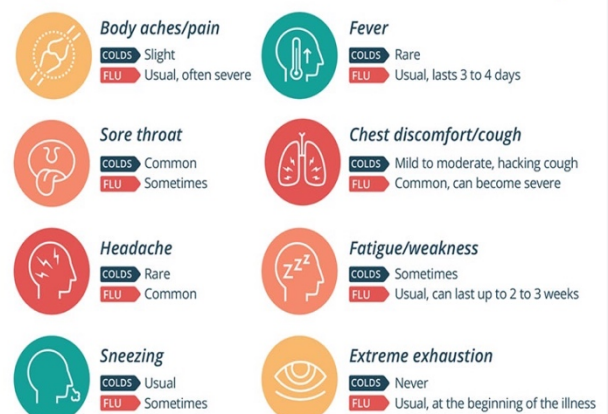
Decreasing STI/BBV rates

- High and increased testing
- High treatment coverage – undetectable viral load
- Pre-exposure prophylaxis

COVID-19 rates:

- Reduced influenza cases (2020)
- Individual cases
- Clusters
- Outbreaks

Understand the symptoms



Outbreak Investigation

Outbreak: “occurrence of disease cases in **EXCESS** of normal **expectancy**”

Examples:

- 1 Ebola case in US
- 2x influenzas cases in Aus. winter
- 5x Gastro cases in

Steps of an outbreak investigation (CDC) → many of steps happen **CONCURRENTLY**

1. Prepare for field work 2. Establish outbreak existence 3. Verify diagnosis	Is this an outbreak? • Expected incidence of disease vs # currently infected • Severity of the disease & transmissibility potential Confirm diagnosis • Identify causative disease + confirm that it IS an actual increase (based on clinical features, lab results – sub-typing and descriptive statistics)				
4. Construct working case definition/criteria WHO, WHAT ,WHERE, WHEN?	• Standard Criteria classifying people as possible outbreak case (inc. S+S, lab results, person, place & time) • Consistency = Must use SAME criteria → Can be probable or confirmed A case was initially defined as • Person: any person who ate breakfast • Place: at the implicated restaurant • Time: between the 10 February and 25 February 2014 Probable case definition= 'any person who ate at the restaurant 10 February and 25 February 2014 and developed symptoms of gastroenteritis, defined as two or more gastrointestinal symptoms'. Confirmed case definition= 'any person who ate at the restaurant 10 February and 25 February 2014 and developed symptoms of gastroenteritis, defined as two or more gastrointestinal symptoms and had a faecal sample that was positive for <i>Salmonella</i>'.				
5. Find cases systematically & record info [contact tracing]	• Identifying cases w/ help from clinicians, hospitals, labs, affected → may need to issue public media alert • Recording info: demographics (i.e. age, sex, address), clinical info (S+S – duration), possible exposures (i.e. close contacts)				
6. Use descriptive epidemiology 7. Develop hypotheses	• Describe outbreaks → person, time, place (epidemiology) ◦ Create an epidemic curve: # of cases in an outbreak, plotted over time • Hypothesis → what do you know about the disease? ◦ Contact affected → e.g. interviews with confirmed & probable cases of Salmonella ◦ Use info gathered to develop hypothesis & test it ◦ E.g. Case control study was developed based upon the restaurant's breakfast menu to determine causes of salmonella outbreak				
Point-source outbreak E.g. COVID, Flu Person to person E.g. Food-borne outbreak					
8. Refine and re-evaluate hypothesis epidemiologically 9. Compare & reconcile w/ lab and/or environmental studies	• Epidemiological study designs: case control, cohort, descriptive → IDENTIFY CAUSE <table border="1"> <thead> <tr> <th>Case-control</th><th>Cohort Study</th></tr> </thead> <tbody> <tr> <td> • Based on disease status (cases & controls) • Generates odds ratio → measure of association • OR = 1.0 shows the same odds of exposure • OR > 1.0 shows a higher odds of exposure among ill (e.g. OR = 5 → 5x risk of being exposed → ill) </td><td> • Based on exposure status (exposed vs. non exposed) • Must be include every person in cohort (i.e. wedding) • Generates a relative risk as a measure of association • RR = 1.0 shows the same risk in exposed and unexposed • RR > 1.0 shows risk is higher in those exposed </td></tr> </tbody> </table>	Case-control	Cohort Study	• Based on disease status (cases & controls) • Generates odds ratio → measure of association • OR = 1.0 shows the same odds of exposure • OR > 1.0 shows a higher odds of exposure among ill (e.g. OR = 5 → 5x risk of being exposed → ill)	• Based on exposure status (exposed vs. non exposed) • Must be include every person in cohort (i.e. wedding) • Generates a relative risk as a measure of association • RR = 1.0 shows the same risk in exposed and unexposed • RR > 1.0 shows risk is higher in those exposed
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10. Implement control measures	• As early as possible → can include (beware of confidentiality): ◦ Sending warning/advice about control/prevention to clinicians ◦ Quarantine ◦ Recall of contaminated products ◦ Recommendations (e.g. decrease temp. in storage fridge or don't use eggs in salmonella outbreak)				
11. Initiate/maintain surveillance	• Determine control of outbreak and effectiveness of prevention/control measures • Level of surveillance depends on infectivity and severity of illness (e.g. active case findings in Ebola is critical)				
12. Communicate Findings	• Clinicians LEGALLY required to report & record on Notifiable Disease Data [Public health law] ◦ E.g. influenza, HIV, foodborne illness (> 2 linked cases) • Public Health officials may reach out to clinicians during active case finding → detect those who could be infected + linked ◦ Media attention may be required • Outbreak MDT debriefings (inc. lab personnel, public health team, env. Health officers etc.)				