Infectious Disease

Cytomegalovirus (CMV)
- Common (80% of all adults) usually asymptomatic herpesvirus (HHV5) infection
  - transmitted via bodily fluids e.g. kissing, intercourse
- Symptoms - mild flu-like / EBV-like illness (no pharyngitis or lymphadenopathy)
- Congenital infection (late effects) - deafness, neurological damage, chorioretinitis, jaundice
- Investigations - IgM / IgG, PCR, biopsy (intranuclear inclusions)
- Management - consider IV ganciclovir (also oral as prophylaxis e.g. transplant recipients)
- Complications - Guillain-Barré, encephalitis, pericarditis, GI ulceration, haemolysis

Hepatitis
- Hep. A (RNA virus) - advancing age most significant determinant of severity
  - faecal-oral spread; 2-6wk incubation; transmission highest at 2-3wks; no carrier state
  - prodrome (mild) - low fever anorexia, nausea, fatigue, joint pain, diarrhoea
  - icteric phase - dark urine / pale stools, jaundice (85%), abdominal pain; lasts up to 1yr
  - investigations - IgM (positive for 3-6 months), IgG (positive for life)
  - complications - AIH, fulminant hepatitis, relapsing infection, death (0.2% mortality)
- Hep. E (RNA virus) - as above but may be fatal in pregnancy and causes stillbirth
- Hep. B (dsDNA virus) - commonest worldwide cause of hepatitis
  - blood-borne spread; 2-3 month incubation; chronic infection more likely if young
  - surface antigen (HBsAg) - positive around 4-5wks post-infection; persists if chronic
    - non-infective if HBsAg undetectable; anti-HBsAg IgM in isolation implies vaccination
  - E-antigen (HBeAg) - positive for up to 3 months post-recovery; marker of high infectivity
  - anti-HBcAg IgM - positive around 10wks post-infection; imply acute or past infection
  - symptoms (insidious) - flu-like illness, jaundice (up to 50%), malaise (severe)
  - chronic infection (up to 10%) - risk of cirrhosis, HCC; benign in healthy non-drinkers
  - management (chronic) - if high HBV DNA consider pegylated interferon SC weekly
  - post-exposure prophylaxis (within 48hrs) - hep. B immunoglobulin (HBIG)
- Hep. D (defective RNA virus) - requires HBV (HBsAg) to replicate - 5% of HBV carriers
  - substantially increased risk of cirrhosis (80%) and fulminant hepatic failure
- Hep. C (RNA virus) - 6 genotypes - type 1 commonest in UK, most resistant
  - blood-borne spread esp. IVDU; 6-9wk incubation; chronic infection in up to 85%
  - acute infection usually asymptomatic; chronically may be malaise, anorexia
  - investigations - HCV serology (positive 3-9 months post-exposure) / RNA
  - management - pegylated interferon SC weekly / ribavarin PO (up to 50% effective)
  - complications - cirrhosis (30% in 30 years), HCC, fulminant hepatic failure
  - associations - DM, Sjögren’s, PAN, AIH, thyroiditis, PCT, ITP, glomerulonephritis
Herpes virus

Herpes simplex (HSV)

- Transmission via break in mucous membrane or skin esp. mouth, eye, genitals
  - HSV-1 - widespread infection by aged 2 years, primarily oral infection e.g. cold-sores
  - HSV-2 - with onset of sexual activity, primarily genital infection
- Primary infection - asymptomatic, vesicles, viraemia, life-long latent systemic infection
  - reactivation from CNS sensory ganglia caused by injury, UV light, stress, hormones
- Manifestations:
  - gingivostomatitis - HSV-1, yellow pus-filled mouth ulcers on tongue, palate, gums, lips
  - genital herpes - neuropathic genital pain, genital blisters / ulcers, PV discharge, dysuria
  - herpetic whitlow - solitary finger vesicle e.g. in children’s nurses
  - dendritic ulcer - infectious keratitis causing corneal erosion; sight-threatening
  - eczema herpeticum - superinfection of eczema in children
  - encephalitis - HSV-1 causing fever, seizures, headache, dysphasia, hemiparesis
  - also meningitis - HSV-2, self-limiting; herpes gladiatorum - traumatic vesicles
- Investigations - PCR, viral culture, antibody titres; consider aciclovir if severe

Varicella zoster (chickenpox)

- Highly infectious herpesvirus (HHV3) infection commonly affecting children under 5 years
- Symptoms (after 14 days incubation) - pyrexia, headache, vesicles (relative limb sparing)
  - highly pruritic rash, crusts form and shed, no long-term scarring in children
- Management - fluids, avoid contact with pregnant women / young babies; Ig in pregnancy
- Complications - superinfection / TSS, pneumonia, encephalitis, ataxia, osteomyelitis

Herpes zoster (shingles)

- Reactivation of VZV from CNS sensory ganglia affecting isolated dermatome (esp. thoracic)
- Risks - increasing age, physical or emotional stress, immunocompromise
- Pre-eruptive phase - burning / itching / paraesthesia, no skin lesion, tenderness, malaise
- Eruptive phase - erythematous swelling, plaques, vesicles; acute neuritic pain lasting weeks
- Management - oral aciclovir for 1 week if severe; consider adjunctive prednisolone
- Complications - ophthalmic VZV may cause blindness
- Post-herpetic neuralgia (PHN) - persistent pain 30 days after all lesions crusted
  - significant correlation of incidence with increasing age
  - consider capsaicin, TCAs, gabapentin, methylprednisolone
HIV

- Virus binds to CD4 receptors, CD4 cells migrate to lymphoid tissue and replicate
  - transmission - 0.3% percutaneous exposures, < 0.1% mucocutaneous exposures
  - *seroconversion* (1-6wks) - EBV-like illness, fever, myalgia, headache, lymphadenopathy
  - later - persistent generalised lymphadenopathy (PGL), night sweats, weight loss
- Diagnosis - PCR (p24 antigen, HIV RNA) in early infection; ELISA (IgG anti-HIV antibodies)
- Staging - CD4 count and clinical category A (PGL), B (symptomatic, ARC), C (AIDS)
  - AIDS - CD4 count < 200 or ADI e.g. post-oral candidiasis, CMV, Kaposi’s sarcoma, lymphoma, TB, *pneumocystis jirovecii* pneumonia, cerebral toxoplasmosis

Management - ART if CD4 count < 350 / CNS pathology / ADI
  - initial ART - efavirenz (NNRTI) / tenofovir (NRTI) / emtricitabine (NRTI); PI second-line
  - immunisations - hep. B, pneumococcus, HiB, influenza; no live vaccinations
  - chemoprophylaxis - consider *isoniazid* if high risk for TB, *co-trimoxazole* if AIDS

Post-exposure prophylaxis (PEP) - 2x NRTIs with a PI for 4wks, ELISA 12wks later

- Lipodystrophy syndrome - fat redistribution, insulin resistance, dyslipidaemia
  - risks - PIs / NRTIs in combination, female sex, long duration of disease / treatment
  - symptoms - buffalo hump, neck widening, breast hypertrophy, truncal obesity, fat loss in face / arms / buttocks, superficial venous prominence, emaciation
  - management - lifestyle (Mediterranean diet), metformin, pravastatin, ART changes

Anti-retroviral treatment (ART)

- NNRTIs (efavirenz, etravirine) - may cause SJS, hypercholesterolaemia, hepatitis
- NRTIs (zidovudine, abacavir, tenofovir) - may cause GI upset, headache, blood disorders
- Protease inhibitors (atazanavir, ritonavir) - may cause GI upset, hyperglycaemia, bleeding
- Others - fusion inhibitors (enfuvirtide), *CCR5 antagonists* (maraviroc), *integrate inhibitors*

Leptospirosis (Weil’s disease)

- Caused by *Leptospira* (rat / dog / cattle / wild animal infecting spirochaete) excreted in urine
  - incubation period 1-2wks; *anicteric* (mild, self-limiting) and *icteric* (Weil's disease) forms
- Risks - male sex, young adults, sewage workers, travellers / swimmers, farmers, vets
- Symptoms - flu-like illness, pneumonitis, arthritis, orchitis, cholecystitis, aseptic meningitis
  - icteric form - jaundice, uveitis, abdominal pain, diarrhoea, purpura / epistaxis
- Investigations - LFTs (deranged), PT (prolonged), FBC (leucocytosis), serology / ELISA
- Management - *doxycycline* or *penicillin G* / chloramphenicol if severe, vitamin K
- Complications - miscarriage, hepatic / renal failure, DIC, haemorrhage, rhabdomyolysis
Lyme disease

- Caused by *Borrelia burgdorferi* (tick-borne spirochaete), transmitted via *Ixodes* (deer) ticks
  - reaction associated with HLA-DR4; in Europe - neurological / dermatological disease
- Symptoms (stage 1, localised) - erythema migrans (circular expanding rash around bite)
  - also fever, lymphadenopathy, arthritis / musculoskeletal pain
- stage 2 (disseminated) - flu-like illness, oligoarthralgia / myalgia, facial palsy, syncope
- stage 3 (late) - gout, vasculitis, meningitis, heart block... myriad manifestations
- Investigations (unreliable) - *B. burgdorferi* antibodies, ELISA, PCR
- Management - doxycycline 100mg bd. for 14 days (IV / 30 days if arthritis / CNS / severe)

Malaria

- Parasitic disease caused by species of *Plasmodium* acquired from infected mosquito bite:
  - *falciparum* - commonest, most severe, incubation 1-2wks, quotidian periodicity
  - *vivax / ovale* - benign, incubation 2-3wks, tertian periodicity (every 3 days)
  - *malariae* - benign, incubation 3-4wks, quartan periodicity (every 4 days)
- *Sporozoites* from mosquito saliva go to liver; dormant as hypnozoites, release merozoites
- Risks - poverty, extremes of age, pregnancy (esp. primigravidae), travellers
- Symptoms (within 6 months if *falciparum* / after 6 months otherwise) - cyclical fever
  - also rigors, headache, cough, myalgia, GI upset, jaundice, hepatosplenomegaly
  - if severe - reduced consciousness, dyspnoea, haemorrhage, seizures
- Investigations - Giemsa blood films, FBC (anaemia, thrombocytopenia), LFTs, glucose
- Management (non-falciparum) - chloroquine (not if G6PD) or quinine for 14 days
  - falciparum - quinine 600mg PO tds. with doxycycline 200mg PO od. for 7 days
  - if severe - quinine IV or artesunate IV with doxycycline as above
  - artemisinin derivatives are most effective but should not be used first-line (resistance)
- Complications - cerebral malaria, acidosis, hypoglycaemia, ARDS, splenic rupture, DIC
- Prophylaxis - Awareness, Bite reduction, Chemoprophylaxis, Diagnosis / prompt treatment
  - highest risk areas - Africa, South America, Asia, Middle East
  - bites most often at night; cover arms / legs / DEET, air conditioning, treated nets
  - options - chloroquine with proguanil, mefloquine, Malarone, doxycycline (up to 2 years)
  - side effects (chloroquine, mefloquine) - nausea, diarrhoea, dyspepsia, pruritis
Measles, mumps and rubella (MMR)

Measles
- Acute *Morbillivirus* (single-stranded RNA) infection; very contagious (respiratory droplets)
  - Symptoms (prodrome) - coryza, conjunctivitis, diarrhoea following 2 week incubation period
    - morbilliform rash - maculopapular, *starts behind ears*, head / neck, spreads down
    - Koplik’s spots - pathognomonic buccal red spots with central white speck
    - also high fever, nonproductive cough, periorbital oedema, photophobia
  - Investigations - saliva / serum measles-specific IgM / RNA
  - Complications - pneumonia (*Staph. aureus*), encephalitis (brain damage), low immunity

Mumps
- Acute paramyxovirus infection affecting *salivary glands* (also pancreas, gonads, brain)
  - Symptoms - bilateral parotitis, swelling, jaw pain, high fever, dry mouth; meningism
  - may be followed by bilateral orchitis - testicular pain, rigors, headache, backache
  - Management - supportive; school exclusion for 5 days post-parotid swelling
  - Complications - unilateral deafness (rare, transient), pancreatitis, infertility; rarely fatal

Rubella
- Acute *Rubivirus* (RNA) infection with 2-3wk incubation; contagious via respiratory droplets
  - Symptoms (prodrome) - lethargy, fever, headache, rhinorrhoea, lymphadenopathy
    - macular rash - face, spreading to trunk and extremities; also palatal petechiae
  - Investigations - saliva sample (specific IgM), FBC (leucopenia, lymphocytosis)
  - Complications - rubella encephalopathy (self-limiting, benign), arthralgia, thrombocytopenia

Meningitis
- Risks - CSF shunt, spinal anaesthetic, endocarditis, DM, alcohol, IVDU, CF, crowding
  - May be predominantly meningitic / septicaemic presentation but usually combination of both
- Meningococcal (*N. meningitidis*) - mostly affects aged < 5 years, in winter
  - Symptoms (early) - leg pain, thirst, diarrhoea, skin changes, dyspnoea, cold peripheries
    - late - fever, headache, neck stiffness, photophobia, petechial rash, altered mental state
    - Kernig’s sign - pain on passive knee extension with hips flexed
  - Investigations - PCR, pharyngeal swab, LP (once ICP confirmed not raised e.g. CT)
  - Management - 4 days IV ceftriaxone / cefotaxime; consider dexamethasone, prednisolone
    - GP - IV benzylpenicillin 300mg (age < 1yr) / 600mg (< 10yrs) / 1200mg (> 10yrs)
    - if atypical pathogens (age < 3m or > 50yrs) - also amoxicillin; with gentamicin if *Listeria*
    - outpatient hearing test 4-6 weeks post-discharge
  - Complications - seizures, coma, hydrocephalus, Addison’s (Waterhouse-Friderichsen), deafness, amputations, developmental problems, renal failure, persistent headache
**MRSA**

- *Staph. aureus* - gram-positive bacterium colonising skin; nasal carriage in 30%
  - up to 3% of population colonised with MRSA - resistant to beta-lactams
  - does not pose risk to healthcare workers or close / family contacts of patients
  - Risks - hospital, surgery, critical / chronic illness, ulcers, IV / catheter lines, antibiotics
- Investigations - PCR for mecA gene
- Management - screen all inpatients with nasal swab; ideally perineal swab also
  - if confirmed infection - barrier nursing, contact precautions, ward alert
  - skin / soft tissue infection / UTI - tetracycline with rifampicin
  - pneumonia / sepsis / endocarditis / arthritis - vancomycin / teicoplanin / linezolid
  - nasal carriage elimination - mupirocin nasal ointment

**Osteomyelitis**

- Infection of bone marrow - may spread to cortex, periosteum (via Haversian canals)
  - may be haematogenous (septic, esp. in children) or contiguous (direct / traumatic)
  - majority *Staph. aureus* (90%); also HiB, *Strep., E. coli, Proteus, Pseudomonas*
- Risks - trauma (inc. surgery), DM, PVD, chronic joint disease, alcoholism, IVDU, steroids
- Symptoms - fever; painful, immobile, erythematous, tender limb
- Investigations - MRI, FBC (leucocytosis), CRP / ESR (high), blood / bone / wound cultures
- Management - flucloxacillin with rifampicin for 4-6wks, initially IV
  - if low risk - also benzylpenicillin; if high risk - also gentamicin / ciprofloxacin
  - Complications - bone abscess, sepsis, fracture, septic arthritis, cellulitis, chronic infection

**Sexually transmitted infections (STIs)**

**Chlamydia**

- *Chlamydia trachomatis* - obligate intracellular gram-negative bacterium
- Symptoms - PV discharge / bleeding, fever, abdominal pain, dysuria, dyspareunia
  - in men - urethritis, urethral discharge, fever, acute epididymo-orchitis
- Investigations - urinary nucleic acid amplification (NAAT), enzyme immunoassays (EIA)
  - national screening offered to all aged < 25, annual checkups / change of partner
- Management - azithromycin 1g PO stat / doxycycline 100mg bd. for 7 days
  - abstain from sex for 1wk post-stat dose, ensure partner is also treated; no test of cure
  - contact tracing - up to last 6 months if asymptomatic
- Complications - PID, infertility, ectopic pregnancy, urethral stricture, Reiter’s, PROM
Gonorrhoea

- *Neisseria gonorrhoeae* - gram-negative diplococcus
- Symptoms - *urethritis* (discharge, dysuria), pruritis ani, abdominal pain, PV bleeding
- Investigations - microscopy, swab / culture and sensitivity, NAAT
- Management - azithromycin 1g PO stat with ceftriaxone 500mg IM stat
  - test of cure - culture after 72hrs / NAAT after 2wks
- Complications - PID, infertility, Bartholin’s abscess, urethral stricture, prostatitis

Syphilis

- *Treponema pallidum* - spirochaete, up to 3wk incubation
- **Primary chancre** - painless papule / ulcer, red margin, clear discharge, lymphadenopathy
- Secondary (6wks later) - non-pruritic rash of palms / soles / face forming *condylomata lata*
  - also alopecia, anterior uveitis, meningitis, hepatitis, glomerulonephritis
- Tertiary - *neurological* (tabes dorsalis, dementia), *cardiovascular* (aortitis, AR, aneurysm)
  - also *gummata* - fibrous nodule / plaque esp. bone, skin
- Investigations - EIA (IgM early, IgG > 5wks), VDRL (staging), PCR
- Management - benzathine penicillin 2.4 ‘mega-unit’ IM or azithromycin 1g PO stat
  - if neurosyphilis - procaine penicillin 2.4 units IM for 17 days with probenecid PO qds.
  - **Jarisch-Herxheimer reaction** - acute febrile illness, treat with prednisolone

Septic arthritis

- Infection of a joint (e.g. synovium), usually knee; common in gout, RA, CTDs, steroids
- Symptoms - swollen painful joint (pain on active / passive movement), fever, rigors, effusion
- Investigations - synovial fluid aspirate / culture, blood culture, STD screen
- Management - IV antibiotics for 2-3wks then oral for further 2-3wks, arthroscopy / drainage

Toxoplasmosis

- Parasitic infection of *Toxoplasma gondii* carried by cats and excreted in cat faeces
  - proliferative tachyzoites disseminate to brain, skeletal and cardiac musculature
- Transmission - ingestion / handling cat faeces, raw meat, organ transplant, maternal-foetal
- Primary infection - often subclinical, encased in cysts
  - malaise, lymphadenopathy, *chorioretinitis* (blurring, floaters), pericarditis, hepatitis
- Congenital infection - miscarriage, hydrocephalus, strabismus, blindness, epilepsy, anaemia
- In immunocompromise - *encephalitis*, pneumonitis, respiratory failure, death
- Investigations - IgG, PCR, blood culture, MRI / CT (*ring-enhancing lesions*)
- Management - 4-6wks of pyrimethamine, sulfadiazine, folinic acid
  - acute maternal infection - spiramycin; pyrimethamine teratogenic in 1st trimester