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Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

HIV: diarrhoea Supportive therapy is the mainstay of treatment in Cryptosporidium diarrhoea • Diarrhoea is common in patients with HIV. Causes • Infection, may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections (usually there are fever and wasting) • Malignancy (infiltrative diseases, such as lymphoma or Kaposi's sarcoma.), • Medications (e.g. antiretroviral therapy, particularly when diarrhea is the sole presenting symptom and there is a temporal association.) Ritonavir-containing protease inhibitors (PIs) are the drugs most commonly associated with diarrhoea. Infectious causes • Cryptosporidium (the most common cause of diarrhoea in HIV patients who their CD4+ > 50) It is an intracellular protozoa and has an incubation period of 7 days. Presents as watery diarrhoea, often with severe abdominal pain, commonly lasting

> 7 days. Diagnosis: usually by detection of Cryptosporidium oocysts, antigens, or DNA in stools. Treatment: Supportive therapy is the mainstay of treatment If patient is not on antiretroviral therapy (ART) : initiation of ART is the primary intervention Nitazoxanide may be used for treatment (Antiprotozoal) • Mycobacterium avium intracellulare is an atypical mycobacteria seen with the CD4 count is below 50. Presentation: fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with combination of clarithromycin, ethambutol and rifabutin

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HIV nephropathy Overview • Accounts for up to 10% of end-stage renal failure cases in the United States. • Renal involvement in HIV patients may occur as a consequence of treatment or the virus

itself. • Protease inhibitors such as indinavir can precipitate intra-tubular crystal obstruction Features • Raised creatinine • Nephrotic range proteinuria • Normal sized kidneys on ultrasound scan, • Focal segmental glomerulosclerosis on renal biopsy. • Raised immunoglobulins • Raised cholesterol • Normotension

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Cryptococcal disease in AIDS (Cryptococcosis) Epidemiology • The most common fungal infection of the CNS • The most common fungal disease in HIV Features • May present as: space-occupying lesion, meningitis, or meningoencephalitis. • Symptoms are typically of gradual onset over one to two weeks. Risk factors • usually develops only when CD4+ lymphocyte counts fall below 100 cells/mL. Diagnosis • MRI, with and without contrast, is the preferred diagnostic imaging modality.

• The India ink test is used to diagnose cryptococcal meningitis, • the raised opening pressure, turbid appearance to the CSF, raised protein and mixed lymphocytic/neutrophil picture are relatively typical of the diagnosis. Treatment • Treatment is with amphotericin B and flucytosine (5FC); • patients then require lifetime suppression with fluconazole. Cryptococcus neoformans skin lesions • Most often seen in T cell deficiency states and HIV-infected patients with CD4 counts of <100/mm3. • Gomori's methanamine silver stain shows budding yeasts. • Serum cryptococcal antigen can also be used in diagnosis. • Treatment is with an eight-week course of fluconazole 400 mg /day followed by 200 mg/day.

HIV: immunisation The Department of Health 'Greenbook' on immunisation defers to the British HIV Association for guidelines relating to immunisation of HIV-infected adults Vaccines that can be used in all HIVinfected adults Vaccines that can be used if CD4 > 200 • Measles, Mumps, • Hepatitis A • Hepatitis B • Haemophilus influenzae B (Hib) • Influenza-parenteral • Japanese encephalitis • Meningococcus-MenC • Meningococcus-ACWY I • Pneumococcus-PPV23 • Poliomyelitis-parenteral (IPV) • Rabies • Tetanus-Diphtheria (Td) Rubella (MMR) • Varicella • Yellow Fever Notes & Notes for MRCP
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Contraindicated in HIVinfected adults • Cholera CVD103-HgR • Influenza-intranasal • Poliomyelitis-oral (OPV) • Tuberculosis (BCG)

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Routine vaccines • People with HIV are at risk of Hep B, invasive pneumococcal disease and severe morbidity from influenza. These are all inactivated vaccines and can be given at any CD4 count. • Should be vaccinated against Hepatitis B, pneumococcus, and yearly against influenza Hepatitis B is given as a course of three injections at double dose and booster as required. pneumococcal vaccine PPV23 is a single dose but could be boosted 510 years later. influenza vaccine should be administered yearly. Other vaccines • Men C vaccine → only recommended in people under 25. • polio vaccine the oral polio vaccine is not recommended in HIV as it is a live vaccine. However, the parenteral polio vaccine is acceptable. • MMR vaccine It is a live vaccine that is

contraindicated in patients with a CD4 count of less than 200 cells/µL but could be safely administered in patient with CD4 count above 200 cells/µL. • Haemophilus influenzae B vaccine is an inactivated vaccine that can be given to patients at any CD4 count. Although Haemophilus influenzae is an issue in people with HIV it is the pneumococcal vaccine that is recommended for all HIV patients. it is only recommended for those who have: splenic dysfunction, recurrent pulmonary infections previous Haemophilus influenzae disease with risk of recurrence. • shingles vaccine thought to be safe and immunogenic even in those who have recently had shingles. However, it must be used with caution in any immunocompromised state should not be used in patients with a CD4 count of less than 200 cells/µL.

HIV: Kaposi's sarcoma Overview • Kaposi sarcoma is a neoplasm of endothelial cells (vascular tumor) that is caused by human herpes virus 8 (HHV-8) • most commonly seen in patients with HIV and transplant patients. can be seen in HIV patients with a CD4+ cell count of less than 500/mm3. • Human herpes virus 8, which causes Kaposi sarcoma in HIV patients, is transmitted by sexual contact. • Aside from affecting the skin, Kaposi sarcoma can also affect the gastrointestinal tract and lungs. Feature • presents as purple papules or plaques on the skin or mucosa (e.g. gastrointestinal and respiratory tract) • lesions occur most commonly on the face

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• skin lesions may later ulcerate • respiratory involvement may cause massive haemoptysis and pleural effusion, Chest x ray may show pulmonary nodules. • Histopathology classically show lymphocytic inflammation. proliferation of endothelial cells (spindle cells) Treatment • Radiotherapy + resection Radiotherapy may be used to treat painful or highly visible lesions. • AIDS-related Kaposi's sarcoma becomes smaller as immune function improves such as with treatment with highly active antiretroviral therapy (HAART). • In some circumstances chemotherapy may be added to HAART. • Human herpes virus 8 is also associated with: primary effusion lymphoma (a rare lymphoma of serous cavities) Castleman's disease. Kaposi's sarcoma in a patient with HIV

HIV: Dermatologic conditions (Eosinophilic folliculitis) (EF) Overview • Dermatologic conditions are very common in HIV/AIDS infection; knowing the common infections and their treatment is important. Types • There are three main variants of Eosinophilic folliculitis (EF): • Classic EF immunosuppression-related EF (mostly HIV-associated) and Infancy-associated EF. • The most common type of EF is the immunosuppression-related (HIV-associated) form. • The clinical presentations of EF vary slightly, but histologically the forms are identical. • Classic EF also known as Ofuji disease (eosinophilic pustular folliculitis) more common in individuals of Japanese descent, although anyone can be affected.

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Infectious diseases • Immunosuppression-EF Differs from the classical form in that the eruption is exquisitely pruritic. It also tends to present with erythematous, almost oedematous, papules with

few pustules (whereas the classic form tends to have clusters of pustules). □ Because the eruption is so pruritic the lesions are often excoriated on presentation, making identification of a primary lesion difficult. □ The lesions are found primarily on the face and upper trunk (from the waist up). □ Histologic examination of a papule shows an acute and chronic infiltrate of eosinophils and lymphocytes focused at the level of the follicular isthmus that can rarely progress to complete follicular destruction. □ Men more commonly affected than women. □ may worsen 3 - 6 months after initiation of antiretroviral therapy as part of the immune restoration syndrome and even after the CD4+ cell count rises above 200/µL.

HIV: abnormal vaginal bleeding • Abnormal bleeding can be a sign of cervical dyskaryosis. • Advanced HIV with HPV co-infection is a very strong risk factor for developing cervical dyskaryosis and currently the British HIV association recommend that patients with HIV should have yearly smears. • The US guidelines recommend that HIV positive females under the age of 26 and MSM should be immunised as the HPV vaccine is safe and immunogenic at all CD4 counts. • The risk of HPV infection already present is too great in patients older than 26 for cost effectiveness. • In Britain the national programme now immunises all females aged 12-13 years. • If cervical dyskaryosis is detected it is treated in the same way as in HIV negative patients. • HIV patients should have a yearly smear as per the current BHIVA guidelines. This may change as more information is gathered about cervical disease in patients who are stable on ARVs. • Cervical dyskaryosis is invisible to the naked eye and so a normal speculum examination does not rule out cervical disease.

CMV retinitis in a patient with HIV • AIDS retinitis is typically caused by cytomegalovirus. The slide shows the typical 'cottage cheese and tomato ketchup' or 'pizza' appearance of CMV retinitis in a patient with HIV disease.

Vaginal discharge Vaginal discharge is a common presenting symptom and is not always pathological Common causes Less common causes • physiological • Candida • Trichomonas vaginalis • bacterial vaginosis • cervical cancer • Black women report higher incidence of candidiasis infections compared with white women. Notes & Notes for MRCP
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• Gonorrhoea • Chlamydia can cause a vaginal discharge although this is rarely the presenting symptoms • ectropion • foreign body

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Key features of the common causes are listed below Condition Key features Candida • 'Cottage cheese' discharge • Vulvitis • Itch Trichomonas vaginalis • Offensive, yellow/green, frothy discharge • Vulvovaginitis • Strawberry cervix Bacterial vaginosis • Offensive, thin, white/grey, 'fishy' discharge

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Bacterial vaginosis (BV) Bacterial vaginosis - overgrowth of predominately Gardnerella vaginalis Pathogen • Bacterial vaginosis (BV) describes an overgrowth of predominately anaerobic organisms such as Gardnerella vaginalis. Epidemiology • BV is the commonest cause of abnormal vaginal discharge in women of childbearing age. It is twice as common as vaginal candidiasis. Risk factors • intrauterine coil device, • vaginal douching • number of sexual partners. • Whilst BV is not a sexually transmitted infection it is seen almost exclusively in sexually active women. Features • vaginal discharge: 'fishy', offensive , Gray, thin, and homogeneous • asymptomatic in 50% • This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH. Diagnosis Epithelial cells with a stippled border (Clue cells) are the hallmark microscopic findings of bacterial vaginosis • Amsel's criteria for diagnosis of BV - 3 of the following 4 points should be present

1. thin, white homogenous discharge
2. clue cells on microscopy: stippled vaginal epithelial cells
3. vaginal pH > 4.5
4. positive whiff test (addition of potassium hydroxide results in fishy odour)

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Management Bacterial vaginosis treatment oral metronidazole • Infection resolves spontaneously in one-third of cases • oral metronidazole (400 mg twice daily given for 5-7 days) initial cure rate 70-80% relapse rate > 50% within 3 months • the BNF suggests topical metronidazole or topical clindamycin as alternatives Bacterial vaginosis in pregnancy • complications results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage • treatment it was previously taught that oral metronidazole should be avoided in the first trimester and topical clindamycin used instead. Recent guidelines however recommend that oral metronidazole is used throughout pregnancy. The BNF still advises against the use of high dose metronidazole regimes Comparison of bacterial vaginosis and Trichomonas vaginalis MRCPUK-part-1-January 2020 exam: H/O offensive vaginal discharge. Diagnosed as bacterial vaginosis. What is the most appropriate initial management? Oral metronidazole

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Trichomonas vaginalis Overview • anaerobic flagellated protozoan, which thrive in more alkaline conditions. • incubation period is 5 to 28 days. • transmitted directly, for example, through sexual transmission. Feature • asymptomatic (in most men and 50% of women) • yellow-green, frothy vaginal discharge • vulvar pruritus • dysuria, dyspareunia, and lower abdominal pain. • Punctuate hemorrhages on the cervix, i.e. "strawberry cervix", or along the vaginal wall are less common signs, but are highly suggestive of infection with Trichomonas vaginalis. • The PH of the discharge is greater than 4.5 Diagnosis • The most rapid and practical method for detection is the use of a wet mount in clinic, which demonstrates motile flagellated protozoans. Differential diagnosis • Whilst bacterial vaginosis is also associated with a discharge with a fishy odour, classically there is

no soreness or irritation associated with it. Treatment • A large dose of metronidazole (2 g as a single course), or a seven day course at lower dose is the treatment of choice. Single-dose therapy increases drug adherence. If standard treatment with either single-dose or multidose therapy fails, a regimen of 2 g of oral metronidazole or tinidazole for 5 days may be considered Patients should not consume alcohol during the course of treatment or during the 24 hours after the completion of the medication. Patients on tinidazole therapy should not consume alcohol during therapy or for 72 hours after completion of the medication. Drinking alcohol while taking tinidazole causes disulfiram-like reaction, which includes (nausea, vomiting, headache, ↑BP, flushing, and shortness of breath). Tinidazole has a longer half-life (12-14 h) than metronidazole (6-7 h). metronidazole and tinidazole are equally effective • Partner Partners should be identified and also screened for infection as men rarely exhibit symptoms of a T. vaginalis infection.

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 The epithelial damage caused by T. vaginalis increases susceptibility to HIV virus infection and transmission. Both patient and partner should abstain from sex until pharmacological treatment has been completed and they have no symptoms. • HIV-positive women with Trichomoniasis. the CDC recommends considering the multidose treatment in HIV-positive women with Trichomoniasis. (metronidazole 500 mg twice daily for 7 days) are more effective in treating T vaginalis in HIV-positive women than a single-dose treatment (metronidazole 2 g single dose). • In pregnant women The CDC recommends that infected symptomatic pregnant women be considered for treatment, as metronidazole has not been definitively shown to be harmful during pregnancy and may prevent transmission to the newborn. Infected asymptomatic pregnant women may wish to defer treatment to after 37 weeks' gestation. Pregnant women should be treated with 2 g metronidazole in a single dose, according to the CDC. The safety of tinidazole in pregnancy is not known. Tinidazole is a pregnancy class C agent; animal studies have demonstrated adverse effects on fetal development. Its use is not recommended in pregnant women. • In breastfeeding women In breastfeeding women, the CDC recommends stopping breastfeeding during the course of metronidazole treatment and for 12-24 hours after the last day. For treatment with tinidazole, the CDC recommends stopping breastfeeding for the course of treatment and for 3 days after the last dose. • Screening and Rescreening Patients should be screened for other sexually transmitted infections. the CDC recommends rescreening at 3 months post therapy for sexually active women, as they have a high rate of reinfection.

Genital ulcers (STI) Other causes of genital ulcers • Behcet's disease • carcinoma • granuloma inguinale: Klebsiella granulomatis (previously called Calymmatobacterium granulomatis) Genital ulcers: • Painful: herpes much more common than chancroid • Painless: syphilis more common than lymphogranuloma venereum + granuloma inguinale

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Genital herpes • Causes: most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). • Features: Multiple painful penile vesicles and ulcers are characteristic. Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site. • Diagnosis: Tzanck smear for lesions suspicious of HSV • Treatment: Oral Acyclovir is the treatment of choice. • Prognosis: The lesions generally heal within 2 weeks. Recurrence of painful genital lesions is a characteristic.

Chancroid • Causes: Haemophilus ducreyi. • Features: (Remember the saying: “You do cry with ducreyi”.) painful genital ulcers The ulcers typically have a sharply defined, ragged, undermined border, which readily bleeds on contact. unilateral, painful inguinal lymph node enlargement. • Diagnosis definitive diagnosis based on isolation of H ducreyi on special media polymerase chain reaction (PCR) = rapid detection of H ducreyi test for the other common STDs (syphilis, HSV, gonorrhea, chlamydia) and HIV. • Treatment: Antibiotic treatment: single dose oral azithromycin or IM ceftriaxone Examine and treat sexual partner(s).

Lymphogranuloma venereum (LGV) • Causes: (L1, L2 or L3 serovars of) Chlamydia trachomatis. • Spread: The bacterium gains entry through breaches in the epithelial/mucous membranes, travelling through the lymphatics via macrophages to local nodes. • Stages: three stages: stage 1: small painless pustule which later forms an ulcer at the site of inoculation 3-12 days later. stage 2: painful inguinal lymphadenopathy (Presents 1-6 months later). Enlarged lymph nodes are known as buboes, they are often painful and can lead to thinning of the overlying skin causing abscesses.

 Groove sign is separation inguinal nodes by the inguinal ligament and is characteristic of the disease. stage 3: proctocolitis (if rectally, then tenesmus, proctocolitis, strictures and fistulas can ensue. Cervicitis and urethritis are also common features.) • Diagnosis: enzyme linked immunoassays or polymerase chain reaction of infected sample areas/pus. Acute and convalescent sera can be used, but requires two samples 2 weeks apart. Inclusion bodies in the cytoplasm of scraped tissue cells are identified by iodine staining. • Treatment: Antibiotics either doxycycline or macrolides (azithromycin or erythromycin) the most appropriate intervention Doxycycline for 21 days In patients where this is unsuitable, azithromycin is also thought to be effective. surgical drainage/aspiration of the buboes or abscesses. • Complications: genital elephantiasis, hepatitis, infertility, pelvic inflammatory disease, arthritis fitz hugh curtis syndrome (Perihepatic adhesions).

Syphilis Aetiology • Syphilis is a sexually transmitted infection caused by the spirochaete Treponema pallidum. • Risk and chance of infection after sexual contact: Approximately one-third of sexual contacts of infectious syphilis will develop the disease. • The incubation period is between 9-90 days Stages • Primary syphilis occurs 14 days to three months post exposure chancre - painless ulcer at the site of sexual contact local non-tender lymphadenopathy often not seen in women (the lesion may be on the cervix)

primary chancre associated with syphilis • Secondary syphilis occurs one to six months following the primary infection. caused by dissemination of the bacteria from the chancre, leading to systemic symptoms systemic symptoms: fevers, malaise, lymphadenopathy rash on trunk, palms and soles buccal 'snail track' ulcers (30%) condylomata lata Iritis Hepatitis Early neurosyphilis: Meningovascular syphilis is a form of early neurosyphilis involving the small and medium sized intracranial vessels, most commonly presents as a stroke involving the middle cerebral artery.

Classical palm lesions of secondary syphilis More generalised rash of secondary syphilis • Tertiary syphilis occurs in one-third of untreated patients around 15–30 years after initial infection. It is divided into: Gummatous syphilis (granulomatous lesions of the skin and bones) most common (15% of patients) Cardiovascular syphilis, ascending aortic aneurysms Late neurosyphilis. general paralysis of the insane Gradual onset confusion Hallucinations Tremors Fits Cognitive impairment Hyperreflexia, Argyll-Robertson pupils tabes dorsalis Features of congenital syphilis • blunted upper incisor teeth (Hutchinson's teeth), 'mulberry' molars • rhagades (linear scars at the angle of the mouth) • keratitis • saber shins • saddle nose • deafness Investigation • The diagnosis usually based on clinical features, serology and microscopic examination of infected tissue • Both VDRL and TPHA are often positive in gummatous syphilis. However, in cardiovascular and neurosyphilis, TPHA is positive and VDRL is often negative. • Serological tests can be divided into cardiolipin tests (not treponeme specific)

 syphilis infection leads to the production of non-specific antibodies that react to cardiolipin examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin) insensitive in late syphilis not specific becomes negative after treatment Causes of false positive cardiolipin tests pregnancy SLE, anti-phospholipid syndrome TB leprosy malaria HIV Treponemal specific antibody tests example: TPHA (Treponema pallidum Haem Agglutination test) more specific remains positive after treatment Management • Benzylpenicillin First line treatment benzathine penicillin 2.4 million units given intramuscularly. This is administered either as a single dose or two doses given one week apart. • Alternatives: doxycycline or erythromycin may be given in patients with allergies to penicillins. In case of severe penicillin allergy, a single dose of (2 g) azithromycin is the preferred option because it is effective and doesn’t raise compliance issues. • Jarisch-Herxheimer reaction This is an acute febrile illness with headache, myalgia, chills and rigors starting within 12 hours of the first

dose of treatment and resolving within 24 hours It is thought to be due to the release of endotoxins following bacterial death
  It is usually not important in early syphilis unless there is neurological or ophthalmic involvement or in pregnancy when it may cause fetal distress and premature labour. It occurs in ~50% of patients with primary syphilis, 90% with secondary syphilis and 25% with early latent syphilis. also occurs in Lyme disease and Q fever. Patients should be counselled about the reaction prior to receiving therapy for syphilis. the appropriate management → reassurance and paracetamol for symptom control UK national guidelines on the management of syphilis 2015 • General advice Infected patient should be advised to abstain from sex until any lesions (if any) have resolved or until two weeks after treatment completion • First-line: Benzathine penicillin dose: 2.4 Mega units IM weekly for up to 3 weeks alternative : Procaine dose: 1.8–2.4 mega units IM daily for 14 days. Only if benzathine penicillin is not available (due to the pain and multiple injections associated) • second-line →oral azithromycin single dose. • Treatment during pregnancy: first and second trimesters →give single dose benzathine penicillin;

 third trimester →two doses of benzathine penicillin one week apart. • Neurosyphilis: Procaine penicillin 1.8-2.4 units once daily (IM, for 14 days) with oral probenecid 500 mg four times a day. Tests for monitoring the effect of treatment →RPR/VDRL test Treponemal enzyme immunoassay (EIA)/chemiluminescent assay (CLIA), preferably detecting both IgM and IgG is the screening test of choice.

Genital warts Overview • Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. • They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. • It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer. • HPV 16 is an oncogenic virus and causes squamous cell carcinomas in the oral cavity, cervix, anus and penis. Features • small (2 - 5 mm) fleshy protuberances which are slightly pigmented • may bleed or itch Management • first-line →topical podophyllum or cryotherapy, depending on the location and type of lesion. Multiple, non-keratinised warts →best treated with topical agents solitary, keratinised warts →respond better to cryotherapy • second line →topical imiquimod • genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

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Chlamydia genitourinary infections Pathogenesis: Chlamydia trachomatis, is an obligate intracellular pathogen. Incubation period: 7-21 days Epidemiology • Chlamydia is the most prevalent sexually transmitted infection in the UK. Approximately 1 in 10 young women in the UK have Chlamydia. Features • Asymptomatic in the majority of the patient

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• Women: cervicitis (Muco-purulent discharge, postcoital bleeding), dysuria, dyspareunia → pelvic inflammatory disease, increased incidence of ectopic pregnancies, infertility and perihepatitis (Fitz-Hugh-Curtis syndrome) • Men: urethral discharge, dysuria Diagnosis • Nuclear acid amplification tests (NAATs) is the investigation of choice Management (2018 UK national guideline for the management of infection with Chlamydia trachomatis, published by: British Association for Sexual Health and HIV). • 1st line: Doxycycline 100mg bd for 7 days is now recommended as first line treatment for uncomplicated urogenital, pharyngeal and rectal chlamydia infections. • 2nd line: Azithromycin (1 g as a single dose), for those who cannot take doxycycline. It is also the preferred option for pregnant individuals. • Patients are advised to avoid sexual contact for 7 from starting medication • partner notification all individuals who had sexual contact with the patient within the 60 days prior to infection or the most recent sex partner if the last contact was more than 60 days prior. Contacts of confirmed Chlamydia cases should be offered treatment prior to the results of their investigations being known (treat then test) Chlamydia – Doxycycline is the first line of treatment. September 2008 exam: A swab taken in the clinic showed a Gram-negative diplococcus and treatment with IM ceftriaxone was given. his symptoms have not resolved. What is the most likely explanation? Co-existent Chlamydia infection (Co-existent infection with Chlamydia is extremely common in patients with gonorrhoea).

Gonorrhoea Epidemiology • Gonorrhoea is the second most common bacterial STI in the UK after chlamydia. Pathogen • Neisseria gonorrhoeae (N. gonorrhoeae, gonococcus) • Gram-negative, intracellular, aerobic, diplococci Transmission • Sexual (oral, genital, or anal) • Perinatal Incubation period: 2-5 days Risk factors: multiple sexual partners in recent months, known partner with gonorrhoea, drug use, prior STI, and men who have sex with men.

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Features • Primary infection is symptomatic in 90-95% of men, but only 50% of women. • Urogenital features males: urethral discharge, dysuria females: cervicitis e.g. leading to vaginal discharge rectal and pharyngeal infection is usually asymptomatic • Gonorrhoeae can cause invasive infections such as pelvic inflammatory disease and Fitz-Hugh-Curtis syndrome in women and epididymitis and prostatitis in men. Fitz-Hugh-Curtis syndrome or perihepatitis. This inflammation of the Glisson capsule surrounding the liver can cause sharp pleuritic right upper quadrant pain with nausea, vomiting, and fever. • Disseminated gonococcal infection (DGI) (haematogenous spread from mucosal infection) Arthritis-dermatitis syndrome: a triad of:

1. Polyarthralgias: migratory, asymmetric arthritis that may become purulent
2. Tenosynovitis: simultaneous inflammation of several tendons
3. Dermatitis: vesicular, pustular, or maculopapular lesions Purulent gonococcal arthritis (without skin lesions) Abrupt inflammation in up to 4 joints (commonly knees, ankles, and wrists) Not to be confused with reactive arthritis Diagnosis • Test of choice: nucleic acid amplification testing (NAAT) • Culture: All individuals with gonorrhoea diagnosed by NAAT should have cultures taken for susceptibility testing prior to treatment. Complications • Increased risk of acquiring HIV infection. Individuals diagnosed with gonorrhoea should be tested for all sexually transmitted infections including HIV • local

complications: urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Gonococcal infection being the most common cause of septic arthritis in young adults. • Disseminated gonococcal infection (DGI), septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome). Management (British Society for Sexual Health and HIV (BASHH) guidelines- 2018) • First line empirical treatment is now monotherapy with ceftriaxone 1 g intramuscularly Use Ciprofloxacin 500 mg orally as a single dose as a first line when infection is known to be susceptible in penicillin-allergic patients ceftriaxone and cefixime are suitable treatment options, unless there is a history of severe hypersensitivity (e.g. anaphylactic reaction) to any beta-lactam antibacterial agent (penicillins, cephalosporins, monobactams and carbapenems) Cefixime 400 mg orally as a single dose plus azithromycin 2 g orally. • A test of cure (TOC) is recommended in all cases. if symptomatic → Culture, performed at least 72 hours after completion of therapy if asymptomatic → NAAT, performed 14 days after completion of therapy followed by culture if NAAT-positive.

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Infectious diseases • Sexual partners must be treated simultaneously to avoid reinfections. Who partners should be notified? Male patients with symptomatic urethral infection: All partners within the preceding two weeks, or the last partner if longer than two weeks ago. Patients with infection at other sites or asymptomatic infection: All partners within the preceding three months Who should be treated? For those presenting after 14 days of exposure → treat only following a positive test for gonorrhoea For those presenting within 14 days of exposure: epidemiological treatment based on a clinical risk assessment In asymptomatic individuals, it may be appropriate to not give epidemiological treatment, and to repeat testing 2 weeks after exposure. • DGI →IV ceftriaxone 1 g OD for 7 days.(May be switched to oral 2 days → Cefixime 400 mg or Ciprofloxacin 500 mg twice daily) Acute monoarthritis, a pustular rash and synovial fluid analysis suggestive of joint sepsis in a young woman make gonococcal arthritis the most likely diagnosis. More commonly patients present with co-infection with Chlamydia trachomatis. May 2014 exam: H/O a purulent urethral discharge. A sample of the discharge is shown to be a Gram-negative diplococcus. What is the most appropriate antimicrobial therapy? Intramuscular ceftriaxone stat dose + oral azithromycin stat dose 0BJanuary 2016 exam: What is the most likely complication from repeated Neisseria gonorrhoea infection? 1BInfertility 2B(Infertility secondary to pelvic inflammatory disease (PID) is the most common complication of gonorrhoea)

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Toxoplasmosis Overview • Toxoplasma gondii is an obligate intracellular protozoa which infects the body via the GI tract, lung or broken skin. • It's oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. Transmission (fecal-oral route) • Toxoplasmosis can be contracted through:

1. cysts in meat, (from undercooked meat) The usual animal reservoir is the cat, although other animals such as rats carry the disease. Kittens are the primary host (mature cats are less likely to secrete toxoplasma) sheep and cattle eat food contaminated with soil contaminated by kitten faeces; and humans ingest the organisms in poorly cooked meat. Oocysts excreted with cat faeces can remain in soil for months.
2. oocysts in cat feces, ingestion of fresh food contaminated by toxoplasma excreted in cats' faeces.
3. transplacental →Congenital toxoplasmosis . Epidemiology • 30% risk of reactivation in immunocompromised (especially CD4+ count < 100 cells/µL) in those not receiving prophylaxis or antiretroviral therapy • ~ 30% of the worldwide population is infected Risk factors • HIV patients when the CD4+ count is less than 100cells/microL Toxoplasmosis is the most common central nervous system protozoal infection that presents with brain abscesses in patients with HIV. Pathophysiology • HIV is associated with reactivation of the disease. Feature • Most infections are asymptomatic. • often features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Highly characteristic of toxoplasmosis is asymmetrical lymphadenopathy limited to an isolated lymph node group. • Other less common manifestations include meningio-encephalitis and myocarditis. • Can present with fits in patients with AIDS Most common infection of the central nervous system in patients with AIDS ring-enhancing lesion on head imaging MRI is more sensitive and preferred CD4+ count < 100 cells/µL • Eye manifestations include:

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 Focal choroido-retinitis Granulomatous uveitis Optic atrophy Retinal detachment Cataract Posterior uveitis Glaucoma. • Congenital toxoplasmosis presents with a classic triad of:

1. chorioretinitis,
2. hydrocephalus and
3. intracranial calcifications. Investigation • antibody test: Serology testing for anti-toxoplasma IgM and IgG antibodies via ELISA The serologic diagnosis of toxoplasmosis in immunocompromised patients is based on the presence of IgG antibodies. • Sabin-Feldman dye test • Congenital toxoplasmosis is associated with elevated platelet count. • HIV patients usually presents with multiple ring-enhancing lesions on brain MRI. Treatment • Symptomatic patients usually have a self-limiting infection, • Treatment usually reserved for those with severe infections or patients who are immunosuppressed pyrimethamine plus sulphadiazine for at least 6 weeks Folinic acid, (also known as leucovorin), should be added to prevent pyrimethamine- associated hematologic toxicity Prevention • Trimethoprim-sulfamethoxazole is the therapy of choice for prophylaxis against toxoplasmosis reactivation. • pregnant women Since the protozoal infection is commonly contracted through the handling of cat feces, pregnant women should be advised to avoid contact with cat litter to reduce their fetus's risk for congenital infection. • for infected pregnant to prevent maternal-fetal transmission spiramycin, Risk of fetopathy is reduced by more than 50% if spiramycin, which can prevent maternal-fetal

transmission, is given to mothers Pyrimethamine • MOA →Dihydrofolate Reductase (DHFR) Inhibitor (competitive inhibitor) DHFR is a key enzyme for production of tetrahydrofolate, a cofactor that is required for the synthesis of DNA and proteins. • Indications: used as an antimalarial or with a sulfonamide to treat toxoplasmosis. Sulfadiazine • Bacteriostatic, inhibits bacterial folic acid synthesis by competing with para amino benzoic acid. Spiramycin • Macrolide antibiotics inhibit bacterial growth by targeting the 50S ribosomal subunit • Resistance to spiramycin is commonly attributed to mutations in 50S rRNA

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January 2018 exam: HIV positive man is admitted with right-sided hemiplegia. CT scan shows multiple ring enhancing lesions. A diagnosis of cerebral toxoplasmosis is suspected. What is the most suitable management? Pyrimethamine and sulphadiazine At which CD4 count should prophylaxis against toxoplasmosis begin? <100 cells/µL (with trimethoprim-sulfamethoxazole). although prophylaxis for toxoplasmosis is not required until the CD4 count is <100 cells/microL, the patient will be covered at a CD4 count <200 cells/microL when prophylaxis against P. jiroveci is instituted. What is risk of transmission of HIV to a health care worker after percutaneous exposure? 0.3% with no prophylaxis. the risk is reduced by ~80% when post exposure prophylaxis is administered. HIV- white lesion in oral mucosa • Oral hairy leukoplakia are white oral lesions caused by the Epstein-Barr virus. • a condition seen in HIV-infected patients with a CD4 count between 200 and 500/mm3. • Unlike oral candidiasis (thrush), these lesions cannot be scraped off the tongue and buccal mucosa.

H1N1 influenza pandemic Overview • The H1N1 virus is a subtype of the influenza A virus • the most common cause of flu in humans. • Only influenza type A viruses are known to have caused pandemics. • Influenza A and B viruses circulate and cause outbreaks and epidemics. • The 2009 pandemic was caused by a new strain of the H1N1 virus. • incubation period is about 2 days. • In temperate climates, seasonal epidemics occur mainly during winter, while in tropical regions, influenza may occur throughout the year, causing outbreaks more irregularly. The following groups are particularly at risk: • patients with chronic illnesses and those on immunosuppressants • pregnant women • young children under 5 years old Features: The majority of symptoms are typical of those seen in a flu-like illness: • fever greater than 38ºC • myalgia • lethargy • headache • rhinitis • sore throat • cough • diarrhoea and vomiting A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support. Treatment There is evidence to support the use of oseltamivir as a prophylactic agent against influenza There are two main treatments currently available:

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Infectious diseases

Oseltamivir (Tamiflu) • action neuraminidase inhibitor which prevents new viral particles from being released by infected cells. thus, slowing viral replication down rather than directly killing the

virus particle. This slowing down of replication is important in permitting time for the body's own immune system to deal with the virus. • Administration oral medication • Indications For critically ill patients with confirmed or suspected H1N1, oseltamivir 150 mg bd for ten days is the recommended treatment. 1st line for influenza B prophylaxis against influenza. NICE guidance recommends prophylaxis with oseltamivir within 48 hours of close contact with a patient infected with influenza for high risk patients. Zanamivir can be used within 36 hours of contact with an infected individual. zanamivir is associated with idiopathic bronchial hypersensitivity, as such it is largely considered a second line agent for treatment of influenza. may be used in the prophylactic treatment of healthcare workers during flu epidemics. However, viral replication is rapid and to be effective the drug must be given as early as possible after the development of symptoms of flu and preferably within 48 hours. • side-effects common side-effects include nausea, vomiting, diarrhoea and headaches. Gastrointestinal symptoms are the most common side-effects of oseltamivir (Tamiflu). Zanamivir (Relenza) • action also, a neuraminidase inhibitor • administration inhaled medication intravenous preparations are available for patients who are acutely unwell The only parenteral alternative is zanamivir (300 mg IV for 10 days). can be safely given using peripheral venous access. For hospitalized influenza patients with suspected or known gastric statis, gastric malabsorption, gastrointestinal bleeding, or for patients suspected or confirmed with oseltamivir-resistant influenza virus infection, intravenous zanamivir should be considered. • Indications Zanamivir is a second line therapy for Influenza B, but first line for Influenza A. • Side effects may induce bronchospasm in asthmatics Intensive Care Management of Pandemic (H1N1) Influenza • Ideally patients should be nursed in a negative pressure room. • NIV Whilst there is no evidence that NIV prevents invasive ventilation in H1N1 patients, it is commonly used as bridging therapy.

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 It is important to remember that these are open circuits and still require personal protection for staff. NIV should be started after the mask is secured to the face Ensuring that a well-fitting mask is in place before airflow starts can reduce the amount of aerosol production. Experience with helmet devices is limited but increasing, and it has been successful in patients who are unable to tolerate the nasal or orofacial devices. The advantage is that it may provide a tighter seal than nasal or orofacial devices. • avoiding water humidification and use of a closed hood is also advised. Influenza treatment • Oseltamivir (tamiflu) is the first line treatment recommended for patients with suspected or confirmed Influenza A. • Zanamivir is useful in patients with poor swallow or in those with suspected or confirmed exposure to oseltamivir-resistant influenza.

Infectious mononucleosis & (Epstein-Barr virus) Aetiology • Infectious mononucleosis (glandular fever) is caused by the Epstein-Barr virus (also known as human herpesvirus 4, HHV-4). • The incubation period of EBV infectious mononucleosis is 1-2 months. Epidemiology • most common in adolescents and young adults. Pathophysiology • The CD8+ T-cell response caused by infectious mononucleosis, leads to generalized lymphadenopathy, splenomegaly, and high WBC count with atypical lymphocytes. Features EBV infectious mononucleosis → triad of fever, pharyngitis, and lymphadenopathy. • sore throat • lymphadenopathy Bilateral posterior cervical adenopathy is most highly suggestive of EBV infectious mononucleosis. • Pyrexia, malaise, anorexia, headache • palatal petechiae Palatal petechiae of the posterior oropharynx distinguish infectious

mononucleosis from other causes of viral pharyngitis but do not distinguish it from group A streptococcal pharyngitis, in which palatal petechiae may occur. • Uvular edema is an uncommon, but, if present, it is a helpful sign in distinguishing EBV infectious mononucleosis from other causes of viral pharyngitis or from group A streptococcal pharyngitis. • splenomegaly - occurs in around 50% of patients and may rarely predispose to splenic rupture • hepatitis