Chapter 16

Viruses

GROUP I: dsDNA VIRUSES

Adenoviridae: linear double strand DNA, molecular weight 20-30X10^6 D, 32-35 kb/strand, icosahedral ether-resistant (absence of lipids) capsid with 252 polygonal capsomeres, 60-90 nm diameter, 12 fibres, 4 minor proteins; penetrate host cells by endocytosis; replicate in nucleus of infected cells, producing basophilic inclusions; marked tendency to cause latent infection of tissues such as tonsils and adenoids; several serotypes (notably 12, 18, 31) oncogenic in hamsters and cell cultures; some serotypes agglutinate rat or rhesus erythrocytes; type-specific antibody can be measured by haemagglutination inhibition; related by family cross-reacting soluble antigens (except chicken adenovirus); transfection of cell by adenovirus requires only part of viral genome; important antigens for neutralisation proteins of capsid; proteins: hexon protein (type-specific and family cross reactions, no known biological activity, no haemagglutination, molecular weight 315 000 D, 105 000 polypeptide chains), complete protein (family cross reactive, cytopathic, attachment of virions to cells, partial haemagglutination, molecular weight 419 000), base protein (family cross reactive, cytopathic, no haemagglutination, molecular weight 236 000, 80 000 polypeptide chains), fibre protein (type specific, blocks synthesis of macromolecules, inhibits viral multiplication, partial haemagglutination, molecular weight 83 000), internal proteins (probably act in assembly of viral DNA, no haemagglutination, 19 000-55 000 polypeptide chains); diagnosis: isolation primary method, antigen detection described but not generally available, paired sera required for serology

Mastadenovirus: human adenoviruses; 49 serotypes (species); does not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; 252 capsomeres; survives 50 d in water (source animal and human faeces); causes acute respiratory illness (types 1-7, 11, 14, 21; upper and lower respiratory infection; mainly in children and military recruits; rhinitis, febrile catarrh (types 3, 4, 7, 14), 'influenza-like illness', pharyngitis/sore throat (types 1-3, 5-7, 16 (0.08% of all cases), 21), acute exudative tonsillitis (types 1-5, 7, 14, 16), acute laryngitis, laryngotracheitis, tracheobronchitis (types 1-5, 7), bronchitis, croup, pneumonia (types 1-3, 5, 7), pneumonitis), pharyngoconjunctival fever (types 3, 4, 7, 14), acute haemorrhagic conjunctivitis (type 11), follicular conjunctivitis (types 1-10, 16, 17, 19, 37), keratoconjunctivitis (types 7, 8, 18, 19), alimentary infection (gastroenteritis, acute diarrhoea and/or vomiting; < 4 y; epidemic; types 40, 41, others in AIDS; 15% of nosocomial diarrhoea), arthritis, carditis, myocarditis and pericarditis, acute haemorrhagic cystitis in immunosuppressed (type 11), 6% of encephalitis (especially type 7), non-pyogenic meningitis (15% of cases), hepatitis, intussusception, mesenteric lymphadenitis, maculopapular rash, roseola-like illness, rhabdomyolysis; increased infectiveness in abnormal host (clinical, subclinical and persistent nonlatent infections; T helper lymphocyte dysfunction); attaches to susceptible tissue cell by reaction of viral capsid protein with specific receptor on cell; replicates in intestinal tract, producing diarrhoea; enters across epithelial surface of intestinal tract and subsequently spreads through body; infects lymphocytes; persists in lymphoid tissue (non-infectious, shed to exterior); 80% of cases show transient appearance of autoantibodies to DNA; serum autoantibodies against cytoskeleton, myosin, myoglobin, thyroglobin, transferrin and heart muscle (in acute myocarditis only) also produced; immunity due to antibody (+), cell-mediated immunity (+); 23 genes; subgroup I (types 3, 7, 11, 14, 16, 20, 21, 25, 28) agglutinate rhesus erythrocytes and have moderate oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight 23X10^6 D (35 kbp), 49-52% G+C, penton dodecagons; subgroup II (types 8, 9, 10, 13, 15, 17, 19, 22, 23, 24, 26, 27) agglutinate rat erythrocytes and have low oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight 23-25X10^6 D (35-38 kbp), 57-61% G+C, penton dodecagons; subgroup III (types 1, 2, 4, 5, 6) partially agglutinate rat, but not rhesus, erythrocytes and have low oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight ? 23X10^6 D (35kbp), 57-59% G+C, no penton dodecagons; subgroup IV (types 12, 18, 31) do not agglutinate erythrocytes and have high oncogenic potential, viral DNA 11.6-12.5% of virion, molecular weight ? 21X10^6 D (30 kbp), 48-49% G+C, no penton dodecagons; growth in primary monkey kidney cells +++, human diploid fibroblasts +, Hep2 +++

(6 d to isolation, enlarged, clustered cells like bunches of grapes or lattice; verified by neutralisation test, fluorescent antibody, complement fixation test); diagnosis: complement fixation test, haemagglutination inhibition assay, neutralisation antibody titre, viral isolation from throat swab, conjunctival swab, pharyngeal washing, faeces, CSF

Adenovirus 1: subgroup III; causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia

Adenovirus 2: subgroup III; causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia, left ventricular dysfunction

Adenovirus 3: subgroup I; causes acute respiratory illness, follicular conjunctivitis, coryza, febrile catarrh, pharyngitis, acute exudative tonsillitis, tracheobronchitis, pneumonia, pharyngoconjunctival fever; pharyngitis in 91%, fever in 87%, headache in 70%, nausea in 48%, diarrhoea in 35%, rhinorrhoea / rhinitis in 30%, vomiting in 26% of cases in children

Adenovirus 4: subgroup III; causes acute respiratory illness, febrile catarrh, coryza, acute exudative tonsillitis, pharyngitis / sore throat, pharyngoconjunctival fever, nonpurulent conjunctivitis (in 68% of infections), arthritis (in 8% of infections); fever in 89%, systemic symptoms in 78%, pharyngitis in 56%, tracheobronchitis in 44%, rhinorrhoea / rhinitis in 44%, chest X-ray infiltrates in 22% of adult cases

Adenovirus 5: subgroup III; causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia

Adenovirus 6: subgroup III; causes acute respiratory illness, follicular conjunctivitis, pharyngitis, acute exudative tonsillitis

Adenovirus 7: subgroup I; causes acute respiratory illness, follicular conjunctivitis, febrile catarrh, epidemic keratoconjunctivitis, pharyngitis, coryza, acute exudative tonsillitis, encephalitis, tracheobronchitis, pharyngoconjunctival fever, pneumonia with exanthem; chest X-ray infiltrates in all cases (bilateral in 66% of children and 33% of adults; ? 2 lobes or segments in 79% of children and 17% of adults); cough and fever in all adult cases and 97% of cases in children; pharyngitis in 92%, rhinorrhoea / rhinitis in 75%, nausea in 75%, adenopathy in 50%, conjunctivitis in 33%, myalgia in 33% and headache in 33% of adult cases but none of these in cases in children; dyspnoea in 55%, heart failure in 48%, meningismus in 38% and deaths in 10% of cases in children but none of these in adult cases; diarrhoea in 45% of cases in children and 25% of adult cases

Adenovirus 8: subgroup II; causes epidemic keratoconjunctivitis, nonpurulent conjunctivitis

Adenovirus 9: subgroup II; causes follicular conjunctivitis

Adenovirus 10: subgroup II; causes follicular conjunctivitis

Adenovirus 11: subgroup I; causes acute respiratory illness, acute haemorrhagic conjunctivitis, acute haemorrhagic cystitis

Adenovirus 12: subgroup IV

Adenovirus 13: subgroup II

Adenovirus 14: subgroup I; causes acute respiratory illness, febrile catarrh, coryza, acute exudative tonsillitis, pharyngitis, pharyngoconjunctival fever

Adenovirus 15: subgroup II

Adenovirus 16: subgroup I; causes follicular conjunctivitis (in 50% of infections), acute exudative tonsillitis (0.08% of all cases), pharyngitis

Adenovirus 17: subgroup II; causes nonpurulent conjunctivitis

Adenovirus 18: subgroup IV; causes epidemic keratoconjunctivitis

Adenovirus 19: subgroup II; causes epidemic keratoconjunctivitis, nonpurulent conjunctivitis

Adenovirus 20: subgroup I

Adenovirus 21: subgroup I; causes acute respiratory illness, acute haemorrhagic cystitis

Adenovirus 22: subgroup II

Adenovirus 23: subgroup II

Adenovirus 24: subgroup II

Adenovirus 25: subgroup I

Adenovirus 26: subgroup II

Adenovirus 27: subgroup II

Adenovirus 28: subgroup I
Adenovirus 29: subgroup II
Adenovirus 30: subgroup II
Adenovirus 31: subgroup IV
Adenovirus 37: causes cervicitis (sexually transmitted), nonpurulent conjunctivitis
Adenovirus 40: causes gastroenteritis
Adenovirus 41: causes gastroenteritis
Herpesviridae: double strand DNA; molecular weight 54-102X10^6 D in icosahedral capsid 100 nm diameter with 162 hollow capsomeres surrounded by lipid envelope of host cell origin, 180-250 nm diameter; ether and chloroform sensitive; replicate in nucleus of infected cells (biosynthesis of viral DNA and assembly of viral particles) and acquire outer envelope from infected cell on passage through nuclear membrane; multiply in macrophages; 100 genes; latency (restricted or altered gene expression gives absence of immunogenic proteins, persist in presence of antibodies) and oncogenicity; eosinophilic intranuclear inclusions (Cowdry type A) in infected cells; some species multiply on a variety of cultured cells; antibodies provide some protection against certain strains; infections produce solid immunity; penetrate cells by fusion; no common family antigen

Alphaherpesvirinae

Herpesvirus hominis (Simplexvirus): herpes simplex virus; human herpesvirus 1; types 1 (HHV-1) and 2 (HHV-2); molecular weight $100X10^6$ D, 151 kb/strand, 100 nm, 162 capsomeres, virion 180-200 nm; causes latent infection, grows rapidly in vitro, causes symptomatic reactions by axonal spread from infected ganglion; causes anterior uveitis, arthritis (type 1), balanitis, non-purulent cervicitis (type 2), non-purulent conjunctivitis (uncommon; type 1), disseminated infection associated with atopic eczema in children (exogenous; type 1), dysuria without frequency, 12-21% of encephalitis (all ages; peak incidence > 30 y old; endogenous or exogenous; temporal lobe; types 1 and 2), perinatal and prenatal generalised disease (exogenous; types 1 and 2), genital herpes (type 2; sexually transmitted; very common; reactivates; > 14 y; peak incidence 15-29 y; primary exogenous, recurrent endogenous), acute herpetic gingivostomatitis (type 1; < 15 y; peak incidence 1-4 y; exogenous), adult (associated with pregnancy, thymic dysplasia, coeliac disease, corticosteroid therapy, leukemias and lymphomas, severe burns, renal transplantation, AIDS), neonatal and prenatal hepatitis, infections in abnormal host (T helper lymphocyte dysfunction), iritis, keratoconjunctivitis (type 1; > 1 y; peak incidence > 3 y), localised skin lesions (Kaposi's varicelliform eruption all ages, peak incidence > 15 y; herpes febrilis ('cold sores') type 1, > 4 y, peak incidence > 30 y, endogenous), 4-10% of non-pyogenic meningitis (exogenous; type 2; common in impaired cell-mediated immunity), meningoencephalitis (type 1), papulovesicular rash (neonatal), oesophagitis, proctitis, rhabdomyolysis, acute exudative tonsillitis (type 1), acute chest infection, pneumonia (neonatal and diffuse interstitial in T cell deficiency) with exanthem (type 1), urinary infections, urethritis, vaginitis, vulvitis, whitlow (type 1), systemic infections in cell-mediated immunity disorders, ? cervical carcinoma co-factor, ? psychosis associated with in utero exposure (type 2); increased infectiousness in abnormal host (clinical and latent infections); genital sites: 86% type 2, 14% type 1; orofacial sites: 96% type 1, 4% type 2; finger/hand: 54% type 1, 46% type 2; other non-genital sites: 60% type 1, 40% type 2; type 1 generally decreased incidence but increased proportion of genital; type 2 increased incidence, lower incidence of primary disease but higher incidence of recurrent disease in higher socioeconomic groups; type 1 transmitted by droplets, saliva; type 2 enters across epithelial surface of urinogenital tract and subsequently spreads through body (> 90% of persons with genital HSV-2 shed virus asymptomatically; 60% of infections unrecognised with symptoms, 20% recognised genital herpes, 20% truly asymptomatic); carried in blood associated with mononuclear cells; inhibits phagocytic (macrophage) chemotaxis and secretory function; persistence due to failure to display viral antigen on infected cell surface, residence in cells (eg., neurons) that do not express major histocompatibility antigens prevents T cell recognition; IgG antibodies nonspecifically bind to infected cell and block immune lysis; virally encoded F_c receptor inhibits classical complement pathway; virally encoded complement receptor inhibits alternative complement pathway; antibody binding to surface of virus-containing cell may inhibit viral replication and allow virus to persist; in vitro T cell suppressors; tunicamycin-sensitive viral glycoprotein induces immunosuppression by direct inhibition of lytic activity of natural killer cells; recovery from primary infection due to cell-mediated immunity (delayed type hyperactivity type activated macrophage +++, direct cytotoxicity +++), neutralising antibody (++), antibody-initiated, complement-dependent lysis requiring antiviral IgG and alternative pathway of complement (++); ? resistance to reactivation of latent infection due to antibody; persists in dorsal root ganglia (non-infectious, shed to exterior; activation causes cold sore) and salivary gland (infectious and shed to exterior); diagnosis: isolation in tissue culture (MRC-5 shell vial centrifugation enhancement best method; material from vesicle fluid, throat swab, CSF, corneal scraping; WI38, primary monkey kidney ++, human diploid fibroblasts +++, Hep2 ++, embryonated egg; 3-4 d to isolation, enlarged or shrunken granular cells starting at edge, rapid progression and sloughing, may have giant cells; verified by fluorescent antigen, ELISA; sensitivity 50% for primary, 20% for recurrent), HerpesSelect kit for IgG antibody (types 1 and 2; 50% +ve at 3 w, 98% at 6 w), POCkit for HSV-2 antibody (positive in few weeks), antigen detection (direct immunoperoxidase staining) variably adequate, Tzanck smear, electron microscopy; treatment: aciclovir, valaciclovir, famciclovir, penciclovir, idoxuridine, vidarabine

Herpes B Virus: herpes simiae; causes encephalitis

Poikilovirus: causes pseudorabies, equine rhinopneumonitis

Varicellovirus: varicella-zoster virus (human herpesvirus 3); causes varicella (chickenpox), zoster (shingles), abortion, anterior uveitis, arthritis, non-purulent conjunctivitis, 3% of encephalitis, Guillain-Barré syndrome, adult, paediatric and prenatal hepatitis, iridocyclitis, iritis, keratoconjunctivitis, non-pyogenic meningitis (common in impaired cell-mediated immunity), mouth lesions, myocarditis and pericarditis, oophoritis, pneumonia (including diffuse

interstitial) with exanthem, pneumonitis, prenatal generalised disease, 5-30% of Reye's syndrome, vesicular rash, systemic infections in cell-mediated immunity disorders; increased infectiousness in abnormal host (clinical and latent infections; T helper lymphocyte dysfunction); infects lymphocytes; residence in cells (eg., neurons) that do not express major histocompatibility agents prevents T cell recognition; virally encoded F_c receptor inhibits classical complement pathways; primary bodily defence mechanism cellular immune responses (delayed type hypersensitivity activated macrophage +++, direct cytotoxicity +++), neutralising antibody (++); recovery from primary infection and resistance to reactivation of latent infection due to cell-mediated immunity (+++); persists in dorsal root ganglia (non-infectious, shed to exterior), activation producing zoster; serum autoantibodies against cytoskeleton and insulin produced; diagnosis: serology (complement fixation test, haemagglutination inhibition, indirect fluorescent antibody titre, ELISA, radioimmunoassay) not useful except for immune status, isolation in tissue culture (scrapings from skin lesions, vesicle fluid, sputum; WI38, primary monkey kidney +, human diploid fibroblasts ++, not Hep2) primary method (6-8 d to isolation; discrete, elongated foci of enlarged or shrunken cells, slow contiguous progression, enhanced by use of growth medium; verified by cell association, haematoxylin and eosin, fluorescent antigen, complement fixation test), electron microscopy, Tzanck smear, antigen detection useful; treatment: aciclovir

Betaherpesvirinae

Cytomegalovirus: human herpesvirus 5; may have basophilic inclusion bodies; latent infection; prevalence of antibody in adults varies from 40% in France to 100% in Manila and Uganda; causes abortion, arthritis, cytomegalic inclusion disease, perinatal, prenatal and postnatal generalised disease, adult, neonatal and prenatal hepatitis, mononucleosis, pneumonia and pneumonitis, stillbirth, teratogenic effects, Guillain-Barrè syndrome, prenatal urinary infection; increased infectiousness in abnormal host (clinical, subclinical, latent and persistent nonlatent infections); causes retinochoroiditis, conjunctivitis, acute diarrhoea and/or vomiting, colitis, pancreatitis (59% of cases), encephalitis, myelitis, myocarditis and pericarditis, stomatitis, oesophagitis, gastritis, antral obstruction, cholecystitis/cholangitis/papillary stenosis, hepatic granuloma, hepatitis, ileitis/colitis, otitis media, proctitis, pneumonia, adrenalitis, epididymitis, cervicitis in AIDS; also extremely infrequent encephalitis in impaired cell-mediated immunity, diffuse interstitial pneumonia in allogenic bone marrow transplant recipients, infusion infections, and other infections in T lymphocyte dysfunction), ? atherosclerosis; virus presence in semen and cervix suggests sexual transmission; carried in blood associated with mononuclear cells; infects lymphocytes, affecting functions of T, B, NK cells and macrophages (accessory function, interleukin 2, suppressor activity), decreases polymorphonuclear bactericidal and chemotactic functions, but usually a secondary agent, though evidence that assists HIV infection; virally encoded F_c receptor inhibits classical complement pathways; down-regulation of major histocompatibility class I antigens prevents $CD8^+$ T cell recognition; selective interference of viral antigen processing by another viral protein (eg., protease inhibitors) prevents T cell recognition; virally encoded protein homologous to cellular G protein coupled receptors inhibits inflammatory cell formation; persistent infection of glands, etc, inaccessible to circulating antibody; IgG antibodies nonspecifically bind to infected cell and block immune lysis; primary bodily defence mechanism cellular immune responses (delayed type hypersensitivity activated macrophage ++, direct cytotoxicity +++), neutralising antibody (++), basophil-mast cell (+); recovery from primary infection and resistance to reactivation of latent infection due to cell-mediated immunity; persists in lymphoid tissue (non-infectious, shed to exterior), activation ? disease occurring; cytomegalovirus is a polyclonal B cell activator and triggers B lymphocytes with a broad range of specificities; autoantibodies are common (DNA, erythrocytes, lymphocytes, neutrophils, platelets, immunoglobulin, cytoskeleton, smooth muscle, thyroglobulin); diagnosis: serology (IgM: indirect fluorescent antibody titre, complement fixation test, neutralisation test, ELISA (IgG, IgM, IgM capture); IgG seroconversion or presence of specific IgM useful in nonimmunocomprised), isolation in tissue culture (primary method and only useful method in kidney and liver transplant recipients; human diploid fibroblasts ++, no growth in primary monkey kidney or Hep2; 6-10 d to isolation, compact foci of enlarged cells, slow contiguous progression; verified by cell association, fluorescent antigen, haematoxylin and eosin; first morning's sample of urine most dependable source but may reflect remote infection; also heparinised blood during acute phase and throat swabs; may be cultured from asymptomatic persons— saliva (mostly children), rarely from blood, 1% of normal semen specimens, breast milk specimens in 25% of seropositive women, cervical secretions in 15% of first trimester pregnancies), demonstration of viral antigen or DNA/RNA in diseased lung,

oesophagus, colon or blood (may be only useful method in immunocompromised); treatment: ganciclovir or foscarnet + i.v. immunoglobulin

Roseolovirus: human herpesvirus 6; causes exanthema rubitum (roseola, 'sixth disease') and pneumonitis in infants, disease resembling acute infectious mononucleosis if acquired later in life, bone marrow suppression, pneumonitis, encephalitis, encephalopathy, hepatitis, fever, skin rash, transplant rejection and death in bone marrow, kidney and liver transplant recipients on immunosuppression, disseminated infection, active CNS infection, pneumonitis, retinitis and contributes to death in AIDS; cultivated in mitogen-activated PBL or T cell lines; diagnosis: PCR of serum or plasma; treatment: foscarnet, ganciclovir

Human Herpesvirus 7 : ? causes some cases of roseola

Gammaherpesvirinae

Lymphocryptovirus: Epstein-Barr virus (human herpesvirus 4); causes latent infection; circulating antibody prevents exogenous reinfection; forms circular episomes in nuclei of latently infected cells, transforms cells and causes heterophile mononucleosis; causes infectious mononucleosis (young adults), monocytic angina (older children, young adults, AIDS cases and organ transplant recipients), arthritis (in 5-10% of cases of infectious mononucleosis), encephalitis, adult hepatitis, hepatic granuloma, infusion infection, non-pyogenic meningitis (Duncan's syndrome), Guillain-Barrè syndrome, maculopapular rash, exudative tonsillitis, nonpurulent conjunctivitis, ? urinary infection in infectious mononucleosis, hypersensitivity to mosquito bites; associated with Burkitt's lymphoma, nasopharyngeal carcinoma, B cell lymphomas, Hodgkin's disease, post-transplant lymphoproliferative disease, oral hairy leucoplakia; carried in blood associated with mononuclear cells; infects lymphocytes, causing mainly polyclonal B cell activation, triggering B lymphocytes to produce antibodies with a broad range of specificities, but also affecting T cells; persistence due to failure to display microbial antigen on infected cell surface; virally encoded complement receptor inhibits alternative complement pathway; down-regulation of cell surface adhesins (eg., LFA-3 and ICAM-1) prevents immune cell interactions; virally encoded cytokine (IL-10) homologue induces immunosuppression by inhibition of inflammatory cell formation; persists in lymphoid tissue (non-infectious, not shed to exterior, ? causing Burkitt's lymphoma) and salivary glands (infectious and shed to exterior); autoantibodies in infectious mononucleosis common (cytoskeletal antigen in 97%, nuclear antigen in 66%; also against cardiolipin, erythrocytes, lymphocytes, neutrophils, platelets, immunoglobulin, smooth muscle and thryoglobulin); increased infectiousness in abnormal host (clinical, subclinical, latent and persistent nonlatent infections); major host defence mechanisms basophil-mast cell (+), delayed type hypersensitivity activated macrophage (+++), direct cytotoxicity (+++); diagnosis: serology (indirect fluorescent antibody— Ig M and IgG ? 1:320— to virion capsid antigen, heterophil ? 1:56 (Paul-Bunnell test), ox cell absorption positive (Davidsohn's test), complement fixation test, ELISA, immunodiffusion) primary method, antigen detection not available, isolation not generally available

Kaposi's Sarcoma Associated Herpesvirus (Human Herpesvirus 8): probably causes tumours, including Kaposi's sarcoma, multicentric Castleman's disease and primary effusion lymphoma; transmitted by sexual contact, blood exchange, needle sharing

Papovaviridae: circular double strand DNA, molecular weight 3-5X10^6 D (relatively small) in icosahedral, ether-resistant capsid 43-55 nm diameter; penetrate host cell by endocytosis; replicate within nucleus of infected cell; produce latent and chronic infection in natural hosts; all tumourigenic; 72 capsomeres; cause progressive multifocal leucoencephalopathy (slow viral disease); do not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; oncogenic in experimental animals; persistent infection common; immunity cell-mediated immunity (++); diagnosis: haemagglutination inhibition, indirect fluorescent antibody (brain biopsy; antigen), complement fixation test (significant titre ? 1:8), tissue culture (primary human foetal glial cell culture), electron microscopy, histopathology

Papillomavirus: molecular weight 6X10^6 D, 9 kb/ strand, 55 nm, 72 capsomeres, double strand DNA; characteristically produce benign skin lesions in many species; human papilloma virus, rabbit (Shope) papilloma virus, many papilloma viruses of other mammals

Human Papillomavirus: 70 species; causes or associated with genital warts (sexually transmitted; types 6, 11, 16, 18, 30, 31, 33-35, 39, 40, 42-45, 51-59), cutaneous (types 1-5, 7-10, 12, 14, 15, 17, 19-29, 36-38, 41, 46-50, 60), oral papillomas (types 13, 30, 32, 57), cervical malignancies (sexually transmitted; types 16, 18, 30, 31, 33, 35, 39, 45, 51,

52, 56), squamous cell carcinomas (including oral; types 5, 8, 16, 17, 20, 41, 48), melanoma (type 38), erythroplasia of Queyrat (type 16); clinical and persistent nonlatent infections in abnormal host; cultivated in organ culture of infected skin treated with TPA to increase keratinocyte differentiation; diagnosis: cytology; treatment: cryotherapy, electrosurgery, surgery, 5-fluorouracil, thiotepa, podophyllin, podofilox, imiquimod

Polyomavirus: molecular weight $3.5X10^6$ D, 5 kb/strand, 45 nm, 72 capsomeres, cyclic DNA; can produce cytopathic effects in tissue cultures; widely distributed among humans; progressive multifocal leucoencephalopathy is uncommon manifestation of a common polyoma virus infection of humans; persists in kidney tubules (infectious or noninfectious, shed to exterior); increased infectiousness in abnormal host; 6 genes; polyoma virus of mice, JC and BK viruses of humans, simian virus 40 of rhesus monkey (infection of nonpermissive cells results in permanent transfection of some cells only if viral DNA is integrated into host cell DNA), lymphotropic virus of African green monkey, viruses of mouse, rabbit, hamster and baboon

BK Virus: human *Polyomavirus*; persists in kidney (non-infectious, shed to exterior), activated in pregnancy and immunosuppression; increased infectiousness in abnormal host (subclinical and persistent nonlatent, ? clinical and latent infections); ? cause of bladder carcinoma in transplant recipient

JC Virus: causes progressive multifocal leucoencephalopathy; persists in kidney (non-infectious, shed to exterior), activated in pregnancy and immunosuppression; increased infectiousness in abnormal host (clinical and persistent nonlatent, ? subclinical and latent infections)

Simian Virus 40: increased infectiousness in abnormal host; linked to non-Hodgkin's lymphoma

Poxviridae: large complex viruses; double strand DNA, molecular weight $160X10^6$ D as internal nucleoid in brick-shaped (to ovoid) particle 200-260X250-390 nm with complex capsid symmetry and complex outer coat composed of 2 complete envelope membranes; replicate in cytoplasm of infected cells (host cell nucleus provides functional apparatus for maturation of envelope and internal components), producing eosinophilic inclusion bodies; antigenically complex; nucleoprotein shared by group; agglutination of chicken red cells by lipoprotein complex inhibited by immune serum; produce characteristic pox on chorioallantoic membrane of fertile eggs; protein and lipid present; relatively resistant to inactivation by chemicals (disinfectants) or by heat, cold or drying, inactivated by chloroform, variable inactivation by ether; common family and genus antigens; DNA-dependent RNA polymerase on virion; predilection for epithelial cells; antibodies provide some protection against certain strains; infection produces solid immunity; do not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; multiply in macrophages; control by elimination of viral transmission and immunisation; some species multiply on a variety of cultured cells

Chordopoxvirinae: poxviruses of vertebrates

Orthopoxvirus: virion 250X300 nm, brick-shaped, molecular weight $150\text{-}160X10^6$ D, 231-242 kb/strand, AT/GC = 1.6

Vaccinia Virus: artificially propagated virus used for human vaccination; host range humans, other mammals, birds, but no natural animal hosts; may have evolved from cowpox; causes abortion, encephalitis, nonpyogenic meningitis, skin lesions; increased infectiousness in abnormal host (clinical and persistent nonlatent infections); inhibits phagocytic (macrophage) oxidative burst, suppressor activity; escapes from phagosome; primary bodily defence mechanism cell-mediated immunity (+++); recovery from primary infection due to cell-mediated immunity; 160 genes

Variola, Alastrim: smallpox viruses; double-stranded DNA, brick-shaped to ovoid, 250-390X200-260 nm; DNA-dependent RNA polymerase enzyme for early mRNA production; lipid solvent inactivated, resist inactivation by heat, cold, drying or disinfectants; cause alastrim (mortality 0.25%), smallpox (mortality 5-40%), abortion, haemorrhagic fever; infect epidermal cells; multiply in cell cytoplasm; short incubation period; result in death or complete recovery; if recovery, person usually immune; natural host man but monkeys and mice in host range, including as potential reservoir hosts; laboratory cultivation in animals (especially rabbit, calf, sheep), chick embryo, cell cultures (especially human embryonic kidney, monkey kidney, HeLa); diagnosis: complement fixation test, haemagglutination antibody technique, tissue culture of scrapings from skin lesions, vesicle fluid, pus, blood, crust

Cowpox Virus: causes self-limited localised vesicular lesions; cattle source but host range includes humans and other mammals; occupational illness in livestock workers

Cowpoxlike Viruses: host range rodents, carnivores, elephants, humans; rodents potential reservoir hosts

Monkeypox Virus: causes rare human infections which resemble smallpox (vesicular rash) but very limited spread; host range monkeys, humans, rodents; monkeys and rodents potential reservoir hosts; diagnosis: electron microscopy

Whitepox Virus: probably variant of monkeypox virus; resembles smallpox virus; no recognised human cases; host range and potential reservoir hosts monkeys and rodents

Poxviruses of Buffalo, Camel, Mouse, Elephant, Other Mammals: no human infections recognised

Parapoxvirus

Orf Virus: virion 160X260 nm; causes orf (contagious pustular dermatitis, contagious ecthyma) in sheep and other animal workers; host range sheep, goats, cattle, humans; potential reservoir hosts sheep, goats

Paravaccinia Virus: causes pseudocowpox (milker's nodes, milker's nodules; smooth or warty painless lesions and mild systemic complaints); source cattle; occupational illness in livestock workers

Bovine Papular Stomatitis Virus: causes bovine papular stomatitis; host range cattle, humans; potential reservoir host cattle

***Capripoxvirus*:** 3 viruses of sheep and goats; causes goatpox (host range goats, humans; goats potential reservoir host)

Molluscipoxvirus: molluscum contagiosum virus; causes chronic proliferative lesions (molluscum contagiosum, mouth lesions); clinical and persistent nonlatent infections in abnormal host; infection generally confined to epithelial surface of skin; host range humans, chimpanzees; humans potential reservoir host; diagnosis: cytology

Tanapoxvirus: causes outbreaks of febrile illness with rare upper body pock lesions; Kenya, Africa; host range monkeys, humans; monkeys potential reservoir host

Yabapoxvirus: causes Yaba monkey tumour pox; host range monkeys, humans; monkeys potential reservoir host

GROUP II: ssDNA VIRUSES

Parvoviridae: single strand DNA, molecular weight 1.4-2.2X10^6 D in icosahaedral, ether-resistant capsids about 18-26 nm, 32 capsomeres; positive and negative polarity

Parvovirinae

Parvovirus: survival time in water unknown (source human faeces); causes epidemic viral diarrhoea (in 47% of infections), gastroenteritis; human parvoviruses RA-1 and others, Aleutian mink disease virus and many viruses of rodents, pigs, cattle, cats and dogs

Parvovirus-like Agents: cause water-borne gastroenteritis (19% of outbreaks)

Erythrovirus: Human Parvovirus B19; 24 nm; ssDNA; no envelope; transmission by droplets and by pooled plasma products (solvent-detergent treatment ineffective, effectiveness of heat unknown) and congenital; causes aplastic crisis, erythema infectiosum ('fifth disease', 'slapped face'), stillbirth (rare), anaemia, arthritis (? including rheumatoid arthritis), hydrops foetalis, polymorphous rash, pneumonia, hepatitis, myocarditis; cultivated in dividing erythrocyte progenitors or megakaryocytic cell line + erythropoitin and GM-CSF; diagnosis: PCR, dot hybridisation, capture ELISA on serum

GROUP III: dsRNA VIRUSES

Reoviridae: RNA; double stranded; segmented; icosahedral capsid (60-80 nm)

Orthoreovirus: 3 viruses of humans, monkeys and lower vertebrates, > 5 viruses of birds; double stranded RNA; 70 nm, 72 capsomeres; icosahedral, double capsid, no envelope; 10-segmented; molecular weight 0.5-3X10^6 D/segment (total 15X10^6 D); 46 kb; infectivity stable with lipid solvents; 8 virion polypeptides; recombination by reassortment of subunits of genome; RNA polymerase must be introduced with virus for its replication; penetrates host cell by endocytosis; progeny virus stored in infected cell until its death, each transcribed into complementary, monocistronic messenger by virion transcriptase; inhibits phagocytic oxidative burst, escapes from phagosome; vector contaminated water polluted by animal or human faeces (survival time weeks - months); causes acute respiratory illness, rhinitis, epidemic viral diarrhoea, neonatal hepatitis, maculopapular rash, nonpyogenic meningitis; produces mild illness in most infected persons; in mice, produces virus-induced diabetes as part of a polyendocrine disease with multiple organ reactive autoantibodies prevented by immunosuppression; diagnosis: tissue culture and inoculation of suckling mouse with material from faeces and throat swab; other double stranded RNA viruses similar to *Orthoreovirus* include rice dwarf virus (molecular weight 15X10^6 D, 23 kb/strand, 10 segments) and cytoplasmic polyhedrosis of silkworms (molecular weight 15X10^6 D, 23 kb/strand, 10 segments)

Orthoreovirus 3: exanthem and pulmonary involvement

Orbivirus: > 90 members of 17 subgroups; icosahedral, double capsid (outer skin-like), 70 nm diameter, double stranded RNA, 10 segments each molecular weight 0.3-2.7X10^6 D (total 12X10^6 D); 37 kb; infectivity stable with lipid

solvents; 8 virion polypeptides; carried in blood associated with erythrocytes; includes Corriparta virus, Eubenangee virus, Kemeravo virus, blue tongue virus of sheep, African horse sickness virus

Rotovirus: > 6 members, including > 4 human rotaviruses, many rotaviruses of many mammals, including SA-11 virus of monkeys and Nebraska calf diarrhoea virus; 70 nm; icosahedral with double-shelled capsid, no envelope, double stranded RNA, probably 11 segments of molecular weight 0.23-2.04X10^6 D (total 10X10^6 D), 31 kb; infectivity stable with lipid solvents, fluorocarbon for 5 minutes at 37?C, pH ? 3 for 1 h at 37?C, 56?C for 1 h, –20?C for years; 10 virion polypeptides; survives 2-34 d in water (source animal and human faeces); causes acute epidemic diarrhoea and/or vomiting (most common cause of infantile gastroenteritis; 41 M cases with 873 000 deaths (all < 5 y) globally annually; also traveller's diarrhoea; also in infant mice, calves, piglets, lambs, dogs, foals, infant rabbits, newborn deer, monkeys, goats, guinea pigs), upper respiratory tract infection, ? hakuri; replicates in intestinal epithelium; diarrhoea mechanisms not understood (? lactase deficiency ? lactose intolerance); diagnosis: antigen detection primary method (ELISA (International Diagnostic Laboratories best commercial kit), latex agglutination), isolation (in differentiating human colon carcinoma cell line + trypsin) not generally available, seen by immune electron microscopy in stool, serology not practical for single cases

Coltivirus: Colorado tick fever virus; tick-borne (*Dermacentor andersoni*); western US and Canada; causes 2 periods of abrupt onset high fever, chills, joint and muscle pains, severe headache, ocular pain, conjunctival injection, nausea, occasional vomiting in spring or summer, interrupted by brief, symptom-free interval; diagnosis: seroconversion, electron microscopy, immunofluorescence (antigen), PCR, IgM antibody-capture ELISA; treatment: symptomatic

GROUP IV: POSITIVE SENSE RNA VIRUSES

Astroviridae: RNA; naked icosahedral nucleocapsid; single stranded; positive polarity

Astrovirus: human astroviruses; causes gastroenteritis

Caliciviridae: diameter of virion 35-39 nm, molecular weight of nucleic acid in virion 2.6-2.8X10^6 D; cause gastroenteritis

Calicivirus: 13 vesicular exanthema of swine viruses, many viruses of cats and sea lions, Norwalk gastroenteritis virus of humans; unknown survival time in water (source human faeces); causes gastroenteritis (epidemic viral diarrhoea)

***Norovirus*:** 27 nm; round; density 1.38-1.41 g/cm^2; stable to 20% ether for 24 h, pH 2.7 for 3 h, 60?C for 30 minutes; causes acute epidemic diarrhoea and/or vomiting; ? replicates in intestinal epithelium; Norwalk gastroenteritis virus (USA), Hawaii virus **(**USA), Ditchling virus (England), Cochle virus **(**England), Montgomery County virus **(**USA), W virus **(**England),

Parramatta virus **(**Australia), Colorado virus **(**USA), small round virus **(**Japan), Marin County virus **(**USA); 40% of outbreaks in hospitals and 39% in residential care facilities; 85% of transmission person-to-person

Sapovirus: causes gastroenteritis

***Hepevirus*:** hepatitis E virus; tentatively classified as *Calicivirus* but some features more in common with Alphavirus superfamily; major cause of enterically transmitted hepatitis in developing countries; no chronicity; diagnosis: enzyme immunoassay, Western blot assay

Coronaviridae: single positive strand RNA, 50-160 nm diameter, molecular weight 5-6X10^6 D (18 kb), enveloped particle, spherical, pleomorphic, pedunculate, with petal-like or club-shaped surface projections; replicate in cytoplasm of infected cells; intracytoplasmic membranes site of nucleocapsid development; ether or chloroform inactivates; buds into cytoplasmic vacuoles

Coronavirus: human coronavirus; single strand RNA; envelope from infected cell; 2 types; survival time in water unknown (source human faeces); causes common or feverish cold, URTI, acute chest infection, gastroenteritis, epidemic viral diarrhoea; infection generally confined to epithelial surface of respiratory tract; intestinal coronaviruses (described for pigs, foals, calves, sheep, dogs, mice, man and turkeys; maximum susceptibility in first few weeks of life) replicate in intestinal epithelium, producing lactose intolerance and diarrhoea; group includes mouse hepatitis virus (multiplies in macrophages), infectious bronchitis virus of fowl and > 2 other agents infecting pigs and other vertebrates

Flaviviridae: RNA; enveloped; icosahedral nucleocapsid; single stranded; positive polarity

Flavivirus: 25-50 nm diameter in a lipid envelope; single stranded RNA; molecular weight 3X10^6 D; replicates in cytoplasm and matures by budding from intracytoplasmic membranes; arbovirus group B; 26 mosquito-borne members,

including Alfuy virus, dengue, Edge Hill virus, Japanese B encephalitis, Kokobera virus, Koutango virus, Kunjin virus, Murray Valley encephalitis, St Louis encephalitis, Stratford virus, Usutu virus, West Nile fever, yellow fever; 11 tick-borne viruses, including Kyasanur Forest disease, Omsk haemorrhagic fever, European and Far Eastern tick-borne encephalitis; and 17 vector-unassociated viruses

Japanese Encephalitis Virus: subgroup I; mosquito (*Culex triteniorhynchus* in Asia, *Culex annulirostrus* in Australia) vector and reservoir; other reservoirs pigs, water birds; causes encephalitis (> 50 000 cases annually; fatality rate > 25%); Japan, Guam, E Asian mainland, Malaya, India, Pakistan, Australia; epizootic in temperate and subtropical areas, enzootic in tropical

St Louis Encephalitis Virus: subgroup I; Japanese encephalitis serological complex; vector *Culex* mosquito; host birds, especially English sparrows; Western Hemisphere (USA, Trinidad, Panama); causes St Louis encephalitis (? 60 cases (4 deaths)/y; more severe in older people); diagnosis: IgM and IgG indirect immunofluorescent serum antibody; controlled by mosquito control

Murray Valley Encephalitis Virus: subgroup I; Japanese encephalitis serological complex; mosquito (*Culex annulirostrus*) vector; water birds reservoir; causes Australian encephalitis; Australia, Papua New Guinea, eastern Indonesia

West Nile Fever Virus: subgroup I; Japanese encephalitis serological complex; mosquito vector; birds amplifying host; causes headache, fever (may be haemorrhagic), myalgia, rash, lymphadenopathy, meningoencepahlitis; Egypt, Israel, India, Uganda, S Africa, Southern Europe, Western and South-Western Asia, USA, Australia

Usutu: Japanese encephalitis serological complex; Africa

Koutango: Japanese encephalitis serological complex; Africa

Kunjin: Japanese encephalitis serological complex; vectors and reservoirs as for **Murray Valley Encephalitis Virus**; causes Australian encephalitis; Australia, Papua New Guinea, Borneo

Alfuy: Japanese encephalitis serological complex; Australia

Kokobera: Japanese encephalitis serological complex; Australia, Papua New guinea

Stratford: Japanese encephalitis serological complex; Australia

Cacipacore: Japanese encephalitis serological complex; South America

Yaounde: Japanese encephalitis serological complex; Africa

Ilheus: subgroup I; mosquito vector; causes encephalitis; Brazil, Guatemala, Trinidad, Honduras

Dengue Virus: subgroup II; types 1-4; causes dengue fever (headache, fever, myalgia, maculopapular rash in 31% of cases), dengue haemorrhagic fever (haemorrhagic rash), dengue shock syndrome (prostration), nonpurulent conjunctivitis; antibody bound to microbe enhances infection of phagocyte; affects macrophage suppressor activity; vectors *Aedes aegyptii, Aedes scutellaris, Aedes katherinensis* and *Aedes albopictus* mosquitoes; host humans; widespread (S and SE Asia, Pacific Islands, Central and S America, N Australia, New Guinea, Greece, Caribbean Islands, Nigeria); diagnosis: culture (sensitivity 30-80%), ELISA (IgM positive in 80% by fifth day), immunochromatographic card assay (sensitivity 99% in primary cases, 94% in secondary, specificity 93%), reverse transcription-polymerase chain reaction (being evaluated), hybridisation assay (being evaluated); controlled by mosquito control; live vaccine under test

Yellow Fever Virus: subgroup III; causes yellow fever (haemorrhagic fever, prostration, hepatitis, nephritis); carried in blood free in plasma; recovery from primary infection due to antibody; vector mosquito (*Aedes aegyptii* and other *Aedes*); host humans and nonhuman primates; tropical America, sub-Saharan African, Trinidad; diagnosis: serology (antigen in blood by ELISA, specific IgM or rise in titre by complement fixation test, haemagglutination inhibition antibody technique, neutralisation antibody titre), isolation in tissue culture, histology of liver; treatment: tiazofurin; controlled by immunisation and mosquito control

Edge Hill Virus: related to yellow fever virus; Australia

18 other viruses in subgroup III with mosquito vector

Kyasanur Forest Virus: subgroup IV; causes Kyasanur Forest disease (haemorrhagic fever); India; tick transmission

Omsk Haemorrhagic Fever Virus: subgroup IV**;** causes Omsk haemorrhagic fever; Central Russia, Romania; tick transmission

Powassan Virus: subgroup IV; vectors *Ixodes cookei, Ixodes marxi, Ixodes persulcatus, Ixodes ricinus, Ixodes spinipalpus, Dermacentor andersoni;* host rodents (primarily woodchucks in USA), birds, goats, cattle; NE and Central

Europe, Canada, Northern USA; causes encephalitis (case-fatality rate 10-20%); prevented by protection from tick bite; controlled by tick control

Russian Spring-Summer Encephalitis Group: subgroup IV; 14 viruses; tick vector; cause encephalitis, meningoencephalitis, haemorrhagic fever; Russian spring-summer encephalitis in former Soviet Union, Canada, USA; louping ill in Great Britain; others in Japan, Siberia, Central Europe, Finland, India, Malaya

Rio Bravo Virus: found in bat salivary gland; unrecognised vector; causes encephalitis; California, Texas

Pestivirus: > 3 viruses of cattle and pigs; helical capsid symmetry, enveloped virion, cytoplasm site of capsid assembly, surface membrane site of nucleocapsid envelopment, ether sensitive; helical capsid occurs in animal and plant viruses, but not in animal DNA viruses; helical ribonucleoprotein under capsid is flexible; all animal viruses with helical nucleocapsids also have lipid-containing envelopes

Hepacivirus: hepatitis C virus; 35 nm; ssRNA; envelope; parenterally (including pooled plasma products; inactivated by severe terminal heat and solvent-detergent treatment, sporadic transmissions with pasteurisation) and sexually transmitted non-A, non-B hepatitis; causes hepatitis, haemorrhagic fever, 'influenza-like illness,' infusion infection; chronicity (prolonged carrier state similar to hepatitis B virus exists in some patients; ? associated with hepatocellular carcinoma, splenetic lymphoma; incubation period ? 7 w (range 2-22 w); prevalence varies from < 0.5% in Scandinavia to 8-14% in Egypt; serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; diagnosis: haemagglutination, ELISA, immunoblot, PCR

Hepatitis G Virus: causes acute and chronic hepatitis (mild) in humans; may be same as GB virus-C or very closely related; transmitted by heterosexual intercourse

GB Virus-A: latent tamarin virus

GB Virus-B: definitely causes hepatitis in tamarins; may cause acute hepatitis in humans

GB Virus-C: causes acute and chronic hepatitis in humans; may be same as hepatitis G virus or very closely related

Picornaviridae: positive single strand RNA acts as messenger, translated monodirectionally into giant peptide, subsequently cleaved, no envelope from infected cell, molecular weight $2.3\text{-}2.6 \times 10^6$ D, in icosahedral, ether-resistant capsid with 32 capsomeres, 22-30 nm diameter; replicate in cytoplasm of infected cell; stabilised to heat at 50?C / 1 h by 1M-$MgCl_2$; stable at acid pH; found in enteric tract and hence in sewage; penetrate host cells by endocytosis

***Enterovirus*:** stable at pH 3.9, relatively unstable at 50?C, density 1.33-1.34 g / cm^3 in CsCl; increased infectiousness in abnormal host (clinical infection); enters across epithelial surface of intestinal tract and subsequently spreads through body; immunity due to antibody (++), cell-mediated immunity (+); causes mild summer colds, rhinitis, croup, influenza-like illness, nonexudative pharyngitis and tonsillitis, otitis media, 70-79% of nonpyogenic meningitis (33% of syndromes), meningoencephalitis, 3-40% of encephalitis, neonatal disease, myocarditis, pericarditis, chronic infections in immunocompromised, poliomyelitis-like illness, hand-foot-and-mouth disease, ? acute infective lymphocytosis, ? diabetes type 1

Poliovirus: molecular weight 2.5×10^6 D, 7.5 kb / strand, 1 segment, positive polarity; 3 types; survives 2-130 d in water (source human faeces); causes acute paralytic and bulbar poliomyelitis, carditis, encephalitis (infrequent in impaired cell-mediated immunity), epidemic viral diarrhoea (types 2 and 3), febrile illness, non-pyogenic meningitis, respiratory infection; replicates only in primates or primate-derived cell cultures; viral capsid protein reacts with specific receptor on susceptible tissue cell (eg., neurone); carried in blood free in plasma; replicates in striated muscle and intestinal lymphoid tissue; disseminates to reticuloendothelial tissue (liver, spleen, lymph nodes, bone marrow) via blood; affects macrophage accessory function; ? biliary excretion of virus into intestine; immunity associated with high titres of type-specific neutralising IgA on mucosal surface; recovery from primary infection due to antibody; 5 genes; diagnosis: isolation primary method (primary monkey kidney +++, human diploid fibroblasts +++, Hep2 +++, 5 d to isolation; random, swollen, glassy cells, rapid progression and detachment of cells from glass; neutralisation test), antigen detection not available, serology not generally available (viral isolate required)

Coxsackievirus: 24 coxsackievirus A, 6 coxsackievirus B; pathogenic for baby mice; survives 2 d - 46 w in water (source human faeces); causes acute haemorrhagic conjunctivitis, common or feverish cold, diabetes, encephalitis, epidemic viral diarrhoea (A, B3), fever with exanthem, hand, foot and mouth syndrome, prenatal hepatitis, herpangia + exanthem, macular rash, maculopapular rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, anaphylactoid purpura, chronic or recurrent rash, nonpyogenic meningitis, mouth ulcers, myocarditis of newborn and

interstitial myocarditis and valvulitis in infants and children, pancreatitis, parotitis and submandibular sialadenitis, pericarditis, epidemic pleurodynia, pneumonia with exanthem, acute paralytic poliomyelitis, febrile URTI in military recruits, febrile pharyngitis in children, nonexudative pharyngitis and tonsillitis, rhabdomyolysis, summer febrile illness, pneumonitis, orchitis, generalised disease of newborn infants, 5% of nosocomial diarrhoea; replicates in striated muscle and intestinal lymphoid tissue; ? biliary excretion of virus into intestine; recovery from primary infection due to antibody; serum autoantibodies against heart muscle in patients with acute myocarditis; diagnosis: ELISA

A: causes epidemic viral diarrhoea, aseptic meningitis

A1: no growth in cell cultures; causes herpangia, nonpyogenic meningitis, summer febrile illness

A2: no growth in cell cultures; causes maculopapular rash, nonpyogenic meningitis with exanthem, transient paralytic disease, herpangia, fever with exanthem, summer febrile illness, nonexudative pharyngitis and tonsillitis

A3: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes herpangia, summer febrile illness

A4: no growth in cell cultures; causes nonpyogenic meningitis, herpangia with exanthem, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), petechial or purpuric rash (anaphylactoid), acute paralytic poliomyelitis, fever with exanthem, summer febrile illness, nonexudative pharyngitis and tonsillitis

A5: no growth in cell cultures; causes nonpyogenic meningitis, herpangia, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), summer febrile illness, nonexudative pharyngitis and tonsillitis

A6: no growth in cell cultures; causes nonpyogenic meningitis, herpangia, roseola-like illness, summer febrile illness, nonexudative pharyngitis and tonsillitis, maculopapular rash

A7: may grow in monkey kidney or HeLa cells; causes nonpyogenic meningitis with exanthem, paralytic disease (acute paralytic poliomyelitis), maculopapular rash, vesicular rash (hand, foot and mouth syndrome), pneumonia with exanthem, summer febrile illness

A8: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes herpangia, vesicular rash, summer febrile illness, nonexudative pharyngitis and tonsillitis

A9: grows in monkey kidney and human amnion and embryonic kidney cells, may grow in HeLa cells; causes nonpyogenic meningitis with exanthem, paralytic disease (acute paralytic poliomyelitis), herpangia with exanthem, fever with exanthem, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), petechial or purpuric rash (anaphylactoid), generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, pneumonia with exanthem, pneumonitis, summer febrile illness, nonpurulent conjunctivitis

A10: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, herpangia, acute URTI (cold), maculopapular rash, vesicular rash (hand, foot and mouth syndrome), erythema multiforme or Stevens-Johnson syndrome, summer febrile illness, nonexudative pharyngitis and tonsillitis

A11: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

A12: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, summer febrile illness

A13: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

A14: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, summer febrile illness

A15: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

A16: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, herpangia, fever with exanthem, hand, foot and mouth syndrome, maculopapular rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, chronic or recurrent rash, summer febrile illness

A17: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

A18: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

A19: no growth in cell cultures; causes febrile summer illness

A20: no growth in cell cultures; causes summer febrile illness

A21: no growth in cell cultures; causes herpangia, acute URTI (common or feverish cold; febrile URTI in military recruits), summer febrile illness

A22: no growth in cell cultures; causes herpangia, nonpyogenic meningitis, summer febrile illness

A23: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness, nonpyogenic meningitis, acute paralytic poliomyelitis, maculopapular rash
A24: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes acute haemorrhagic conjunctivitis, acute URTI (cold), summer febrile illness, Bornholm disease (pleurodynia)
B: grows well in primary monkey kidney, human diploid fibroblasts, Hep2, HeLa cells, 4 d to isolation, focal, swollen, glassy cells, detachment from glass (neutralisation test); causes pancreatitis, orchitis, perinatal generalised disease (myocarditis, hepatitis), pleurodynia ('Devil's grip'), aseptic meningitis
B1: causes acute respiratory illness, pneumonia, prenatal hepatitis, nonpyogenic meningitis with exanthem, epidemic pleurodynia or myalgia, macular rash, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), roseola-like illness, infectious myocarditis, infectious pericarditis
B2: causes nonpyogenic meningitis with exanthem, acute URTI (cold), nonexudative pharyngitis and tonsillitis, epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, herpangia with exanthem, macular rash, maculopapular rash, vesicular rash, petechial or purpuric rash, roseola-like illness, orchitis, generalised disease of newborn infants, transient paralysis
B3: causes nonpyogenic meningitis (most frequently reported enterovirus), transient paralytic disease, acute URTI (cold), summer febrile illness, epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, hand, foot and mouth syndrome, maculopapular rash, vesicular rash, petechial or purpuric rash, orchitis, generalised disease of newborn, summer febrile illness, nonexudative pharyngitis and tonsillitis (herpangia), epidemic viral diarrhoea
B4: causes nonpyogenic meningitis with exanthem, paralytic disease, fever with exanthem, acute URTI (cold), epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, maculopapular rash, petechial or purpuric rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, orchitis, generalised disease of newborn, summer febrile illness
B5: causes nonpyogenic meningitis with exanthem, transient paralytic disease, acute URTI (cold), epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, orchitis, generalised disease of newborn, macular rash, maculopapular rash, vesicular rash (hand, foot and mouth disease), petechial or purpuric rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, onychomadesis and/or onycholysis, summer febrile illness, nonexudative pharyngitis and tonsillitis (herpangia)
B6: causes nonpyogenic meningitis, summer febrile illness
Echovirus: 33 types; survives in water 2 d - 46 w (source human faeces); causes arthritis, common or feverish cold, non-purulent conjunctivitis, convulsions (1% of echovirus infections), encephalitis, fever (10% of echovirus infections), postnatal gastroenteritis (diarrhoea and/or vomiting; 36% of echovirus infections), neonatal hepatitis, infections in abnormal host (?-globulin dysfunction), maculopapular rash, non-pyogenic meningitis/meningismus (23% of echovirus infections; 54% of enteroviral cases), myocarditis and pericarditis, paralysis, pleurodynia, acute URTI (4% of echovirus infections), rhabdomyolysis, systemic viral syndrome in agammaglobulinemia, summer febrile illness, ataxia; grows well in primary monkey kidney and human diploid fibroblast cells, not in Hep2 cells; 4 d to isolation, focal, swollen, glassy cells, detachment from glass (neutralisation test); diagnosis: isolation from infected tissue
Echovirus 1: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon sporadic; 3% of echoviral), maculopapular rash, paralysis (uncommon sporadic)
Echovirus 2: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon sporadic), exanthem (macular rash, maculopapular rash), paralysis (uncommon sporadic), encephalitis (uncommon sporadic), ataxia
Echovirus 3: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis with exanthem (uncommon epidemic), maculopapular rash, petechial or purpuric rash, encephalitis (uncommon epidemic)
Echovirus 4: causes nonpyogenic meningitis with exanthem (common epidemic; 6% of echoviral), summer febrile illness with rash (common epidemic), exanthem (macular rash, maculopapular rash, petechial or purpuric rash), paralysis (uncommon epidemic), encephalitis (uncommon sporadic), ataxia, acute URTI (uncommon sporadic), ? vaginitis
Echovirus 5: causes nonpyogenic meningitis (uncommon sporadic), summer febrile illness with rash (uncommon sporadic), macular rash, maculopapular rash, zoster-like rash

Echovirus 6: causes nonpyogenic meningitis with exanthem (common epidemic), paralysis (uncommon sporadic), summer febrile illness with rash (uncommon sporadic), exanthem (maculopapular rash, vesicular (zoster-like) rash, erythema multiforme or Stevens-Johnson syndrome), encephalitis (uncommon sporadic), ataxia, enteritis (common epidemic), perinatal hepatitis, pleurodynia (uncommon sporadic), myocarditis (uncommon sporadic)
Echovirus 7: 15% of enterovirus isolates; causes nonpyogenic meningitis (52% of echovirus 7 infections; 21% of echoviral cases; common sporadic), upper respiratory tract disease (14%), encephalitis (9% of echovirus 7 infections, 9% of enteroviral encephalitis; uncommon sporadic), nonspecific febrile illness (7%), rash (maculopapular, petechial or purpuric; 2%), carditis (1%), paralysis (0.6%), epidemic viral diarrhoea
Echovirus 8: 7% of nonpolio enterovirus isolates; causes acute URTI (uncommon sporadic), enteritis (uncommon sporadic)
Echovirus 9: 9% of nonpolio enterovirus isolates; causes nonpyogenic meningitis with exanthem (uncommon epidemic), epidemic viral diarrhoea, fever with rash (common epidemic), otitis media, paralysis (uncommon sporadic), pharyngitis in children, acute exudative tonsillitis, rash (maculopapular, vesicular, petechial or purpuric, roseola-like illness, anaphylactoid purpura), summer febrile illness, encephalitis, ataxia, pneumonia with exanthem
Echovirus 11: 14% of nonpolio enterovirus isolates; causes nonpyogenic meningitis with exanthem (46% of echovirus 11 infections; 38% of echoviral cases; common epidemic), epidemic viral diarrhoea (23%), encephalitis (15% of echovirus 11 infections, 15% of enteroviral cases), common cold (9%), nonspecific febrile illness (8%), rash (maculopapular, vesicular, urticarial, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, chronic or recurrent rash; 2%), pneumonia with exanthem (1%; uncommon sporadic), carditis (0.6%), paralysis (0.4%; uncommon sporadic), ataxia, perinatal hepatitis; diagnosis: PCR
Echovirus 12: causes summer febrile illness, epidemic viral diarrhoea
Echovirus 13: causes summer febrile illness, macular rash, maculopapular rash, nonpyogenic meningitis (uncommon sporadic), coryza, pharyngitis, bronchitis, broncholitis, poliomyelitis-like illness, diarrhoea with fever, encephalitis, enteroviral sepsis
Echovirus 14: causes nonpyogenic meningitis with exanthem (uncommon sporadic), summer febrile illness, exanthem (macular rash, maculopapular rash), enteritis (uncommon epidemic viral diarrhoea, perinatal hepatitis)
Echovirus 15: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)
Echovirus 16: causes nonpyogenic meningitis (uncommon epidemic), summer febrile illness with rash (uncommon epidemic), exanthem (maculopapular rash, roseola-like illness), paralysis (uncommon sporadic), encephalitis, ataxia, herpangia with exanthem
Echovirus 17: causes summer febrile illness, nonpyogenic meningitis with exanthem (uncommon sporadic; 3% of echoviral), macular rash, maculopapular rash, vesicular rash, herpangia with exanthem, nonpurulent conjunctivitis
Echovirus 18: causes summer febrile illness with rash (uncommon epidemic), nonpyogenic meningitis with exanthem (uncommon epidemic), exanthem (macular rash, maculopapular rash, anaphylactoid purpura), paralysis (uncommon sporadic), encephalitis (uncommon sporadic), ataxia, enteritis (uncommon epidemic viral diarrhoea), nonpurulent conjunctivitis
Echovirus 19: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon epidemic), macular rash, maculopapular rash, encephalitis (uncommon sporadic), acute URTI (uncommon epidemic), enteritis (uncommon sporadic), myocarditis (uncommon sporadic), perinatal hepatitis
Echovirus 20: causes summer febrile illness, acute URTI (common cold; common epidemic), nonpyogenic meningitis (uncommon sporadic), enteritis (uncommon sporadic)
Echovirus 21: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)
Echovirus 22: causes summer febrile illness, maculopapular rash, nonpyogenic meningitis (uncommon sporadic), acute URTI (uncommon sporadic), enteritis (uncommon sporadic)
Echovirus 23: causes summer febrile illness, nonpyogenic meningitis, enteritis (uncommon sporadic)
Echovirus 24: 3% of echovirus isolates; 44% associated with nonpyogenic meningitis; also causes summer febrile illness, enteritis (uncommon sporadic)
Echovirus 25: causes summer febrile illness, maculopapular rash, nonpyogenic meningitis with exanthem (uncommon sporadic; 3% of echoviral), haemangioma-like lesions, roseola-like illness, acute URTI (uncommon sporadic)
Echovirus 26: causes summer febrile illness

Echovirus 27: causes summer febrile illness, maculopapular rash, roseola-like illness
Echovirus 29: causes summer febrile illness
Echovirus 30: causes nonpyogenic meningitis with exanthem (third most frequently reported enterovirus; common epidemic), carditis, encephalitis, gastroenteritis, respiratory tract illness, summer febrile illness, paralysis (uncommon epidemic), ataxia, macular rash, maculopapular rash, roseola-like illness; 28% of nonpolio enterovirus isolates (40% of isolates from faeces or rectal swabs, 21% from CSF, 19% from throat swabs, 16% from tissues, 1% from nasopharynx, 1% from urine, 5% from other sources)
Echovirus 31: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)
Echovirus 32: causes summer febrile illness, haemangioma-like lesions, enteritis (uncommon sporadic)
Echovirus 33: causes maculopapular rash, nonpyogenic meningitis with exanthem
Enterovirus 70: causes nonpurulent conjunctivitis, acute haemorrhagic conjunctivitis
Enterovirus 71: causes macular rash, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), nonpyogenic meningitis with exanthem
Hepatovirus: hepatitis A virus; virus 30 nm; ssDNA; no envelope; survives > 24 d in water (source human faeces); causes infectious hepatitis (short incubation hepatitis; entero (faecal-oral) transmission and transmission by pooled plasma products (inactivated by severe terminal heat or pasteurisation, not by solvent-detergent treatment); incubation period 15-40 d; acute onset; fever common; autumn and winter; commonest in children and young adults), arthritis, hepatic granuloma, haemorrhagic fever, nonpyogenic meningitis, myocarditis and pericarditis; replicates in liver; biliary excretion of virus into intestine; increased infectiousness in abnormal host; serum antibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; no chronicity; virus in faeces and blood incubation period and acute phase; prophylactic value of ?-globulin (passive immunity); diagnosis: ELISA for hepatitis A IgM antibody + total hepatitis A antibody, immune adherence haemagglutination test for hepatitis A IgM antibody, seroconversion of hepatitis A IgG antibody, counterimmunoelectrophoresis, immune electron microscopy of stool, indirect fluorescent antibody titre, radioimmunoassay
Cardiovirus
Encephalomyocarditis Virus: causes encephalomyocarditis; major host defence mechanism interference with adherence (++++)
Mengovirus: causes non-pyogenic meningitis
Rhinovirus: common cold virus; causes cold (++++), croup, febrile upper respiratory infection (++), otitis media, rhinitis, acute sinusitis, nonexudative pharyngitis and tonsillitis, clinical infection in abnormal host, asthma exacerbation;
> 115 types infecting humans, 2 viruses of cattle; acid labile (unstable below pH 5-6), relatively stable at 50?C, density 1.38-1.41 g/cm^2 in CsCl; disease-producing dose in man: nasal cavity 1 TCID 50, conjunctiva 16 TCID 50, posterior pharyngeal wall 200 TCID 50; infection generally confined to epithelial surface of respiratory tract; replicates only in primates or in primate-derived cell cultures (primary monkey kidney +, human diploid fibroblasts +++, Hep2 negative; 7 d to isolation; focal, swollen or granular cells; pH 3 stability, neutralisation test); immunity is associated with high titre of type-specific neutralising IgA on mucosal surface
Togaviridae: positive single strand RNA (infectious), lipid envelope from infected cell; site of nucleocapsid envelopment surface membrane or intracytoplasmic membranes; ether sensitive; diameter of virion 20-70 nm, molecular weight of nucleic acid in virion $3\text{-}4.6X10^6$ D, 12 kb; icosahedral symmetry; multiplies in arthropods; penetrates cell wall by endocytosis; 200 different types; unstable without added protein but survives several months at –20?C, indefinitely at –70?C or if lyophilised; haemagglutinates red blood cells from newborn chicks or geese; diagnosis: serology primary method (only primary togavirus infection of individuals not previously exposed to similar togavirus can be diagnosed reliably by rises in antibody titre), isolation not generally available (best animal host suckling mouse), antigen detection not available
Alphavirus: arbovirus group A; 23 members; 27-70 nm diameter, with 32 capsomeres in a lipid envelope; single stranded RNA, molecular weight $3X10^6$ D; replicates in cytoplasm and matures by budding from surface membrane; causes Eastern equine encephalitis, Venezuelan equine encephalitis, Western equine encephalitis (includes Sindbis),

Getah, Semliki; mosquito-borne; replicates in arthropods; adsorption by temperature-independent process, synthesis of large polypeptide cleaved to give structural polypeptides, attachment to inner surface of host cell membrane

Eastern Equine Encephalitis Virus: subgroup I; Atlantic and Gulf coasts of USA (freshwater swamps; (? 3 cases (2 deaths)/y)), Canada, Brazil, Cuba, Panama, Philippines, Dominican Republic, Trinidad; reservoir wild birds; vector *Culex melanura* mosquito; causes encephalitis (summer and early autumn; ? 42-50% case-fatality rate)

Venezuelan Equine Encephalitis: subgroup I; Central and S America (Brazil, Colombia, Ecuador, Trinidad, Venezuela, Mexico), southern USA (Florida, Texas); reservoir rodents and horses; vector *Culex* and other mosquitoes; also infectious as aerosol and possible biowarfare agent (10-100 organisms required for infection); causes encephalitis (< 3 cases/y in USA; fatalities rare)

Western Equine Encephalitis Virus: subgroup I; freshwater swamps and irrigated areas west of Mississippi River, Canada, Mexico, Argentina, Brazil, British Guiana; reservoir wild birds, especially English sparrows; vector *Culisetta melanura* and *Culex tarsalis* mosquitos; causes Western equine encephalitis (summer and early autumn; ? 20 cases (mainly infants and children)/y; < 3% case-fatality rate)

Sindbis: subgroup I; mosquito vector; causes haemorrhagic fever but usually subclinical; ? 35 cases (< 1 death)/y; Egypt, India, S Africa, Australia

Chikungunya: subgroup II; mosquito vector; headache, fever (may be haemorrhagic), rash, joint and muscle pains; E Africa, S Africa, SE Asia

Semliki Forest: subgroup II: mosquito vector; fever or no symptoms; E Africa, W Africa

Magaro: subgroup II; mosquito vector; headache, fever, joint and muscle pains; Bolivia, Brazil, Colombia, Trinidad

Ross River Virus: mosquito vector (*Aedes vigilax* and *Aedes camptorhynchus* in salt marshes, *Culex annulirostris* in fresh water; also *Ades normanensis*, *Coquillettidia linealis* and *Aedes notoscriptus*); Australia, New Guinea, Solomon Islands; causes Ross River fever, arthritis, 'influenza-like illness,' macular rash; diagnosis: culture of serum, ELISA (IgG and IgM)

Barmah Forest Virus: mosquito vectors as for **Ross River Virus**; Australia (? 700 notified cases/y (55% in Queensland)); causes arthritis, arthralgia, rash, fever, lethargy, malaise

3 others named with mosquito vector and subclinical or asymptomatic infection

Rubivirus: rubella virus; enveloped particle 60 nm diameter with 33 nm internal core of ribonucleoprotein; causes rubella (German measles), abortion, arthritis (usually adult women; fingers, wrists and knees), carpal tunnel syndrome (11% of total due to virus and 14% due to vaccine), catarrh, coryza, encephalitis (progressive rubella panencephalitis— slow viral disease), meningoencephalitis (rare), nonpyogenic meningitis, prenatal generalised disease (including hepatitis, urinary infection), stillbirth, teratogenic effects, Guillain-Barré syndrome, myocarditis and pericarditis, nonpurulent conjunctivitis, erythematous rash, maculopapular rash; increased infectiousness in abnormal host; infects lymphocytes and macrophages; chronic infection; immunity cell mediated (+++); diagnosis: negative passive haemagglutination with positive ELISA (IgG, IgM and IgM capture), haemagglutination inhibition (diagnostic titre ? 1:8), tissue culture of urine, throat swab, amniotic fluid, placenta

GROUP V: NEGATIVE SENSE RNA VIRUSES

Bornaviridae

Bornavirus: Borna disease virus; causes progressive polioencephalomyelitis in horses and sheep; possibly linked to schizophrenia-like disease and major depressive disorder in humans

Filoviridae

Filovirus

Ebola Virus: causes Ebola haemorrhagic fever; Subsaharan Africa; means of transmission unknown; diagnosis: antigen test by immunofluorescent agglutination test, antibody ELISA, reverse transcriptase polymerase chain reaction

Marburg Virus: causes Marburg haemorrhagic fever; Subsaharan Africa; means of transmission unknown; acquired after exposure to tissues of infected African monkeys; diagnosis: direct visualisation on electron microscopy of infected tissues, virus specific immunofluorescence or electron microscopy of isolate (grows readily in Vero cells) from blood or serum or suspensions of heart, kidney, liver or spleen, complement fixation test

Paramyxoviridae: single negative strand RNA antimessenger on which virion transcriptase initiates transcription at single promoter to yield 5-8 complementary messengers (positive strand); molecular weight 5-7X10^6 D (17-20 kb) in an

internal coiled ribonucleoprotein helix 18 nm diameter (except respiratory syncytial virus— 14 nm) embedded in lipid of host cell origin, which also contains viral haemagglutinin; particle about 125-300 nm (range 100-800 nm) diameter with surface spikes; RNA synthesised in nucleus of infected cell, other components in cytoplasm; virus maturation at cell surface; ether sensitive; haemagglutinate red cells; penetrate host cells by fusion; do not require intact nucleus to reproduce; nucleocapsid localised in cytoplasm, not fragmented; virion (viral-coded) RNA polymerase; no separate haemagglutinin and neuraminidase; haemagglutinins attach to host cell nuclear membrane before budding of virus during viral replication; neuraminidases induce antibody that decreases size, but not number, of plaques in vitro; filamentous forms observed; haemolysin present (except in respiratory syncytial virus); prominent cytoplasmic inclusions (also nuclear in measles); syncytial formation; disrupt with lipid solvents; cytoplasm site of multiplication

Paramyxovirinae

Paramyxovirus: causes respiratory ? generalised infection

Parainfluenza Virus: types 1-4 + Sendai virus (Simian SV5); haemagglutination +, haemadsorption +, haemolysis +, neuraminidase +, antigenic relationship to mumps; causes acute respiratory illness— croup in infants and young children (type 1 ++++, 2 and 3 +), pneumonia (types 1 and 3 ++++), ‘influenza-like illness’ (type 1 +++, type 3 +), common or feverish cold (types 1 and 3 ++), minor URTI (types 1 and 3 ++, 4), bronchitis (types 1, 3), acute bronchiolitis, bronchopneumonia (types 1, 3), laryngotracheitis, pneumonitis, sore throat, acute exudative tonsillitis, coryza, rhinitis; also epidemic viral diarrhoea (in 15% of cases), otitis media, rhabdomyolysis, roseola-like illness; decreases polymorphonuclear bactericidal and secretory functions; diagnosis: isolation primary method (primary monkey kidney +++, Hep2 +, human diploid fibroblasts negative; 6-11 d to isolation, no cytopathic effect or focal rounding and multinucleate giant cells (types 2 and 3); haemadsorption at 4?C < at 20?C), antigen detection described but not generally available, paired sera required for serology (haemagglutination inhibition, fluorescent antibody, complement fixation test, radioimmunoassay, ELISA); treatment: ribavirin aerosol (when warranted)

Parainfluenza 1: nearly all cases in children < 5 y; epidemic usually every other year; causes bronchitis, acute bronchiolitis and bronchopneumonia, pneumonia, croup, minor URTI, acute laryngitis, common or feverish cold, ‘influenza-like illness,’ pneumonia, tracheobronchitis, febrile nasopharyngitis, parotitis and submandibular sialadenitis; 3% of respiratory viral isolates in hospitalised children

Parainfluenza 2: about ½ of cases in children < 5 y; epidemic usually every other year; causes croup, tracheobroncitis, febrile nasopharyngitis, acute sinusitis, acute chest infection; 0.9% of respiratory viral isolates in hospitalised children

Parainfluenza 3: about ½ of cases in children < 1 y; endemic; causes minor URTI, acute laryngitis, bronchitis, acute bronchiolitis and bronchopneumonia, pneumonia, croup, common or feverish cold, tracheobronchitis, acute sinusitis, parotitis and submandibular sialadenitis, influenza-like illness, meningitis; 12% of respiratory viral isolates in hospitalised children

Parainfluenza 4: about ½ of cases in children < 5 y; endemic; causes common cold, minor URTI, pertussis-like syndrome, meningoencephalitis; 0.6% of respiratory viral isolates in hospitalised children

Rubulavirus: mumps virus; haemagglutinins and neuraminidases found on a single glycoprotein antigen; haemagglutination +, haemadsorption +, haemolysis +, neuraminidase +; 1 antigenic type, antigenic relationship to parainfluenza; causes mumps, anterior uveitis, arthritis, 6-10% of encephalitis, hydrocephalus and mental retardation, 1-4% of non-pyogenic meningitis, meningoencephalitis, myocarditis and pericarditis (in 0.04% of mumps cases), oophoritis, orchitis, pancreatitis, epidemic parotitis, respiratory infections; > 66% of cases have antibodies to smooth muscle and cytoplasmic filaments; serum autoantibodies against DNA, lymphocytes, insulin, pancreatic ?-cells and heart muscle (in acute myocarditis only) also produced; immunisation with live attenuated virus against mumps may be successfully combined with immunisation against measles and rubella; rarely isolated but can be cultured from blood, saliva, throat swab, secretions from Hansen’s duct, CSF, urine; grows in primary monkey kidney (+++), human diploid fibroblasts (+), not in Hep2; 7 d to isolation, enlarged syncytial giant cells; diagnosis: complement fixation test, indirect fluorescent antibody titre for IgG and IgM, ELISA (IgM), haemadsorption, passive haemagglutination, haemagglutination inhibition, neutralisation test (not routine)

Newcastle Disease Virus: molecular weight $6X10^6$; 18 kb/strand; 1 segment negative polarity 18 nm diameter, virion 125-250 nm; causes disease in fowl, non-purulent conjunctivitis in man; inhibits phagocytic oxidative burst > 5 other diseases of birds and mammals

Morbillivirus: measles virus; more contagious than mumps; haemagglutination +, haemadsorption +, haemolysis +, neuraminidase –; 1 antigenic type; causes measles (morbilli, rubeola), anterior uveitis, bronchopneumonia, coryza, catarrh, croup, 6-7% of encephalitis, epidemic viral diarrhoea, neonatal hepatitis (fatal in children with leukemia), 4% of non-pyogenic meningitis, mouth lesions, myocarditis and pericarditis, otitis media, giant cell pneumonia with exanthem, pneumonitis, mesenteric lymphadenitis (in 15% of hospitalised cases), subacute sclerosing panencephalitis (chronic neurologic condition with characteristics of both ‘chronic’ and ‘slow’ infection), maculopapular rash, roseola-like illness, urinary infection, nonpurulent conjunctivitis; atypical measles follows infection in persons previously immunised with formalin-inactivated measles vaccine (gives polymorphous rash); clinical and persistent nonlatent infection in

abnormal host (T helper lymphocyte dysfunction); enters across epithelial surfaces of respiratory tract and conjunctiva and subsequently spreads through body; multiplies in macrophages; infects lymphocytes, affecting functions (not 'luxury' functions) of T, B and NK cells; decreases polymophonuclear chemotactic functions; carried in blood associated with mononuclear cells; loss of viral antigen by capping; recovery from primary infection due to cell-mediated immunity, resistance to reinfection due to antibody; persists in brain (may be infectious, not shed to exterior), causing subacute sclerosing panencephalitis; > 66% of cases have antibodies to smooth muscle and cytoplasmic filaments; serum autoantibodies against DNA, lymphocytes, insulin, pancreatic ?-cells and heart muscle (in acute myocarditis only) also produced; diagnosis: haemagglutination inhibition (significant titre ? 1:10 or 4X rise), complement fixation test, staphylococcal protein A adsorption (specific IgM), sucrose gradient ultracentrifugation, ELISA (IgG, IgM), tissue culture (WI38, primary monkey kidney, Hep2; no growth in human diploid fibroblasts; vacuolated, syncytial giant cells; rarely isolated but may be cultured from throat swab or washings collected soon after rash appears; verified by neutralisation test, fluorescent antibody); treatment: ribavirin

Rinderpest Virus: causes rinderpest in cattle

Distemper Virus: causes distemper in dogs; multiplies in macrophages, causing profound suppression of T and B cells and macrophages

Peste-Des-Petite Ruminant Virus: causes disease in sheep and goats

Hendra Virus: equine morbillivirus; causes respiratory disease in horses and humans

Nipah Virus: causes encephalitis (often fatal); spread from pigs to humans; Malaysia and Singapore; diagnosis: immunohistochemistry + serology

Pneumovirinae

Pneumovirus: human respiratory syncytial virus; haemagglutination +, haemadsorption –, haemolysis –, neuraminidase – 1 antigenic type; causes acute respiratory illness— acute bronchiolitis, bronchopneumonia, pneumonia and pneumonitis in infants (+++), common or feverish cold (++), URTI (++), croup (+), influenza-like illness (+), bronchitis, rhinitis, acute exudative tonsillitis; causes airway hyperresponsiveness and enhanced airway sensitisation to allergen; 66% of respiratory viral isolates in hospitalised children; major cause of lower respiratory tract infection in young children; most frequent nosocomial infection on paediatric wards; decreases polymorphonuclear bactericidal, chemotactic, oxidative and secretory functions; natural immunity incomplete; diagnosis: isolation primary method (primary monkey kidney +++, human diploid fibroblast +, Hep2 +++, 6-8 d for isolation, enlarged, glassy, syncytial giant cells or granular rounded cells; verified by fluorescent antigen, neutralisation test, ELISA), antigen detection useful for rapid diagnosis (ELISA (Vidas sensitivity 66%, specificity 94%), radioimmunoassay), paired sera required for serology; treatment: ribavirin

Metapneumovirus: human metapneumovirus causes mild to severe respiratory disease in children (bronchiolitis in 68%, pneumonitis in 17%)

Rhabdoviridae: negative polarity single strand RNA (noninfectious), molecular weight 3-4.6X10^6 D (11-24 kb) in an internal coiled ribonucleoprotein helix 18-50 nm embedded in lipid of host cell origin, making a bullet-shaped particle 60-80X130-240 nm with surface spikes; penetrate cells by endocytosis; most harmless to humans; virion enzyme (RNA dependent) RNA transcriptase; lipid solvents disrupt virions, inactivate infectivity; maturation by budding at cytoplasmic membranes; hosts wide range of mammals, fish, invertebrates and plants; no common antigens; diagnosis: antigen detection and isolation in reference laboratories primary methods, serology useful for assessment of immunity

Vesiculovirus: several vesicular stomatitis viruses infecting horses, cattle, swine and occasionally humans; molecular weight 4X10^6 D, 13 kb/strand, 1 segment, negative polarity, virion 68X175 nm, bullet-shaped

Lyssavirus: rabies virus; causes rabies, encephalitis, myocarditis and pericarditis; transmitted by bite from infected animal; persistent infection of glands, etc inaccessible to circulating antibody

AMBISENSE RNA VIRUSES

Arenaviridae: molecular weight 3.5X10^6 D; contained in a set of granules about 20 nm diameter similar to ribosomes; particle 50-300 nm diameter (average 110-130 nm) with lipid envelope with surface spikes; develop in cytoplasm of infected cells; surface membrane site of helical nucleocapsid development; single strand RNA; spherical, pleomorphic, 2 segments virus specific 3.6 and 1.6X10^6 D (11 and 4.8 kb); in 3 species, host RNA also in virions; 2 glycoproteins 72 000 and 1200 D; lipid solvents inactivate; unstable; no haemagglutination; best animal hosts various

rodents; budded from surfaces of cells; geographically restricted to range of host mammals; able to code for new antigens on surface of infected cells; person-to-person transmission rare

Arenavirus: single strand RNA; envelope from infected cell; diameter of virion 50-300 nm; normally infects rodents; may give serious disease in man

Lymphocytic Choriomeningitis Virus: normally infects mice; may give serious disease in man; causes 'influenza-like illness,' birth defects, encephalitis, non-pyogenic meningitis, parotitis and submandibular sialadenitis; multiplies in macrophages; carried in blood in platelets, leucocytes and plasma; infects lymphocytes and macrophages (affects accessory function of macrophages); antibody of poor specificity or affinity fails to neutralise or opsonise; viral invasion of lymphoid tissue leads to suppressor T cell induction or clonal deletion of T cells; persistent, but harmless, carriage of virus for laboratory rodents; persistent infection leads to a continuous immune complex formation and trapping, causing glomerulonephritis, vasculitis, and uveitis, as well as possibly deleterious production of autoantibodies and interferon; recovery from primary infection due to cell-mediated immunity (antibody-initiated, complement-dependent lysis requiring specific antiviral IgG and alternative pathway of complement)

Lassavirus: causes Lassa fever (haemorrhagic fever), abortion, encephalitis, myocarditis and pericarditis, adult hepatitis; found in W and Central Africa; maintained in nature by rodent, transmitted by rodent, easily transmitted from person to person; diagnosis: isolation from blood, throat or urine, serology (fluorescent antibody staining of conjunctival scrapings); treatment and prophylaxis: ribavirin

Tacaribe Complex: 8 members (Tacaribe, Junin, Tanian, Machupo, Pichide and 3 other viruses of S American haemorrhagic fevers); headache, fever, neuralgia, haemorrhagic signs; S and Central America

Junin Virus: causes Argentinian haemorrhagic fever; Argentina; case-fatality rate 20%; no arthropod vector; rodent transmission; diagnosis: serology; treatment: postconvalescent plasma

Machupo Virus: causes Bolivian haemorrhagic fever; Bolivia; case-fatality rate 20%; rodent transmission; diagnosis: serology

Guanarito Virus: causes Venezuelan haemorrhagic fever; Venezuela

Bunyaviridae: 90-100 nm diameter, molecular weight $6\text{-}7X10^6$ D; arboviruses; spherical, enveloped, helical nucleocapsid; single stranded RNA, 3 segments of 4, 2 and $0.8X10^6$ D (12, 6 and 2.4 kb); 2 glycoproteins 115 000 and 38 000 D, 1 nonglyoxylated protein 19 000 D; lipid solvents inactivate; unstable below pH 7; haemagglutinate 1 d chick or goose red blood cells; cause encephalitis; best animal host suckling mice, chicken

Bunyavirus: Bunyamwera and 17 others; mosquito vector; headache, fever, myalgia, fever only or no symptoms; Uganda, S Africa, India, Malaya, Colombia, Brazil, Trinidad, W Africa, Finland, USA

California Group: California encephalitis virus, LaCrosse virus and 9 others; mosquito vector; encephalitis or no symptoms; USA, Trinidad, Brazil, Canada, Czechoslovakia, Mozambique

California Encephalitis Virus: causes California encephalitis (? 60 cases (< 1 death)/y; *Aedes melaninon* vector; ground squirrel principal vertebrate host; California, Texas, Utah)

La Crosse Virus: causes La Crosse encephalitis; mosquito (*Aedes triseriatus*) vector; chipmunk and squirrels principal vertebrate hosts; Upper Mississippi River Valley

Tahyna Virus: *Culiseta annulata* and *Aedes* vectors; hares principal vertebrate host; Europe

> 154 viruses of other serogroups

Hantavirus: Hantaan and several other viruses (especially Seoul virus, Belgrade virus and Puumula virus); causes haemorrhagic fever with renal syndrome (epidemic haemorrhagic fever, Korean haemorrhagic fever); Pulmonary Syndrome Hantavirus causes pulmonary illness (can be lethal); Asia, Balkans, former Soviet Union, Europe, USA, Africa; rodents, bats, birds reservoir; transmission via aerosol; many members; diagnosis: immunofluorescent antibody test, ELISA; treatment: ribavirin; prevention: combined Hantaan/Puumula vaccine

Puumala Virus: causes nephropathia epidemica (mild form of haemorrhagic fever with renal syndrome occurring in Scandinavia); diagnosis: serology, histology; treatment: ribavirin

Nairovirus: Crimean-Congo haemorrhagic fever virus; causes Crimean-Congo haemorrhagic fever (headache, fever, myalgia, haemorrhagic signs, meningoencephalitis, nonpurulent conjunctivitis); Africa, Asia, Southern former Soviet Union; mosquito-borne; diagnosis: isolation of virus from blood, 4X rise in antibody titre, presence and decline of IgM antibody; also viruses of 5 other serogroups (> 27 members) including virus of Nairobi sheep disease

Phlebovirus: sandfly fever virus (> 30 members) and other viruses of humans and animals, including of sheep and other ruminants, which may cause human disease (Phlebotomus fever, nonpurulent conjunctivitis)

Uukuvirus: Uunkeniemi and other viruses (7 members), all belonging to same serogroup; infects rodents and ticks; Finland

Rift Valley Fever Virus: causes Rift Valley fever (headache, fever, myalgia, joint pains, haemorrhagic signs, rash, 'influenza-like illness', encephalitis in <1% of infections); mosquito-borne; Subsaharan Africa, Middle East, India, Egypt, Sudan; diagnosis: serology, isolation by tissue culture or inoculation of suckling mice during febrile stage

Silverwater: tick vector; no disease known; Canada

Orthomyxoviridae: single stranded RNA in several distinct non-overlapping messenger (negative strand) pieces, each 1 gene, each separately transcribed by virion transcriptase into complementary, noncistronic messenger; molecular weight 2-5X10^6 D in 6 separable components, in an internal coiled ribonucleoprotein helix 6-15 nm diameter embedded in lipid of host cell origin, which also contains viral components, haemagglutinin and neuraminidase; protein component of greatest molecular weight (73%); particle about 80-120 nm diameter with surface spikes; ribonucleoprotein synthesised in nucleus of infected cell, other components in cytoplasm; matures at cell surface; ether sensitive; haemagglutinate red cells (human group O, chick, guinea pig); grow in chick embryo amniotic cavity and in cultures of monkey kidney cells; ribonucleoprotein is complement fixing antigen common to all strains within A, B, C types; complex antigenic makeup of major and minor antigens and rapid antigenic variation allow virus to recirculate throughout community (antigenic drift by small mutational changes, antigenic shift by hybridisation between human virus and virus from animal reservoirs); penetrate cell by endocytosis; nucleoprotein localised in nucleus; virion (viral-coded) RNA polymerase; separate haemagglutinin and neuraminidase (enzyme that cleaves N-acetylmuramic acid, glycoprotein coded by discrete segment of RNA, thought to enhance penetration of mucus, capable of varying independently of viral haemagglutinin); filamentous forms common; haemolysin absent; prominent cytoplasmic inclusions absent; syncytial formation; regularly produce pandemics; diagnosis: isolation primary method, antigen detection described but not generally available, paired sera required for serology

Influenzavirus: molecular weight 6X10^6 D, 18 kb/strand, 8 segments; types A (many members), B (several members) and C (1 member; probably a separate genus); causes acute respiratory illness (influenza), pneumonia, Reye's syndrome, rhabdomyolysis; increased infectiousness in abnormal host; attaches to respiratory epithelial cell by reaction of viral haemagglutinin with neuraminic acid receptor on cell; infection generally confined to epithelial surface of respiratory tract; inhibits phagocytic (macrophage) chemotaxis, bactericidal and oxidative functions, attachment, ingestion despite attachment, lysosome fusion, accessory function; immunity due to antibody (+), cell-mediated (+); 10 genes; viral antigens vary within host population; avian influenza viruses replicate in intestinal epithelium without causing diarrhoea, destroy T and B lymphoid cells; 80% of cases show transient appearance of antibodies to DNA; serum antibodies against cytoskeleton, myosin, myoglobin, thyroglobin, transferrin and heart muscle (in acute myocarditis only) also produced; grows in primary monkey kidney cells (not in human diploid fibroblast or Hep2; 4 d to isolation, no cytopathic effect or focal enlarged granular cells followed by sloughing, rapid progression; haemadsorption at 4?C = that at 20?C); serology: haemagglutination inhibition, fluorescent antibody, complement fixation test

Influenza A Virus: H_0N_1 (A_0, human), H_1N_1 (A_1), H_2N_2 (A_2), H_3N_2 (A_{HK}, A_3), $H_{sw}N_1$ (swine), $H_{eq}N$ (2 equine), $H_{av}N$ (8 avian); causes influenza (++++), croup (+++), pneumonia (++), URTI (++), common or feverish cold (+), bronchitis, acute bronchiolitis and bronchopneumonia, laryngotracheitis, pneumonitis, coryza, tracheobronchitis, acute sinusitis, acute exudative tonsillitis, otitis media, parotitis and submandibular sialadenitis, 6% of nonpyogenic meningitis, postinfectious encephalomyelitis, Guillain-Barré syndrome, myocarditis and pericarditis, nonpurulent conjunctivitis, Reye's syndrome; 4% of respiratory viral isolates in hospitalised children; clinical infection in abnormal host; inhibits lysosome-phagosome fusion and phagocyte oxidative response; pandemics in 1890-1892 (H_2N_2), 1902-1903 (H_3N_2), 1918-1919 ($H_{sw}N_{sw}$, swine-like; 22 M deaths), 1929 (H_0N_1), 1947 (H_1N_1, A prime), 1957-1958 (H_2N_2, Asian, A/Japan/57; 70 000 excess deaths), 1968-69 (H_3N_2, Hong Kong, A/Hong Kong/68; 34 000 excess deaths), 1973 (A/England/72; 25 000 excess deaths), 1976 (A/Victoria/75; 27 000 excess deaths), 1977 (H_1N_1, Russian); detection: haemagglutination inhibition, indirect fluorescent antibody titre, radioimmunoassay, ELISA, tissue culture (WI38, primary monkey kidney); treatment: ribavirin aerosol (i.v. in myocarditis and pericarditis), amantadine, rimantidine

Influenza B Virus: causes influenza, bronchitis, acute bronchiolitis and bronchopneumonia, tracheobronchitis, common or feverish cold, coryza, croup, pneumonia, pneumonitis, URTI, nonexudative pharyngitis and tonsillitis, acute laryngitis, otitis media, myocarditis and pericarditis, hepatic granuloma, nonpurulent conjunctivitis; 2% of respiratory viral isolates in hospitalised children; diagnosis: radioimmunoassay, ELISA; treatment: ribavirin aerosol (i.v. in myocarditis and pericarditis)

Influenza C Virus: causes influenza, upper respiratory tract infection, coryza, pneumonia

GROUP VI: RNA REVERSE TRANSCRIBING VIRUSES

Retroviridae: about 100 nm diameter, molecular weight 6-7X10^6 D; surface membrane site of nucleocapsid development; diploid viruses; genome alternates between RNA in virion and proviral DNA in host cell; 2 identical messenger single strand RNA segments (positive strand), each transcribed into DNA by reverse transcriptase in virion; functional mRNAs transcribed from this; ? cause mucocutaneous lymph node syndrome, implicated in schizophrenia

Oncovirinae: positive strand single strand RNA; envelope from infected cell; diameter of virion about 100 nm; RNA tumour virus group

Type A Oncovirus Group

***Cisternavirus*:** mice, hamster, guinea pigs

Type B Oncovirus Group: mammary carcinomas in mice (mouse mammary tumour virus MMTV-S (Buttner's virus), MMTV-P (GR virus), MMTV-L) and ? humans

Type C Oncovirus Group: > 15 sarcoma and leukemia viruses of mice, cats, cattle, birds, snakes and primates, including human T-lymphocyte virus

Human T-Lymphocyte Virus (HTLV): causes infusion infections

HTLV-I: causes adult T cell leukemia, infusion infections, HTLV-I-associated myelopathy, T cell lymphoma, tropical spastic paraparesis, ? multiple sclerosis; affects mainly T helper cells; endemic in SE USA, Japan, S America, Carribean; transmitted in blood and sexually; diagnosis: competitive ELISA, radioimmunoassay, immunoprecipitation

HTLV-II: causes T cell hairy cell leukemia, infusion infections; endemic in England and New York City in i.v. drug abusers, sexually transmitted

HTLV-V: ? causes Sézary syndrome; endemic in Southern Italy

Leukemia Viruses: mouse, cat, etc; infect lymphocytes and macrophages; persist in lymphoid and other tissues (may be infectious, not shed to exterior), causing late leukemia

Feline Leukemia Virus (Feline Leukosis Virus): infects cats; kidney deposits (may cause glomerulonephritis) and vascular deposits of circulating immune complexes; diagnosis: isolation, immunofluorescent antibody, ELISA

Murine Leukemia Virus (Murine Leukosis Viruses F, M, R (Friend, Moloney, Rausner Viruses): carried in blood associated with platelets; kidney deposits of circulating immune complexes may cause glomerulonephritis (also murine radiation leukemia virus, murine endogenous virus, rat leukosis virus, reptilian-viper virus)

Avian Leukosis/Sarcoma Viruses: cause lymphoid, haematopoietic, vascular, renal, hepatic and connective tissue neoplasms; Rous sarcoma virus (molecular weight 3.5X10^6 D, 10.5 kb/strand, 1 segment, positive polarity), Rous sarcoma associated virus, other chicken sarcoma viruses, RE viruses, pheasant virus (also feline sarcoma virus, feline endogenous virus (RD114), hamster leukosis virus, porcine leukosis virus, bovine leukosis virus, primate sarcoma viruses (woolly monkeys, gibbon ape), primate sarcoma associated virus, primate endogenous viruses (baboon endogenous virus (BaEV), stumptail monkey virus (MAC-1), owl monkey virus (OMC-1))

Type D Oncovirus Group: primates; monkey (? mammary tumour) virus (Mason-Pfizer monkey virus), Langur virus, squirrel monkey virus

Simian Immunodeficiency Virus: causes AIDS-like syndromes in Asian monkeys, affecting T, B and NK cells; African monkeys natural hosts, disease not produced

Lentivirinae

Lentivirus

Human Immunodeficiency Virus (HIV): 110 nm; ssRNA; envelope; causes acquired immunodeficiency syndrome (AIDS), AIDS dementia complex (HIV encephalopathy), AIDS enteropathy, Guillain-Barrè syndrome, reactive arthritis, vasculitis, teratogenic effects; produces profound helper T cell dysfunction; macrophages also affected;

decreases polymorphonuclear chemotactic and secretory functions; serum antibodies against DNA, erythrocytes, lymphocytes, neutrophils, platelets and immunoglobulins produced (may reflect coinfections with other viruses and microorganisms as well as an effect of HIV; in some cases, antibody-related autoimmune diseases may appear); transmitted in blood and in pooled plasma products (inactivated by severe terminal heat and solvent-detergent treatment) and sexually; cultivated in mitogen-activated PBL or T cell lines; diagnosis: ELISA, Western blot, p24 antigen capture, culture of peripheral blood lymphocytes, test for proviral DNA; treatment: zidovudine, didanosine, zalcitabine, ganciclovir

HIV-I: causes AIDS and AIDS-related complex; endemic in Central Africa, Europe, USA

HIV-II: causes AIDS; endemic in W Africa, Cape Verde

Maedo-Visna Virus: 'slow virus', infects sheep, causing maedi and visna, progressive pneumonia; infects lymphocytes and macrophages

Caprine Arthritis-Encephalitis Virus: causes retrovirus-mediated synovitis in goats that resembles rheumatoid arthritis; multisystem disease may be associated

Equine Infectious Anaemia Virus: infects horses; infects macrophages; autoimmune reactions against retroviral antigens on the surface of erythrocytes cause haemolytic anaemia; kidney deposits (causing glomerulonephritis) and vascular deposits of circulating immune complexes; diagnosis: agar gel immunodiffusion test

Spumavirinae

Spumavirus: foamy virus group; > 4 syncytial and foamy viruses of humans, monkeys, cattle and cats; includes avian reticuloendotheliosis virus (chicken syncytial virus); no disease known in humans

GROUP VII: DNA REVERSE TRANSCRIBING VIRUSES

Hepadnaviridae: double stranded DNA with RNA intermediate; cause infusion infections

Orthohepadnavirus: hepatitis B virus; small icosahedral particles (nucleic acid-free, possibly aggregate of virus capsomeres) about 22 nm diameter (Australia antigen) in acute phase serum hepatitis; virus particle (including nucleic acid) possibly about 2 nm diameter; 22 nm sphere buoyant density (CsCl) 1.2 g/cm^3, sedimentation coefficient 543, protein, glycoprotein, lipid; filamentous forms buoyant density (CsCl) 1.2 g/cm^3; Dane particles (42 nm spheres) buoyant density (CsCl) 1.25 g/cm^3, sedimentation coefficient 58-59, protein, glycoprotein, lipid, circular interrupted double strand DNA; core particles buoyant density (CsCl) 1.36 g/cm^3, sedimentation coefficient 1105, protein, circular interrupted double strand DNA; contains both single strand and double strand DNA; envelope from infected cell; not readily grown in vitro; causes serum hepatitis (long incubation hepatitis), cirrhosis, abortion, arthritis, Guillain-Barré syndrome, haemorrhagic fever, hepatic granuloma, infusion infections, myocarditis and pericarditis, non-pyogenic meningitis, rhabdomyolitis, stillbirth; associated with hepatocellular carcinoma; usually transmitted in blood and in pooled plasma products (inactivated by severe terminal heat or solvent-detergent treatment; sporadic transmissions after pasteurisation) by parenteral inoculation, but also sexually; incubation period 60-160 d; onset insidious; fever > 38?C uncommon; year-round; all ages, commonest in adults; virus not demonstrated in faeces; primary bodily defence mechanism humoral immune responses (antibody ++), cell-mediated immunity (+); antigen-antibody complexes circulate in serum, deposit in tissue, bind complement and produce injury (glomerulonephritis, arthritis, vasculitis) in a classic model of viral immune complex disease in humans; acute arthritis due entirely to host immune response; necrotising vasculitis with chronic infection (important that virus persists systemically, host immune response; ? cross reactive antigen not important; sequence: virus replication systemically, immune response, immune complexes, kidney and vascular deposits of circulating immune complexes, inflammation, virus persistence); viral surface antigens in extracellular fluids combine with and 'divert' antibodies; persists in liver (virus shed into blood, which remains infectious); serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; increased infectiousness in abnormal host (clinical, subclinical and persistent nonlatent infections); decreases polymorphonuclear bactericidal, chemotactic and oxidative functions; diagnosis: reverse passive indirect haemagglutination, radioimmunoassay (antibody and antigen), ELISA (antibody and antigen), counterimmunoelectrophoresis; HBsAg (surface antigen) appears 30-50 d after infection; detection of HBsAg in blood, less often in faeces, urine, semen, bile; detection of HBsAg 60 d - years; HBsAg contains strain specific antigenic determinants that may vary geographically and are combinations of several determinants (multiple serologic types of coat proteins); prophylactic value of ?-globulin good if titre of anti-HBs antigen high (passive immunity)

SUBVIRAL AGENTS: SATELLITES, VIROIDS AND PRIONS

Dependovirus: adenosatellite virus; adenoassociated virus; defective, cannot replicate in absence of helper adenovirus; human (types 1-3), monkey (type 4), > 4 others of cattle, dogs, birds; molecular weight $1.5X10^6$ D, 4.5 kb/strand, 20 nm, 12 capsomeres, single strand DNA; useful for gene therapy; integrates into chromosome

Deltavirus: hepatitis D (Delta) Virus; RNA satellite virus; transmitted parenterally with hepatitis B virus; requires HBV to grow; causes hepatitis, liver cancer; chronicity; serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced

PRIONS: Spongiform Viral Encephalopathy Agents; increased infectiousness in abnormal host (clinical, ? subclinical, latent and persistent nonlatent infections)

Creutzfeldt-Jakob: slow agent distinct from conventional viruses; mean age at death 65 y, median duration of illness
4 mo, psychiatric presentations uncommon, typical periodicity on EEG seen in 65-70%, pulvinar sign on brain MRI scan in
< 10%, prion protein plaques rare in brain, absent from tonsils

Kuru: slow agent distinct from conventional viruses; long incubation; lethal

Scrapie: slow agent distinct from conventional viruses; ? infects lymphoreticular tissues; no detectable antibody; mean doubling time 4-7 d in mouse brain

Bovine Spongiform Encephalopathy: causes "mad cow disease" (200 000 cases in UK since 1986, due to contaminated feed), condition similar to Creutzfeld-Jakob disease in humans (> 80 cases in UK, 3 in France, 1 in Republic of Ireland; median age at death 29 y, median duration of illness 14 mo, psychiatric presentations very common, typical periodicity on EEG absent, pulvinar sign on brain MRI scan in > 70%, numerous florid prion protein plaques throughout the brain characteristic and also present in tonsils)

SITUATIONS IN WHICH VIRAL DIAGNOSIS CAN BE HELPFUL: severe pneumonia unresponsive to antimicrobials and no bacterial aetiology determined (influenza A, adenovirus, parainfluenza, respiratory syncytial virus), myopericarditis (coxsackievirus B), acute gastroenteritis (*Rotovirus*— especially in infants and children), macular and maculopapular exanthems and enanthems (rubella, measles, enteroviruses, adenovirus), vesicular exanthems and enanthems (herpes simplex and varicella-zoster), congenital or perinatally acquired illness (cytomegalovirus, herpes simplex, rubella, enteroviruses), febrile mononucleosis-like or sepsis-like syndromes (Epstein-Barr virus, cytomegalovirus, adenovirus, enteroviruses), conjunctivitis and keratitis (adenovirus, herpes simplex), hepatitis (hepatitis A, B, C, cytomegalovirus, Epstein-Barr virus, adenovirus, coxsackievirus B)