Human Herpes Viruses

Name comes from the Greek 'Herpein' - 'to creep' = chronic/latent/recurrent infections.

Types

- HHV-1: Herpes simplex type I
- HHV-2: Herpes simplex type II
- HHV-3: Varicella-zoster virus (VZV)
- HHV-4: Epstein-Barr virus (EBV)
- HHV-5: Cytomegalovirus (CMV)
- HHV-6: Human herpesvirus type 6 (HBLV)
- HHV-7: Human herpesvirus type 7
- HHV-8: Kaposi's sarcoma herpesvirus (KSHV)

They belong to the following three families:

- Alphaherpesviruses: HSV I & II; VZV
- Betaherpesviruses: CMV, HHV-6 and HHV-7
- Gammaherpesviruses: EBV and HHV-8

Herpes simplex virus types I and II (HHV1 & 2)

Primary infection usually by 2yr of age through mucosal break in mouth, eye or genitals or via minor abrasions in the skin. Asymptomatic or minor local vesicular lesions. Local multiplication → viraemia and systemic infection → migration along peripheral sensory axons to ganglia in the CNS → subsequent life-long latent infection with periodic reactivation → virus travels back down sensory nerves to surface of body and replicates, causing tissue damage:

Manifestations of primary HSV infection

- **Systemic infection**, e.g. fever, sore throat, and lymphadenopathy may pass unnoticed. If immunocompromised it may be life-threatening pneumonitis, and hepatitis.
- **Gingivostomatitis:** Ulcers filled with yellow slough appear in the mouth.
- **Herpetic whitlow:** Finger vesicles. Often affects childrens' nurses.
- **Traumatic herpes (herpes gladiatorum):** Vesicles develop at any site where HSV is ground into the skin by brute force. E.g. wrestlers.
- **Eczema herpeticum:** HSV infection of eczematous skin; usually children.
- **Herpes simplex meningitis:** This is uncommon and usually self-limiting (typically HSV II in women during a primary attack)
- **Genital herpes:** Usually HSV type II
- **HSV keratitis:** Corneal dendritic ulcers. Avoid steroids.
- **Herpes Simplex Encephalitis:** Usually HSV type I. Spreads centripetally, e.g. from cranial nerve ganglia, to frontal and temporal lobes. Suspect if fever, fits, headaches, odd behaviour, dysphasia, hemiparesis, or coma or subacute brainstem encephalitis, meningitis, or myelitis.

Diagnosis

- Rising antibody titres in 1° infection
- Vesicle fluid, culture or PCR for fast diagnosis.

Treatment

- 1°genital heres: 5 days of **aciclovir** 400mg PO q8h (topical not as effective) or **valiciclovir** 500mg PO bd x 5d or **famciclovir** 125mg PO bd x 5-10d. If sev → IV acyclovir.
- Recurrent genital herpes: As above if <72hr post onset. Consider prophylaxis if >6x/yr
- Herpes keratitis: ophthalmic 3% **aciclovir** ointment 5x/day x 14d.
- HSV gingostomatitis/oral labialis: Normally Rx not reqd. If sev. or not drinking early PO/IV (or TOP if mild) **aciclovir** may aid healing.
- Neonatal herpes/HSV encephalitis: **aciclovir** 5-20mg/kg IV q8h x 14d
- Immunocompromise/severe genital herpes in pregnancy: IV **aciclovir** as above.
- Although painful, most recurrent infections resolve spontaneously, usually to recur later.

Varicella-zoster virus (VZV/HHV-3)

Gives rise to 2 distinct clinical syndromes:

Varicella Zoster (Chickenpox) – 90% in childhood, entering via respiratory tract or conjunctiva, spreads to bloodstream and RES. Secondary multiplication involves skin and mucosa, producing vesicles with very high infectious titres. Cx rarely pneumonia & encephalitis.

Treatment

Most will not need antivirals. However aciclovir may be used:

- Intravenous **aciclovir** (10 mg/kg IV q8h x7-10d)
    - High risk patients who are immunocompromised or on high dose steroids.
    - Systemic disease (for example affecting heart, lungs).
    - New lesions appearing after 8 days.
- Oral **aciclovir** (800 mg 5x/day adults, 20 mg/kg up to 800 mg qds for children) :
    - Patients with a chronic medical condition (lung or heart disease for example).
    - Patients over 12 years of age to reduce the complication rate.
    - When the patient is a secondary case in a household.
    - Pregnant patients, although use is not licensed. No evidence of teratogenicity.
- Varicella contacts (>4h face-face contact) should have PO **aciclovir** if:
    - No previous varicella exposure (or rapid serological testing confirms exposure) and 5-7d post-exposure and high risk (immunocompromised or pregnant) or possible transmission on to high risk contact (e.g. parent of immunocompromised child)
    - NB: high risk and under 96 hours after exposure, give specific varicella zoster immunization (**VZIG**).

Herpes Zoster (Shingles) - After 1° infection, persists in sensory ganglia of CNS. 'Reactivation' after many years → infection to dermatome - more serious with cranial nerves.

Treatment – Herpes Zoster

- Supportive – clean lesions with saline, fluids, analgesics, segregation
- Antiviral if <72hr onset, immunocompromised or ophthalmic zoster (doesn't reduce post herpetic neuralgia): 1 week of **aciclovir** 800mg PO 5 times/day (consider IV if sev or ophthalmic) or **valiciclovir** 1g PO q8h or **famciclovir** 250mg PO bd/tds. [VZV 4-10x less sensitive to aciclovir than HSV]

  Post herpetic neuralgia: (Burning pain in area of previous shingles, >3mo after rash resolution, worse in elderly, DM, trigeminal area, immunosuppressed.) : **paracetamol**, opioids, **aspirin**, TENS (of limited use), **amitriptyline** 10-100mg on, **gabapentin** 300mg od-tds, **capsaicin** 0.075% cream TOP (**SE:** burning sensation), **lidocaine** 5% patches. Varicella vaccine may reduce incidence of HZV & post-herpetic neuralgia.

Epstein-Barr virus (EBV/HHV-4)

~90% of adults in W. Europe and N. America carry EBV. Infection persists for life with virus regularly shed in saliva which is the usual route of transmission. It can persist for a lifetime in an asymptomatic state. In vivo it affects human B-lymphocytes (generally non-productive infection) and epithelial cells (productive infection). It is linked with several tumours:
Presentation: Low grade fever, fatigue and prolonged malaise. Sore throat. Tonsillar enlargement is common and may be massive. Palatal petechiae, uvular oedema. Fine, macular non-pruritic rash, which rapidly disappears. Transient bilateral upper lid oedema. Lymphadenopathy, especially neck glands. Nausea and anorexia. Mild hepatomegaly and splenomegaly Jaundice
Invs: FBC (↑WCC, lymphocytosis; atypical lymphocytes>20%), ↑ESR, mild ↑AST & ALT Monospot +ve (horse RBC agglutination test as EBV induces a variety of unrelated non-EBV heterophile antibodies may be negative early on), IgM EBV antibodies, USS for HSM
Associated diseases: Burkitt's lymphoma, Hodgkin's disease, B-lymphoproliferative disease, nasopharyngeal carcinoma, X-linked lymphoproliferative syndrome, oral hairy leukoplakia (HIV)
Mx:

- Advise paracetamol for analgesia and control of fever.
- Patients may require hospital admission for intravenous fluids.
- Short course of corticosteroids are beneficial for haemolytic anaemia, CNS involvement or extreme tonsillar enlargement.
- Advise patients to avoid contact sports for 6 weeks - because of risk of splenic rupture.
- Avoid: EtOH, contact sports (splenic rupture risk), amp/amoxicillin (rash)
- No specific antiviral therapy is available.

Cx: airway obstruction, prolonged fatigue, depression, neurological (optic neuritis, transverse myelitis, meningitis/encephalitis, CN palsies (esp VIIn) or Guillain-Barre syndrome), splenic rupture, haemolytic anaemia, thrombocytopenia.

Cytomegalovirus (CMV/HHV-5)

Common asymptomatic infection. Apart from during pregnancy and newborn infants exposed in utero, active (as opposed to latent) CMV infection only occurs in fetus & immunocompromised. May cause post-transfusion fever.
Invs: Urine culture, serology.
Treatment: Ganciclovir for life- or sight-threatening infections.

Human herpesvirus 6 (HBLV/HHV-6)

Primary infection in childhood causes Roseola Infantum - "sixth disease". Cx: mild in childhood (may cause febrile convulsions) but 1° infections of adults (rare) have more severe Cx - mononucleosis and hepatitis, and is a particular problem in immunocompromised patients.

Human herpesvirus 7 (HHV-7)

HHV-7 is a recently (1990) described T-lymphotropic. It infects almost all children by 3yo and persists lifelong, with the shedding of infectious virus in saliva. Similar to HHV-6, including the ability to cause at least some cases of exanthem subitum (Roseola Infantum).

Kaposi's sarcoma herpesvirus (KSHV/HHV-8)

This is detectable in Kaposi's sarcoma lesions, and may also be associated with body cavity-based lymphomas (BCBLs) of B-cell origin, and a subset of Castleman's disease (a rare non-neoplastic condition where collections of lymph gland tissue (plasma cell type) develop throughout the body), hyperplastic lymphadenopathy.