HERPESVIRIDAE (1)

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Herpesviridae (1)

7- Immunity

1) innate immunity: includes natural killer cells and INF-γ, important in controlling primary and recurrent infections
2) Adaptive immunity: T cells are important in killing infected cells
→ B cells produce antibodies to fight the infection
During primary infections, IgM antibodies appear transiently and are followed by IgG and IgA antibodies that persist for long periods.
→ After primary infection, the virus hide in the neurons to escape from the circulating antibodies, and it's released when the immunity is suppressed
→ Circulating antibodies will not prevent reinfection, even if they will weaken it
→ Many newborns acquire passively transferred maternal IgG.

8- Diagnosis

- PCR: used for CNS infection detection
- Cell culture; basic method but not enough by itself
- Cell culture: May be confused with other herpes viruses
- Serological test: such as chemiluminescent assays, immunofluorescence assay, and enzyme linked immunosorbent assay
Not preferred as there are some antigens that are similar between HSV-1 & HSV-2, even similar antigens between HSVs & varicella-zoster viruses

9- Epidemiology

- For HSV-1:
The highest incidence of HSV-1 occurs among children 6 months to 3 years of age.
By adulthood, 70–90% of persons HSV-1 IgG.
- For HSV-2
usually considered an STI, so antibodies to this virus are seldom found before puberty.
Less common than HSV-1
- For pregnant women:
Maternal genital HSV infections pose risks to both the mother and the fetus.
Rarely, pregnant women may develop disseminated disease after primary infection, with a high mortality rate.

10- Treatment

- Antiviral drugs (e.g. acyclovir):
Acyclovir which is a nucleoside analog, is monophosphorylated by the HSV thymidine kinase and is then converted to the triphosphate form by cellular kinases. The acyclovir triphosphate is efficiently incorporated into viral DNA by the HSV polymerase, where it then prevents chain elongation.
Note: anti-viral drug resistance may occur
- Vaccines are under experiment
- Sanitation is important

7- Immunity

- Remember: Immune system is divided into two parts: 1) innate & 2) adaptive
- 1) innate immunity: includes natural killer cells and INF-γ, important in controlling primary and recurrent infections
  2) Adaptive immunity: T cells are important in killing infected cells
  → B cells produce antibodies to fight the infection
  During primary infections, IgM antibodies appear transiently and are followed by IgG and IgA antibodies that persist for long periods.
  → After primary infection, the virus hide in the neurons to escape from the circulating antibodies, and it's released when the immunity is suppressed
  → Circulating antibodies will not prevent reinfection, even if they will weaken it
  → Many newborns acquire passively transferred maternal IgG.
  → The period of greatest susceptibility to primary herpes infection occurs between ages 6 months and 2 years.
  → Trans-placentally acquired IgG from the mother are not totally protective against infection of newborns, but they seem to ameliorate infection if not prevent it.
  → HSV-1 antibodies begin to appear in the population in early childhood, while HSV-2 rise during the age of adolescence and sexual activity

8- Diagnosis

- PCR: Used nowadays instead of viral isolation as the standard assay for specific diagnosis of HSV infections of the CNS by detecting the virus in the cerebro-spinal fluid sample.
- Virus isolation: remains the definitive diagnostic approach. Virus may be isolated from herpetic lesions and may also be found in throat washings, CSF, both during primary infection and during asymptomatic periods.
  → Note: the isolation of HSV is not in itself sufficient evidence to indicate that the virus is the causative agent of a disease under investigation, as their might similar clinical disease with other virus, and there is asymptomatic reactivation of the virus
- Cell culture: rapid cytologic method is to stain scrapings obtained from the base of a vesicle (e.g., with Giemsa's stain); the presence of multinucleated giant cells indicates that herpesvirus (HSV-1, HSV-2, or varicella-zoster) is present, distinguishing lesions from those caused by coxsackieviruses (Tzanck smear)

8- Diagnosis

- Serological tests:
- Antibodies appear in 4–7 days after infection and reach a peak in 2–4 weeks, IgM will rise first followed by IgG that will persist for the rest of the life
- They persist with minor fluctuations for the life of the host.
- Detection methods available include chemiluminescent assays, immunofluorescence assay, and enzyme linked immunosorbent assay.
- The diagnostic value of serologic assays is limited by the multiple antigens shared by HSV-1 and HSV-2.
- There may also be some heterotypic anamnestic responses to VZV in persons infected with HSV and vice versa.
- The use of HSV type-specific Abs, available in some research laboratories, allows more meaningful serologic tests.

9- Epidemiology

- For HSV-1:
- The highest incidence of HSV-1 occurs among children 6 months to 3 years of age.
- By adulthood, 70–90% of persons HSV-1 IgG.
- Middle-class individuals in developed countries acquire antibodies later in life than those in lower socioeconomic populations (crowding, poor hygiene).
- The virus is spread by direct contact with infected saliva or through utensils contaminated with the saliva of a virus shedder.
- The source of infection for children is usually an adult with a symptomatic herpetic lesion or with asymptomatic viral shedding in saliva. The frequency of recurrent HSV-1 infections varies widely among individuals.
- At any given time, 1–5% of normal adults are excreting virus.

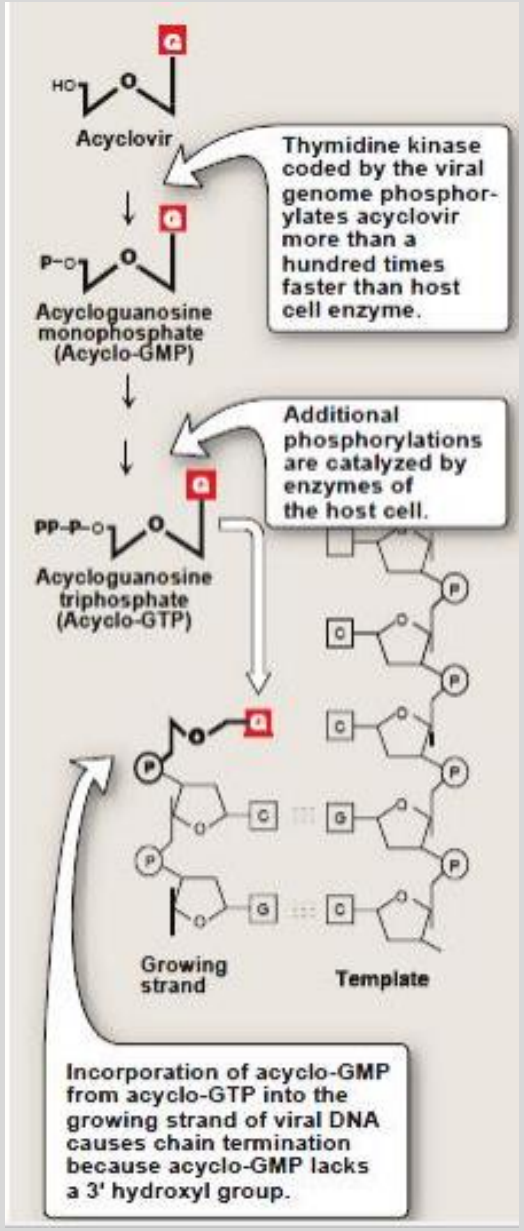
9- Epidemiology

- For HSV-2
- usually considered an STI, so antibodies to this virus are seldom found before puberty.
- Antibody prevalence studies have been complicated by the crossreactivity between HSV types 1 and 2. Surveys using type-specific glycoproteins Ags determined that 17% of adults in the US possess HSV-2 IgG, with seroprevalence higher among women, blacks, and older individuals, reaching 56% in blacks 30–49 years.
- Frequent subclinical reactivations for both types occur in immunocompetent hosts lasting less than 12 hours.
- Both symptomatic and asymptomatic infections provide a reservoir of virus for transmission to susceptible persons.
- Studies have estimated that transmission of genital herpes in more than 50% of cases resulted from sexual contact in the absence of lesions or symptoms.

9- Epidemiology

- For pregnant women:
- Maternal genital HSV infections pose risks to both the mother and the fetus.
- Rarely, pregnant women may develop disseminated disease after primary infection, with a high mortality rate.
- Primary infection before 20 weeks of gestation has been associated with spontaneous abortion.
- The fetus may acquire infection as a result of viral shedding from recurrent lesions in the mother's birth canal at the time of delivery.
- Estimates of the frequency of cervical shedding of virus among pregnant women vary widely.
- Genital HSV infections increase acquisition of HIV infections

10- Treatment



- Effective antivirals include acyclovir, valacyclovir, and vidarabine, all of which are inhibitors of viral DNA synthesis.
- Acyclovir which is a nucleoside analog, is monophosphorylated by the HSV thymidine kinase and is then converted to the triphosphate form by cellular kinases. The acyclovir triphosphate is efficiently incorporated into viral DNA by the HSV polymerase, where it then prevents chain elongation.
- The drugs may suppress clinical manifestations, shorten time to healing, and reduce recurrences of genital herpes. However, HSV remains latent in sensory ganglia.
- Drug-resistant virus strains may emerge.
- Counselling, antiviral therapy and condom usage to prevent genital herpes.
- Experimental vaccines of various types are still under development.