Microbiology

Sheet no. :15

Refer to :Herpes viruses slides ( 30-32)+Hepatitis slides(1-13)

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**Herpes virus 6 & 7**

* Less important than previous types.
* Fewer complications.
* Play an important role in T cells infections (Mainly CD4 cells) and lymphocytes.
* Can be recognized in blood and infected cells.
* Genetically, related to Cytomegaloviruses (CMV) but with different clinical features.
* Majority of children acquire their infection in their first 3 years(by close contact with any infected individual).
* Not necessary for the infection to be associated with clinical features of the disease, similar to CMV **to some extent**, Asymptomatic can’t be recognized easily **unless** associated with fever or adenopathies.
* Classical features of **Rosella Infants disease** “Presence of skin rashes especially on the face” usually skin rashes cover the face with macular lesions recognized easily with fever and certain adenopathies in some cases & rarely associated with neurological disorders “so no meningitis or encephalitis”. Also, the presence of erythema is noticeable.
* An important complication associated with Herpes 6&7 is: Hepatitis, esp. Hepatitis F ,in adults and old children.
* Main route of infection: Direct contact with infected saliva during acute stage and the carrier stage.
* Herpes 6&7 might produce some complications, rarely, results in rejection of transplanted kidneys.

**Herpes 8**

* Related 70% to EBV.
* Complications associated with malignancies, Sarcoma cutaneous lesions, oral cavity lesions and may spread to any internal organ especially to nose and anus.
* Can be transmitted by sexual contact or other means.
* Sarcoma cutaneous lesions could be seen with skin lesions **“Blue or dark brown rashes”.**
* Can’t be treated easily.
* No global antiviral drug, so treated in early stages ***(Not second),*** by surgical treatment, Cryotherapy **“the local or general use of low temperatures in medical therapy”**, Radiotherapy, Topical immunotherapy and Ganciclovir.

**Hepatitis**

* Keep in mind that hepatitis is very important to us as dentists because it is very serious and is easily encountered during our job.
* The incidence of hepatitis B virus among dentists in Jordan is increasing, 2 cases of death were recently reported.
* Fortunately, we are all immunized against hepatitis B virus but always keep in mind that:

“IMMUNIZATION with hepatitis B is NOT NECESSARILY associated with COMPLETE IMMUNITY”.

Few percentages may not develop sufficient immune response against the virus. It is a must to test a sample of your blood to check the level of AntiHBsAg.

* Hepatitis in general means inflammation of hepatocytes, which could be mild or severe associated with liver cirrhosis .
* The causative agent of hepatitis infection doesn’t only rely on the presence of hepatitis A, B, C, D, or E viruses (direct infection to hepatocyte). It can be in association with other viruses(Indirect infection) that play a role in developing complications of this infection.
* An important virus is Herpes Simplex virus 1, 2 that can be highly associated with complications of hepatitis viral infection. Herpes Simplex virus doesn’t actually cause cirrhosis like hepatitis viruses but it does develop **yellow fever** which is usually more dangerous. Other viruses including CMV, Epstein Barr virus, Rubella virus, and many special types of Enteroviruses can cause hepatitis.
* Hepatitis might not be recognized directly as it takes few months to years for infection to appear.
* Clinically, in general, hepatitis can be recognized on patients developing jaundice –yellow skin-, yellow eyes, dark urine, fatigue, vomiting and fever.

All these clinical features indicate the presence of hepatitis viral infection.

* Recognition of hepatitis infection should not depend on the clinical features only (jaundice and yellow fever), it should be tested through blood samples to know if the infection is from hepatitis virus or any other type.
* In general, jaundice is associated with two main features:
1. The accumulation of bilirubin: As it is responsible for the yellowing

of the skin.

1. The presence of alanin aminotransferases –liver enzymes- in the blood.

**Hepatitis A Virus**

* A very special type of viruses, as it does not really belong to the hepatitis viruses group. It is part of another group of viruses which is Enteroviruses and picorna viruses, as part of theenteroviruses. It is under the group of hepatitis viruses for easier explanations but in reality it is from another type of viruses.
* It is ss+veRNA.
* Non-enveloped.
* More stable than other viruses under acidic environment or even under wide range of high temperatures (from 0-25 C).
* It is not easily eliminated from water and fresh food contamination (salads). This is the reason why infection with hepatitis A can be in form of outbreak disease.
* Very common in countries with low standards of hygiene especially the developing countries, unfortunately, including Jordan. It is very important to increase the standards of hygiene to prevent the spread of such infections.
* It is not found in single cases –not sporadic-. A +ve single case, then you should expect many other cases. All cases originate from the same source such as coughing or direct contact.
* Fecal-oral route.
* Hepatitis A is found in contaminated water and contaminated fresh food and dietary products. It is very commonly found in fresh yoghurt.
* One genotype can produce infection in humans so you’ll be immunized once you are infected with hepatitis A.
* Clinical manifestations are very mild in 5% of children of age up to 15 years old. Jaundice **might be recognized and might not**. Children are presented with mild abdominal pain, vomiting 1-2 times only, or mild fever. And it rarely develops to liver cirrhosis.
* 50% of adults above the age of 15 develop jaundice and few percentages continue to liver cirrhosis.
* In hepatitis A and other types, liver cirrhosis maybe extensive in normal people more than immunocompromized patients, due to high amounts of Cytotoxic T-Cells & release of cytokines to produce hypersensitivity in normal people.

* Why the virus cannot survive in the blood after 6-7 weeks? due to the presence of specific antibodies –IgM in the early stages and IgG in later stages-. IgG antibodies persist longer but that doesn’t mean that infection with HAV develops chronic stage.
* There are NO healthy carriers for HAV as it gets eliminated through liver or intestines.
* Hepatitis A infection does not develop to chronic phase. 6-7 weeks are enough for the virus to get eradicated. There are no healthy carriers for hepatitis A virus except for hepatitis B, C, D viruses.
* The presence of infections is related to the presence of the virus in the blood and hepatocytes. Usually HAV goes from the bile duct into the intestine without passing to the blood for the second time. Mostly HAV is excreted in the feces.
* To examine the presence of the virus in a patient, we do not usually look for the virus in the stool. It is very important to look for the presence of specific antibodies; an example is Anti-hepatitis IgM that is found in the acute early stage of the disease. Another choice is the IgG that could be found in the healthy or recovery stage following the developing symptoms

**Hepatitis B Virus**

* HBV is more important and much more dangerous. Despite the fact that hepatitis B virus is the smallest virus among all human viruses, it has a very complex structure.
* Its structure contains a core that is composed of a dsDNA associated with a proteinous capsule that is composed of different types of proteins.
* Also it contains a specific DNA polymerase.
* The assembly of the virus containing the core is called HBc –the c in relation to core- and its antigen is HBcAg. The core antigen circulates in the hepatocytes and does not reach blood. This core is considered the infectious part of the virus in association with the envelope.
* The envelope of HBV which is important for attachment is more complex than any other envelop of hepatitis viruses. It is composed of different types of glycoproteins. It contains three important surface antigens –HBsAg-; M, S, and L; those are important to know the genotype of the virus in different countries. Once the HBsAg is circulated in the blood; it is associated with the clinical features of the infection.
* DURING the infection process, hepatitis virus develops HBeAg that is usually tested during infection in the blood. The presence of HBeAg in the host’s serum is associated with much higher rates of viral replication and enhanced infectivity.
* During multiplication in the nucleus of hepatocytes, there will be developing of another specific antigen knows as HBeAg (a product of HBcAg) it can be separated during infection in the blood into two major forms:

|  |  |
| --- | --- |
| Circular formThe production of the Ag isn’t completed so no developing for hepatitis clinical features  | Filamentous formElongation= “Completed production of AgE” |
|  |  |

* Survival of HBV:

Notice that HBV is more stable than HAV, you need at least 2 hours of boiling to inactivate the virus, UV light cant inactivate it too.

Hepatitis B virus is very hard to kill using disinfectants or UV light. In dental clinics, they provide them with autoclaves with UV light that is not enough to kill the hepatitis B virus. It can be enough in the case of using a very strong chlorine disinfectant agent such as hypochlorite. Equipments are washed in 10% of hypochlorite for 1 day with the disinfectant and then placed in the autoclave. Some devices use diluted Formalin but it is usually not effective as formalin evaporates producing hypersensitivity to the respiratory tracts of dentists.

* Routes of infection:
* Parenteral:

 In the past, the transmission of HBV was mostly through blood transfusion but nowadays this problem is not available anymore as it is controlled very well because they never donate blood until they examine the sample and make sure that this sample is free of HBV, HCV, syphilis, and HIV.

Another way is the transmission of the virus through IV injections commonly among drug abusers.

* Perinatal:

 from the mother “Crossing the placenta/During delivery” to produce neonatal infection that can’t be discovered in first 3 years, clinical manifestations start in the second 3 years.

The only way to know is to detect the presence of the virus in the blood during infectious cases –acute or chronic-, at least HBsAg, Anti-HBc (IgM in early stages and IgG in later recovery stage), and HBeAg should be tested.

* Sexual contact from healthy carriers:

The husband is infected with hepatitis B; the woman will develop the infection.

* HBV is rarely transmitted through bites, traumatic injuries, or direct contact. Those routes are not considered serious. Dentists and surgeons are the most susceptible to infection with HBV as they mainly deal with blood during accidents in surgical manipulation and of what is called **“The needlestick injuries”.** If a patient is found to be a +ve HBV, he/she should be reported directly to the hospital to have quick recommended treatment.
* Saliva can be source of infection in acute stage.
* All antigens of hepatitis B virus are found at the infective process but not at the same time. Each antigen presents a specific timing of infection.
* The following explains a table in slide #12:
* If there is NO infection, -ve results are shown for HBsAg.
* In vaccination, also –ve results are shown and might be +ve during the very early stages of the disease. In general they will be –ve but you will have Anti-HBsAg (antibodies against the surface antigen).The level of the antibodies after vaccination indicates the level of someone’s immune response. You might find HBsAg alone circulating in the blood but this is not enough. Anti-HBsAg should be seen to report +ve immune response and demonstrate its level.
* In cases of acute mild infection, the main symptom to appear is jaundice. It might also occur in late stages of the infection especially in the starting of recovery of the disease that will indicate that the body has started producing specific antibodies against the virus. The presence of jaundice does not really indicate the progression to liver cirrhosis but if jaundice has extended for few months (3 months and more) rather than few weeks –the normal interval (2-8 weeks) for jaundice appearance- the progression to liver cirrhosis appears.
* In chronic stages, HBsAg is –ve but Anti-HbsAg, Anti-HBcAg, and Anti-HBeAg are present.
* These +ves and –ves are the mean values in 90% of patients but in some cases, you might recognize only one or two of the antibodies.
* This sheet contains **extra** notes that were mentioned during the lecture, you have to refer back to the mentioned slides.