***Sheet no:14***

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In relation to HSV we have 8 groups of herpes , that important in association with human infection ( some of HSV related to the animals ) the other only to the human for example **Herpes Varicella-Zoster virus** .

varicella mean: chicken pox which we think for the first impression it is related to birds, chickens because there is a virus special for chicken ..etc might produce some clinical feature similar to varicella .

zoster means: not a new type of virus but this virus following latent infection in specific tissue target reactivate and produce clinical feature of zoster or shingle , so those have2 clinical manifestation.

Varicella-zoster virus belong to the group of **alpha** which means related to HSV1 and HSV2, and in fact the virus mainly complicate the lymphoid cells in the respiratory tract mainly , it might produce vital effect damage the infected cells , the clinical feature of infection should be separated .

 in relation to chicken pox (vraicella) we have the **primary** infection followed **droplet infection** from persons who carry the virus in salivaor in the respiratory tract and spread in the environment to young children mainly (age between 5-10 years) who are more susceptible to acquire infection **.**

might also associated with **conjunctiva**, the same procedure that the virus multiply slowly in the lymph tissue where produce large number of particle, which later carried to the lymphatic system, reticular endothelial cells and the blood stream associated with **viremia** , once it reach the blood it reach the skin manifesting in **skin rushes** .

 **the infection not always present with the infection of skin( rarly), but mainly the respiratory tract in the acute stage (which in the incubation period often between 1-2 weeks)**

the process of infection differ from healthy patient.

 (children mainly up to 90% but in certain condition young adults )in our country often the children acquire natural infection without any complication , the clinical manifestation some sore throat , fever , sometimes enlargement of lymph nodes but it is not so serious ,later the patient develop skin rushes easily distinguished from other type like measles **…** , but in certain percentage ( less than 0.1% ) if children suffering from any immune deficiency or immune suppress disease related to cell mediated , might varicella produce complication , and this complication:

1- manifest 1st and 2ndry bacterial viral infection in respiratory tract in form of pneumonia ,

 2-also might reach the heart muscles and produce myocarditis and later produce arthritis,

3- and rarely affect the CNS which mean meningitis or encephalitis

On the other hand , neonatal or congenital varicella ( neonatal means : once the neonate , following delivery in 1st 30 minute -30 days , if the mother acquire or exposed to varicella virus might at the same time infect the baby ) OR ( congenital : during pregnancy infection the fetus might develop the infection) , in such case to escape any complication the only way to give the new born baby **passive immunization with Ig** which obtained from a patient who have high level of IgM and IgG antibodies , this immunization to reduce the severity of infection , especially prevent complication which associated with chicken pox.

Now the **latency** during the infection either asymptomatic ( no observing of skin rushes ,just inflammation in the RT) or symptomatic, despite this fact the virus later travel and produce latent infection in dorsal sensory root ganglia ,(later at any time during life might develop the second clinical manifestation zoster ), example : during the activation, the DNA of the virus inside the ganglia retain back to the dermatophyte ,it might affect **especially thoracic dermatophyte** only 1 or 2 or 3 dermatophyte it depend on the severity of infection . and **rarely reach the upper lumber dermatomes** ,and might **affect the trigeminal ganglia** which mean it might affect the eyes in patient who develop the reactivation of varicella , -remember 1st from the periphery ( skin or RT) reside to the ganglia –

During **primary infection** most children developed immune response except few percentage , and this **immunity** mainly of 2 type : cell mediated immunity and specific antibodies which include **IgG and IgM** , might in certain cases only recognize IgG or IgM , but in general better to have both in order to prevent developing of complication and later to reduce the activation with varicella virus .

Herpes **zoster shingle** recognize in 5% of all infected persons in the age above 50s , and zoster is a very **painful** disease , at first it might not recognized , just hypersensitivity in the infected area in relation to dermatophye or dermatomes of the trunk and later there is eruption in the skin by the presence of **erythema** in most of them , also might associated with **fever** and it will be more painful because of the **inflammation in the ending of the nerves ,** which produce more damage in certain number of patient with **localized ulceration in the skin (rarely) ,**

 but the more dangerous if the virus reach the area of eye which we called **ocular zoster ,** it is limited to few number (5-10%) not necessary to be recognized **,** so the virus affect the ophthalmic trigeminal nerve and produce inflammation , and if the patient not rapidly treated with antiviral drug then he must later **result in severe damage in the cornea and the retina and might become blind** ,( it treated by Aciclovir the drug of choice) ,

almost each year only in US there is between 20-30 thousand cases of blindness associated with zoster , and in the world 100,000 cases including our country in elderly persons

the other clinical feature which might be associated with zoster that affect the CNS (the most dangerous) called **acute zoster neuritis** , produce **pain** in the CNS and might spread to the internal organs affect the lung , brain producing **damage and death** , this is a very serious complication associated with reactivation of varicella . therefore the only way to prevent complication to treat the patient with antiviral drug or to have a vaccine for such persons who suffering from immune suppress condition , this vaccine is not 100% protected but at least reduce the severity of infection .

**HSV 4\*\***

HSV 4 related to another group called **gamma**, and the infection route duplication is more specific , it is related to RT especially oropharyngeal epithelial cells where the first infection can be started, it might be started in the salivary gland , and might later infect directly reach B lymphocyte and reside it and begin the replication cycle , but generally due to the fact in contrast to other herpes virus **excrete a large number of glycoprotein** ,these glycoprotein has antigenic structure response for invasive as well as for developing of clinical feature , and these called as amorphous protienous layer associated with the capsule and the envelope, and this layer responsible for the clinical features as well as for introduction and inducing immune response during infection , but due to the presence of large glycoprotiens therefore we might recognize variety of clinical feature .

In relation to **latency** , following the infection in the RT or the salivary gland tissue , we might recognize the latent in memorial B lymphocyte , in such case the patient develop a variety of clinical feature .

The infection could be symptomatic or **asymptomatic** , and according to a study almost **in the 1st 5 years** the children(50-70%) get infection without knowing that they are infected , because there is **no clinical** feature other than some respiratory tract infection and fever , so we have to expect a large number of population they are infected with a **mild form** of Epstein-Barr virus , despite this fact the virus reside in the B lymphocyte memory and later associated after activation in a furious clinical feature,

 **one of the most clinical feature** : infectious mononucleosis which known as glandular fever , this means there is inflammatory reaction in the epithelial cells of soft palate mostly

, and **also** might be with oral lesions , and with specific type of disease recognized in any immune suppress condition like who infected with HIV and this known as oral hairy leucoplakia , this is white lesions with cheek mucosa and with the edge of the tongue( very rare ) , and often in immunocompromised patient or patient infected with HIV, in addition (this is the problem) following a symptomatic , we have latent stage and this latent stage may happen later after (10-20)years in a type of autoimmune disease and it ( autoimmune disease) can be serious and some times and it depend on health condition of the patient and patient immune response …….etc .

In addition epstein viruses might produce variety of infection in parts of the body and in different parts of the world , with a variety of infection manifested later in form of malignancy (cancer disease) for example  **hodgkin disease lymphoma** is associated with Epstein viruses in all ages and following latent infection and it is a serious disease and usually the patient will respond to the treatment , often in association with patient who recieve transplanted organs (e.g kidney ) are susceptible to develop such type of disease , why ? because the patient who recieve organ must always take preventive drugs against rejection of organ like cyclosporine and this allow Epstein viruses and cytomeglo viruses in certain cases to be inactivated to produce complications in relation to Hodgkin disease or B –cell lymphoma and it is common in our country ( there is specific % that appear in age 60s or 70 s).

Burkitts lymphoma is recognized in relation to tumors of jaw but only in certain African countries (tropical African children ) and not recognized in our country ☺.

Nasopharyngeal carcinoma is complication of Epstein viruses but often recognized in china and other south east countries mainly in males than female .
 As we see,in eoisten viruses , the problem is not the primary infection but suppression of immunity and in order to establish diagnosis of infection the first important step to consider saliva in a source of infection.
|In relation to Epstein viruses like herpes complex 1 and 2 and in addition to other types of viruses so we can use saliva or throat washing to confirm the presence of such viruses (in the past they use tissue culture but now PCR to detect DNA of viruses) ,but if there is advanced technique we can use **blood sample** –**aypical b-lymphocyte** or looking for **heterophile antibodies** (develop against antigen but at the same time it will develop as immune response ( auto) against certain antigen which related to heart or other part of body (e.g rheumatic fever)
. it can be possible to detect capsules or nuclear by using PCR and there is vaccine available , the treatment could be effective in early stages ,**DOC(drug of choice ) is aciclovir .

Cytomegloviruses** is the most common type infected all human everywhere , so it considered (present with us) as children , adult, eldery … everywhere it is long-life infected and might not necessary under certain conditions , it belong to a group of beta-herpes viruses and we have specific characteristic of this virus( e.g in relation to varicella zoster virus, herpes1 and 2 as well as Epstein virus that we do not have many genotype ( we have only few genotype( mostly called subtypes such as influenza virus we have H1 ,H2……)) .
In CMv,when we infected with one genotype later on we might be infected with second genotype if we travel from Jordan to another country which mean ( infection with one genotype will result in development of patient immunity against another genotype but not complete , therefore we might be always susceptible to acquire new genotype and acquire another infection but with less complication) .  **CMV** means : produce enlargement in the cells (multi-nucleated gaint cell) particularly in endothelial cells and this might result in damage of infected organs and it is endemic everywhere and easily to be excited and often according to standard of hygiene in each country . In our country we have low to moderate standard of hygiene ☹ so infection with CMVis more common than in developing country where there is high standard of hygiene .

this virus can be excreted in saliva ,very common in urine but not in feces , and may present in blood ,tears,sexual contact might be associated with development of CMVinfection so **urine and saliva account for the majority of infection .**generally CMVinfection is mild, asymptomatic , not associated with any clinical features ,but might be associated in certain category of patient with complication especially if it related to kidney it might associated with inflammation and it usually recognized by presence inflammatory cells in urine and might be associated with liver cirrhosis and in lung, often it persist for along time in mono-nucleas cells which mean will be associated with blood especially in donating blood ( it should be controlled by presence of cmv espically if it should be used for patient who will acquire kidney transplantation .)
congenital cmv is very common, can be during pregnancy acquired following delivery , it might be primary inheritance infection ( during pregnancy in any month ) but it is more dangerous in the first and less complication later but infection with cmv associated with very very serious complication especially due to presence of cytemegalic inclusion body which often damage brain tissue during circulation of virus in blood and associated with down syndrome ( in Jordan we have recorded about 50-100 cases of down syndrome each year ☹.
\*CMV infection might be associated with hearing or vision loss particularly or complete as well as complication in GI , so these infections are serious ,should be prevented as possible .

\*we have tests that can control primary infection of cmv , herpes virus,….. .

\*in healty patient , infection with cmv is not serious but often should be controlled espically if there is pregnancy ( pregnant women should be aware that she have sufficient immune antibodies in order to prevent infection in newborn babies .

\*most and serious complication associated with **organ transplant** and **immunosuppressant** .

\*immune response to cmv infection involve **humoral antidodies and cell-mediated immunity** and you might recognize both of them or one , not necessary to have both at the same level ,in early infection you will recognize high level of **IgG** later you recognize **IgM** .

\*lack of immune response in certain % of the infected person might be late result in complications espically in relation to eye (**retinitis** ) which means severe inflammation in the retina and cornea and blindness , **pneumonitis** ( with bacteria **),colitis (**related to inflammation in large intestine caused by clostridium difficile),**hepatitis C or B and** cause severe **cirrhosis** or **caicinoma** and it is more dangerous in **encephalitis** and **pancreatitis** .

**DIGNOSIS :
\***you have to detect infection in newborn babies especially if there is signs and symptoms that the patient ( mom or baby) they have some clinical features related to cmv therefore a test called **TORCH TEST(** it is antigenic as a detection test) , you have only to collect 2 drop of cord blood during or following delivery and its should be placed on a simple slide where at the same time we can use urine but it not accurate
\*this test can be used for detection rubella , toxoplasma ,HSV2 ,…… .
\*finally it is important to use rapidly anti-viral drug (**aciclovir** ) and (**ganciclovir**) which it is more effective
\*recently , available vaccine can be pretentive up to 90 %.
good luck every one ☺