

**Sheet no :11**

**Refer to slide no : 4+5**

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**\*The doctor said a note about the influenza virus: the spikes are projected from the envelope not from the capsule. \*He also said that if there is a difference between the slides and the sheets we have to follow to the slides :)**

**Adenoviruses**

**\*Now we will talk about a new group of viruses which are known as Adenoviruses. \*They are related to infections in our adenoids. \*This type of viruses is special due to: 1-It is widely distributed in nature. 2- it can easily infect any person starting from the children, young adults, and elderly. \*The infection established directly following: 1-contact with infected person. 2-drinking contaminated water or drinks or eating contaminated vegetables, etc. \*This infection might survive for along time in different body tissues especially in: 1-payer’s patches (intestinal tract). 2- Adenoids. \*This infection might be excreted later (not necessarily during the presence of infection) if there is a feature related to activation of the virus due to immuno compromised condition or other conditions. \*This virus has a linear, double stranded DNA, so it is not related to RNA viruses (Paramyxovirus and Orthomyxovirus). \*This virus doesn’t have an envelope, and has a special capsid associated with alarge number of capsomers (up to 256 capsomers but in the slides it’s up to 252), and these capsomers are found like a shell surrounded the capsid.**

**\*In addition to that, there are projected tube like structures: they are special peptidoglycane layers responsible for the attachment to the surface of mucosa of the upper respiratory tract and the intestinal tract, which means that this virus is acquired by direct contact or contaminated water, drinks, and fresh types of food. \*The pathogenicity of this virus is associated only with humans, it can be associated with certain types of animals. \*There are large numbers of serotypes =47 serotypes (the numbers of the serotypes might differ from one reference to another but in general it’s within 50 serotypes). \*There are few serotypes associated with human infections, and each country has it’s own serotypes (serotypes which found in our country are not necessarily to be the same in another country especially western and European countries), therefore infection and developing of immune response are related to a specific serotype (which means if we travel from Jordan to another country we might be infected later by another serotype and develop asymptomatic infection). \*Adenoviruses infection in general is mild, and not recognized. \*It might recognized only in a form of infection in the respiratory tract especially in relation to the tonsils and adenoids where you might recognized some inflammation and some fever but it’s not easily to be differentiated like other types of viruses. But at the same time it might reach the intestines associate with a form of gastroenteritis especially in children (vomiting and mild to medium form of diarrhea). \*It might be associated with a form of a urinary tract infection but without the presence of inflammatory cells and pus cells like bacteria. \*So this virus affects many parts of the body and it can be established in certain parts of our body especially: kidney, intestines, and tonsils, where it might be excreted for along time. \*This infection can be established in any person but it’s more dangerous with immune compromised people (in those people it might produce severe form of infection and complications).**

**\*\*\*Clinical manifestations: \*In general they are very mild. \*Only few percentage (1%-5%) which might require clinical attention but the others are very mild. \*The doctor said he’s sure that all of us have exposed to adenovirus without knowing that we are infected with it!!! \*But in certain cases we might recognize more dangerous and severe infections especially in relation to upper respiratory tract like pharyngitis. 1)Pharyngitis: it cannot be easily distinguished from other respiratory tract viruses (influenza, parainfluenza, rhinovirus, corona virus, etc). \*the only way to know that the infection is related to adenovirus requires certain experience from the examined physician especially pediatricians because at the same time there is pharyngitis associated with conjunctivitis. This is very confirmative for the presence of adenovirus despite the fact that other viruses (like measles and mumps) might produce conjunctivitis, but in relation to adenovirus pharyngeo-conjunctivitis is common especially with children. 2)Conjunctivitis: it is more dangerous and more painful if the infection is only related to the eye and produce conjunctivitis, there will be very severe pain and require medical attention. \*there can be sporadic case (single case) or outbreak of cases especially in military camps, schools, etc. 3)Acute gastroenteritis: it’s found only in patients:1-with underlying diseases. 2-lack of nutrition. 3-immune compromised (very dangerous). where it might produce a chronic form of diarrhea, it can be so severe and require going to the hospital. \*Generally, other features are very rare, and each type of these clinical manifestations (pharungitis, pharyngeo-conjunctivitis, conjunctivitis) is related only to a few number of serotypes, not all serotypes of adenovirus produce the same feature, so according to the presence of these serotypes we might recognize the severity of the infection. 4)Acute hemorrhagic cystitis: It’s another form of infection which is not easily detected and require a lot of investigation to prove that this infection is due to this type of viruses. \*The infection might reach any part of the genital tract (Cervicitis , Urethriti , Urinary bladder hemorrhagic cystitis), and often associated with releasing of red blood cells in the urine without pus cells. \*\*A very simple routine test: If we examine the urine for the presence of any type of infection whether viral or bacterial, if there are only red blood cells without pus cells neutrophils and without any type of bacteria, the causative agent is probably adenovirus (there are other types of viruses can cause this thing like leukovirus and toxantovirus (I’m not sure abot it’s name) but more common the cause is adenovirus). \*\*Adenovirus is associated with mild infections in healthy children and adults, and produce severe form of complications only in immune compromised conditions especially patients who receive kidney or any other transplant, therefore before the donor donates a kidney he must be examined for the presence of adenovirus, otherwise the transplantation will produce complications and death to the receiver of the kidney. \*\*\*Immunity: \*Following the infection there is a specific immunity which is a “humoral immunity” composed of two types: 1-the first is in relation to the mucosa which is mainly IgA antibodies. 2-the second is mainly associated with IgG antibodies. \*so this immunity prevents infection with only a specific serotype (the serotype which the person has infected with it previously), BUT there is a cross reactivity between few serotypes, therefore one specific serotype might reduce -to some extent- the infectivity and the manifestations of the clinical features of the infection of another serotypes by the presence of antibodies against them. \*So one serotype of adenovirus might decrease the infection with other serotypes but it cannot prevent it 100%. \*\*\*Diagnosis: \*Diagnosis of adenoviruses is not easy. \*There are few laboratories that have the capability to detect specific antibodies by ELISA for example (It’s used to detect specific substances), recently they have introduced DNA PCR which is easily to be done to the urine, respiratory tract, and blood, to recognize if there is an active virus during the infection. \*\*\*Treatment: \*Antiviral treatment (drugs) is very important especially in: 1-Conjunctivitis (eye infection): because adenovirus infection in the eye is very severe and it might affect the cornea. 2-a patient who has a transplanted kidney to prevent any diseases with adenovirus. \* Ribavirin is an excellent drug which can reduce the severity and the pain of infection, it must be used at least for two weeks in order to control the infection.**

**Gasrtoenteric viruses**

**\*\*\*Enteroviruses: \*It’s name is related to the intestines. Despite the fact that infection with these viruses is not related to the intestine only. \*We have two routes for the infection: 1- Starts in the respiratory tract and ends in the intestinal tract. 2- Starts in the intestinal tract and not necessarily to end in the respiratory tract. \*The infection: 1-often starts in the respiratory tract and later it can disseminate to the intestinal tract directly. 2-or it might establish in the respiratory tract and then disseminate to the lymph system then to the blood stream and from the blood it goes to the gastrointestinal system. \*This group of viruses composed of 71 serotypes, each serotype is associated with a specific type of infection, or each few serotypes might have the same clinical features, therefore it’s not easily to classify this large number of enteric viruses serotypes. \*Because many of these viruses are not so important and rarely produce infection in each country, we will concentrate only on four enteroviruses which are associated with the majority of infections related to the enteroviruses and associated with millions of cases each year everywhere in the world. Some of these viruses can be so dangerous and associated with severe form of infections in the central nervous system which result in paralysis and death of the infected person. \*The major four enteroviruses: Polioviruses, Coxsackieviruses, Echoviruses, and Hepatitis A virus. \*** **Rhinovirus is considered part of enteroviruses. \*Enteroviruses belong to a family called picorna viruses family due to the fact that these very small viruses are not recognized easily even by the electron microscope. \*All these viruses are similar in the structure. \*Structure: -single stranded +ve RNA viruses. -four important polypeptides (the doctor said glycoproteins!!! but I followed the slides) associated with the capsule known as (VP1, VP2, VP3, VP4). The difference between them is the antigenicity (production of specific antibodies), not each VP protein results in the same antibodies production, but there is similarity so sometimes it might cross react during the infection with a different type, despite of this fact each virus is associated with a very specific type of infection. \*The structure of these viruses is exactly like Haemophilus influenza and Parainfluenza and other viruses. \*Once these viruses reach the respiratory tract mucosa, they attach to the mucosal cells and penetrate them by the presence of the specific polypeptides resulted in infection in the cytoplasm and within the cytoplasm of the virus the production of more virus particles begin which will be released from the infected cells by the body later (like Haemophilus influenza and Parainfluenza). \*The infection of all these viruses often -not necessarily all the time- starts in the respiratory tract, and attaches to the mucosal cells there, after the incubation period (between 3 days and 3 weeks) the infection will be established. The infected respiratory tract releases large numbers of viruses, some of these viruses will be swallowed and reach the intestinal tract, others will disseminate to the lymphatic system then to the blood stream and produce viremia. \*If the virus is established in the intestine directly not via the respiratory tract the viruses will increase in the number within the payer’s patches and they will be released in large numbers and again via the mesenteric lymph nodes of the intestine it will reach the blood stream and produce viremia. \*So, the two routes (respiratory tract or intestinal tract) at the end will lead to viremia (viruses in the blood stream). \*The presence of the virus in the blood stream results in immune response, if this immune response can’t control the replication of the virus, we might recognize the clinical features of the infection [during potent features of the viruses Polioviruses, Coxsackieviruses, Echoviruses and even the Hepatitis A viruses (Hepatitis A virus has been separated from the enteric viruses and becomes part of the hapatoviruses group, and it’s not recorded as a part of enteric viruses in the references).]. \*All these viruses can survive for a long period in the environment especially in the cold water. Once the water (mainly in the environment) becomes contaminated with these viruses , they might survive for a long period (few weeks to few months). But the virus can be easily deactivated by heating the water up to 60 degrees, this can be enough to deactivate the virus. \*The water becomes contaminated by these viruses because it is exposed to humans and animals feces (there are certain enteroviruses related to the animals, others are related to the humans and animals), contamination with the feces will increase the presence of these viruses.The water might be contaminated from the fresh products also (vegetables especially the green ones, etc), the viruses can survive on the shells of these vegetables. \*So the infection by these viruses is very common, but generally most of these enteroviruses are associated with mild infection to the gastrointestinal tract (mild diarrhea, and some fever for 24-48 hours), and often it’s self limited and doesn’t require a treatment. \*Despite this fact, there are some of these viruses produce more severe infection (especially Polioviruses, Coxsackieviruses) and might result in outbreak of enteroviruses infections. \*Enteroviruses generally are considered highly contiguous viruses which means that the viruses which are mainly found in the urine and feces can contaminate our fingers or our food, etc and this might be enough to produce infection in any susceptible person. \*The route of infection is known as fecal oral route, which means that the viruses are often found in the intestine, when they are excreted from the intestine they can contaminate water, food, anything we use, etc and produce infection. \*These viruses might be acquired via droplet infection, but it’s mainly fecal oral route. \*Structure: complex cubic structure with a large number of capsid. \*Note: in the slides there is a picture for Rota virus, it’s not a part of enteric viruses but to some extent it’s structure is similar to their structure. \*In relation to our country and many developing countries, the enteroviruses infection is more than developed countries, due to lack of hygiene (the standard of hygiene is not very high especially in relation to the restaurants, food products, etc). \*Travelers who come from the western countries to our country acquired diarrhea, this form of diarrhea can be due to: 1-enteroviruses. 2- enterotoxigenic E. coli. It’s called “travelers diarrhea”. \*The infection often starts in the form of mild diarrhea, later it might result in other features especially CNS disorders. \*In general the clinical features of ALL the enteroviruses: 1-mild Pharyngitis. 2-mild Pharyngitis and skin rashes. 3-Acute hemorrhagic conjunctivitis (exactly like Adenoviruses). 4-Pneumonia. 5-CNS infection. 6-conjunctivitis. 7-encephalitis. 8-Mild paralysis (for few days). So it might be associated with a variety of infections. \*In general, infection with these enteroviruses resulted in developing of a specific humoral antibodies which might protect against a lot of types of enteroviruses not against a single type. \*\*\*Polioviruses: \*The causative agent of Poliomeylitis. \*In the past, Poliomeylitis was known as the causative agent of paralysis, especially before the introduction of the vaccine which we have in our country, this vaccine covers the majority of newborn babies. \*We’re lucky because Poliomeylitis cases are not recorded since thirty years. \* In Jordan, there is no one clinical case of Poliomeylitis which is caused by polioviruses. But there are some cases related to Poliomeylitis but they are not due to true polioviruses as causative agents, it’s a paralytic disease due to other enteroviruses like Coxsackieviruses, which might give impression that it’s a poliovirus but during the investigation we will find that it’s not a true poliovirus. \*Often polioviruses are associated with water contamination especially during winter months because they can survive in cold temperature. \*Polioviruses are generally considered -to some extent- resistant to the disinfectants (like dettol and other detergents, the diluted dittol is ineffective, but in high concentrations it will be effective against polioviruses), therefore polioviruses might survive more than other viruses in the environment of humans and result in infection especially in young children. \*The age of the infected person should be considered. Young children (up to 10 years old) often develop mild general symptoms like gastrointestinal symptoms, respiratory tract symptoms, and fever, it’s rarely associated with aseptic meningitis. \*Clinical features of Poliomeylitis are divided into three parts: 1- Asymptomatic Poliomeylitis: it means that there is intestinal infection associated with mild diarrhea, some fever, mainly associated with upper respiratory tract like sore throat, running nose, and RARELY associated with aseptic meningitis (the virus doesn’t reach the spinal cord or the brain cells). 2-Abortive Poliomeylitis: second step of general Poliomeylitis (the general might not be recognized / asymptomatic). \* 0.5-1 % of infected children might develop abortive Poliomeylitis. \*In addition to the clinical features (diarrhea, sore throat,etc), the infected person might have aseptic meningitis which means that the virus has reached the central nervous system and it might associated with a mild paralysis for few days (suddenly, the patient will have some problems in moving his hands, legs, and muscles). \*Children develop neutralizing antibodies and recover without any damage in the nerve endings and the central nervous system, so it’s not dangerous but it’s recognized and sometimes requires going to the hospital. 3-Paralytic Poliomeylitis: it depends whethere the infection is in children or in adults. \*Normally the number of Paralytic Poliomeylitis in the children (age less than 10 or 12 years old), is 1/1000 from the asymptomatic meningitis, so it’s very rare. \*Whereas this can be 1/75 in adults, which means that the adults associated with** **Paralytic Poliomeylitis more than the children and this infection in adults is more dangerous. \*Paralytic Poliomeylitis is associated with two important clinical features: 1- Acute flaccid paralysis:**

**\*The limb becomes floppy, the muscles are weak. \*This will persist for life and there is no reverse. \*It’s associated with damage to the lower motor neurons.**

**2-Bulbar poliomyelitis: \*It’s more dangerous because the damage is followed in the spinal cord brain stem cells. \*It causes death to the infected child or adult. \*It’s more dangerous, and recognized in adults more than children, children rarely develop this type of infection. \*If the contact with poliovirus happens during the pregnancy, will it affects the fetus??? The answer is yes, and it is more dangerous during the first trimester and it will decrease with the duration of pregnancy. There are very rare cases associated with the damage in the brain of the fetus if the infection is in a woman who is susceptible to infection (means that she lacks specific neutralizing antibodies to poliovirus). This thing is rarely recognized in our country and many other countries who have complete immunization against poliovirus.**