بسم الله الرحمن الرحيم

- This lecture is a continuation of the last lecture under the topic of Viral agents causing gastrointeritis,these are :

1- Rotaviruses 2-Adenovirus 3-CALICIVIRUS.(MOST DECSRIBTED NORWALK VIRUS 4-Astroviruses 5- Toroviruses.

2) Adenovirus Gastroenteritis

- **First Isolated in 1953 from adenoidal tissue so that it's called adeno virus**
- **Virion:**
  - **– Icosahedral, Naked (non-enveloped), it has 252 capsomeres and Fibers projecting from penton bases which is formed by capsid. There is repeating of the capsomers, they either meet as pentones or hexones as we took in the last semester.**
  - **– Genome: Double-stranded DNA, linear, infectious.**
  - **– Proteins: Important antigens (hexon, penton base, fibers projecting from the pentose bases and they have a circular ends, these fibers play a role in attachment to cells of an epithelial origin and they are also toxic to the cells as well.**
  - **– Replication: as it is a DNA virus so it replicates in the nucleus**
  - **– Virus classification: Double stranded DNA; Family: Adenoviridae; Genus: Mastadenovirus; Species: Human adenovirus (H Ad)**
- **There are more than 100 serotypes, but those which makes disease in human are around (50-55) serotypes**
- **They are classified into 6 subgenera from A to F.**
- **Fig 1 show how the adenovirus looks under the electron microscope**

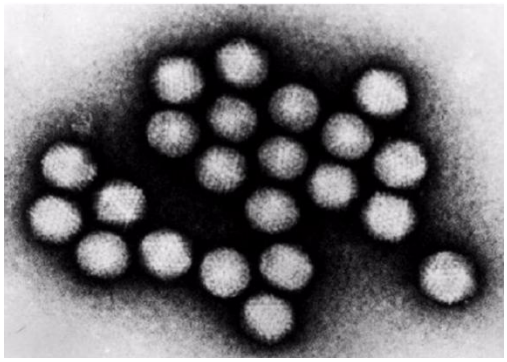


Fig 1

- **Known oncogenic potential of some serotypes which is exclusively seen in animals but not in humans (natural host).**
- **Commonly used as vectors in gene therapy and vaccine delivery**

Adenoviral structure

- **Penton bases associated with fibers projecting form it and has a circular end aid in attachment and a Double stranded DNA inside**
- **Look at pic number two to distinguish the aforementioned structures**

*** *Outstanding characteristics***

-Excellent models for **molecular** & **biochemical** studies of eukaryotic cell processes

- The largest viruses (maximum size able to be transported through the endosome by receptor mediated endocytosis).

-virion has unique "spike" or fiber associated with each penton base of the capsid that aids in attachment to the host cell and it is toxic to the cell.

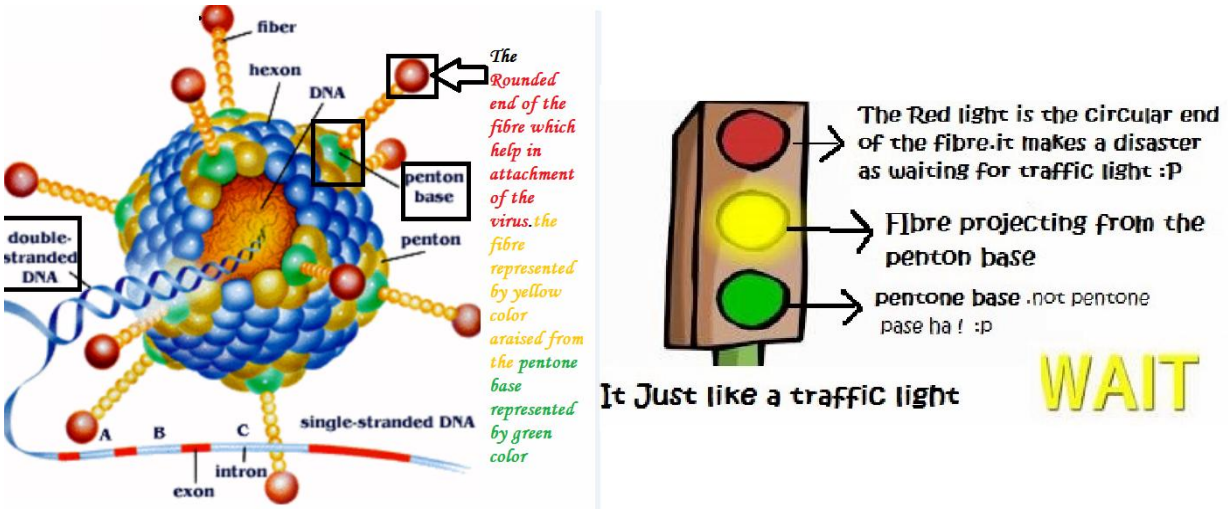
-has tropism for cells of epithelial origin

-**Replicative cycle is sharply divided into EARLY & LATE events**.

1- **The early phase** or even is responsible for **structural** protein formation.

2- **Late phase** responsible for **nonstructural** protein formation.

- **Fig 2 show the structure of the adenovirus**



PIC 2

Adenovirus pathogenesis

- Adenovirus can make a wide range of infections in the body, eg, pharyngitis conjunctivitis upper respiratory tract infections, gastroenteritis and cystitis. This indicates that adenoviruses have ***tropism*** for **cells** of epithelial origin.
  - N.B. remember, Tissue tropism is the cells and tissues of a host which support growth of a particular virus or bacteria.
- **ONCE Adenovirus replicates in epithelial cells, it is producing inflammation and then as a result cell necrosis.**
- **After acute infection, the virus may remain latent in some tissues (tonsils, adenoids, payer's patches) and become reactivated and shedding asymptomatically there for 6-18 months or even up to 2 years.**
- **Reactivation of virus, once** it lies in the latent stage**, enhanced by stressful events or drop in the immune system.**
- **• Integration of adenoviral DNA into host cell genome may occur leading to latency in tonsils and peripheral lymphocytes**
- **As it is a DNA virus, sometimes smudgy intranuclear inclusions may be seen as aggregates of capsid proteins.**

** N.B: as a general role. *Viruses may form inclusion bodies according to the site where it replicates.so that, **DNA** viruses tend to cause **intranuclear inclusion**s while **RNA** viruses tend to cause **Intracytoplasmic** inclusions with some exceptions like CMV*

which is DNA virus that makes both intracellular and intracytoplasmic inclusion bodies.

- **Adenovirus infection leads to the following:**

  -Penton bases with its fibers have toxic effects on host cells especially in GI tract Encode proteins in the E3 genomic region that binds MHC class 1 antigens in the ER which restricts their expression on the surface of infected cells and interfere with recognition and targeting by cytotoxic T cells. (Helps in latency) what does this statement mean? –once the virus enters the cell there are several cellular protease that work on cleaving(cut) the proteins encoded by E3 genomic region of penton base into smaller proteins, these proteins attach to the MHC class 1 antigen forming a complex in the endoplasmic reticulum. Then, travels to Golgi, MHC class 1 antigens are present in all nucleated cells; the complex then goes to the surface of the infected cell. The cytotoxic T-cells comes because CDA binds to MHC class 1, recognize it as foreign antigen and produce perforins and granzymes which lead to killing of the infected cells.

  -N.B. CD4 binds to MHC class 2 antigens.

  - E1A protein has been associated with increased susceptibility of infected cells to destruction by TNF and other cytokines

  - Adenovirus death protein; important for efficient lysis of infected cells and release of progeny virions.since it is a naked virus and newly produced viruses are released after cell lysis. So, these proteins aids in spread of infection

***Diarrhea due to* Enteric Adenovirus:**

- Adenovirus **Causes 5-15% of all viral gastroenteritis. It is the second common viral agent causing gastroenteritis after ROTAVIRUS .Belong to serogroup F • Most of patients affected Age below 4 years old. •It is Year round infection, there is no season or preference so it is seen all around the year.it is mainly spreads via fecal-oral route as all other viruses causing gastroenteritis. Isolation requires special media which is Graham 29.ELISA can be used for rapid detection of the** Adenovirus.

***CLINICAL FEATURES OF Adenovirus gastroenteritis**

- **Incubation period extends from (3 -10 day) .it has one of the longest incubation periods along viruses causing gastroenteritis**
- **Diarrhea lasts for 10 -14 days (up to 2 weeks)**

- **Can also cause intussusception(commonly seen in small intestine in small children or infants, mesenteric adenitis is developed because of spreaded virema reached lymph nodes of the mesentery ,Adenovirus might be associated with abdominal pain might be missed for appendicitis**
- **Treatment: There is no specific treatment of Adenovirus but supportive treatment by replacing fluids and electrolytes. Treatment by cidofovir is promising for severe disease in immunocompromised while in immuncompmetent patient there is no need of use the antiviral drugs.**

3) HUMAN CALICIVIRUS (HuCV)

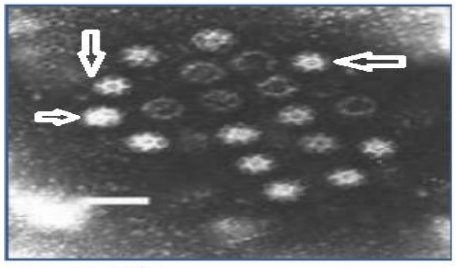
- **Family Caliciviridae .they are a naked (Non-enveloped) viruses so that they can resist after exposure to acids, ether or heat (Remember naked viruses are more virulent). They have Single stranded positive sense RNA .27-35 nm in diameter. They have icosahedral capsid containing single capsid protein. Have not been effectively propagated in cell culture as all other viral agents causing gastroenteritis.**
- **Caliciviridae divided into two groups (genera):**

1- SLV (Sapovirus)pr (Saporovirus) **2- NLV (Norovirus) .**

1- SLV (SAPOVIRUS)PR (SAPOROVIRUS

- **It is considers as a (typical) virus causing gastroenteritis.**
- **Morphology**
  - **E/M pic reveals**

  1-It is star shaped virus (pointed by white arrows in pic 3. 2-It size 31-35 nm and it is larger than noroviruses. 3-32 cup-like depressions.
- **E.g.- Sapporo-like viruses**



SAPOROVIRUS

2-NOROVIRUSES

- **Morphology of HuCV- atypical (Noroviruses)**

1- **approx. 27 nm.2-Rough, feathery surface but no internal pattern .3-Small Round Structured viruses**

- **e.g.- Norwalk-like viruses**
- **Norwalk virus Nomenclature: As they were first associated with an outbreak in Norwalk Ohio.so that it is called Norwalk virus**
- **EPIDEMIOLOGY:**

  Winter vomiting disease" 1968, Norwalk OH • Cause 40% of nonbacterial epidemics. It contribute with 45% foodborne infections so that it is the most common cause of foodborne infections, 52% of foodborne infection caused by Norwalk virus is contributed raw shell fish and associated outbreaks or it could either be caused by contamination of water sources .it is mostly associated with Explosive epidemics in camps, cruise ships and nursing homes(closed sittings).it is distributed worldwide and can infect all ages. Worldwide distribution • Affects all ages .Major cause of food-borne outbreaks of Gastroenteritis (>50%).The Prevalence of antibodies reaches 50% by the fifth decade (people who age 50 years, so it rises slowly and if we compare it with Abs prevalence of Rotavirus we will exclude that antibody prevalence of Rotavirus is more evident and high by 90 % of people have humoral antibodies by the age of 4 years. It is associated with asymptomatic infections.so if you test for antibodies you might find patients have anti bodies against the virus but he would not get develop gastroenteritis. Viral shedding 3-4 days. Mucosal changes revert in ~2 weeks while Rotavirus might take up to 8 weeks. Protective immunity short-lived, reinfection can occur but the symptoms will be milder.NLV have no cross protection (immunity), It means when different viruses from the same ''Norovirus'' subfamily infect t the cell it won't develop immunity and protect from other viruses within the same subfamily because each virus have antigen specific immunity. Subfamily doesn't protect other one.

NORWALK VIRUS: CLINICAL FEATURES

- It has a Short incubation period extends from 24 hours up to 2-3 days (range 10-50hr). Incubation period starts by Vomiting followed by diarrhea which lasts for 1-3 days. Patient might have other Constitutional symptoms like Headache, myalgia and fever. Less severe than rotavirus .It is associated with complications more in immunocompromised patients

- **Treatment OF symptomatic (ALSO SUPPORTIVE) rehydration, antidiarrheal ((**fluid and electrolyte replacement.

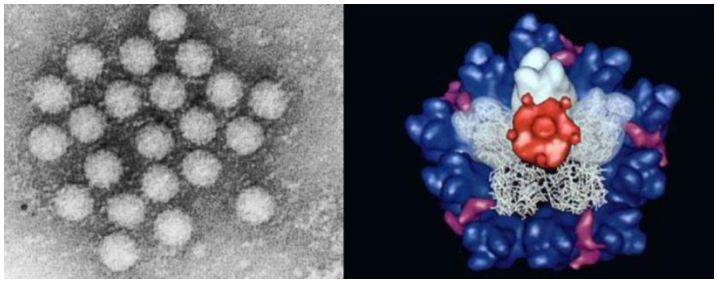
- **Spread, it is spreading by fecal oral route.**
- **Diagnosis: -**

  Specimen is taking either from stools, vomitus, food or environmental swabs in the case of outbreaks and then can be detected by electron microscopy .PCR is also used for detection. Serology also can be used for epidemiologic purposes.

  4) **Human Astrovirus:**
- **Described in relation to an outbreak of gastroenteritis in 1975**
- **It was Detected by EM**
- **Immunologically distinct from HuCV (Human Calicivirus) at the beginning they thought that it was a member of caliciviredae family**
- **It can infect animals as well as human.**
- **Classification of Astrovirus**

  - Family Astroviridae Genus Astrovirus, 8 Human serotypes (1-8)
- **ASTROVIRUS- structure**

-it is a single stranded positive sense RNA virus.it is naked virus so that it is heat stable and acid resistant. Its virion is rounded with star shape in the middile.it contains 3 structural proteins.pic 4 shows how it loos under E/M.



Pic 4

- **ASTROVIRUS - Clinical Features**

  - Infants and children are most often affected, Elderly and immune compromised persons as well .Short incubation period 1-4 days starts with Nausea and vomiting followed by abdominal cramping pain and watery diarrhea.it might be associated with Constitutional symptoms-fever, malaise, headache .Symptoms last 3-4 day which is considered as short period of time.
- **ASTROVIRUS – Epidemiology**

  -Endemic worldwide.Astroviruses are associated with 5%–9% of cases of gastroenteritis in young children, mainly in children <7 years of age.it is Transmitted from person-person via fecal oral route. Outbreaks mostly due to fecal contamination of sea-food or water resources.

- **ASTROVIRUS – Diagnosis**
  - **EM (virus shed in stool in great numbers)**
  - **EIA) Immunoassay)**
  - **RT-PCR**

5) Toroviruses

- **Family Coronaviridae .Genus Torovirus • They cause gastroenteritis in mammals, but rarely in humans associated with Watery diarrhea in 2 – 12 months old infants and it is not as severe as in Rotavirus. The only Enveloped virus along viruses causing gastroenteritis.it is single stranded positive sense RNA virus. The illness lasts for short duration (3-4 days). Diagnosis: EM, ELISA, Hemaglutination inhibition (HI).Treatment: the same as all other viruses cause gastroenteritis it is supportive with not specific antiviral treatment.**

- **Infection By which of the following is localized to the duodenum and upper jejunum?**

  -A-Rotavirus. B- Norovirus. C-Sapovirus D- Astrovirus F- Adenovirus

  * The answer is (A) since: -the sites of infection: Rotavirus ➔duodenum & Proximal jejunum

  Calicivirus ➔jejunum the rest➔small intestines.

''انا اللي طول عمري بقول أن المحبة عمرها طويل'' "ليث المهيرات "

ذكرى مرور عام . اللهم اغفر له وارحمه واجعل قبره روضه من رياض الجنة وأكرم نزله وأسكنه الفردوس... اللهم آمين .