MICROBIOLOGY

بسم الله الرحمن الرحيم

Final – Lecture #1

# Adenoviruses

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا


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# Objectives

- Understand the structure, properties, classification, replication, and pathogenesis of Adenoviruses
- Discuss the epidemiology, clinical presentation, laboratory diagnosis and management of Adenoviruses

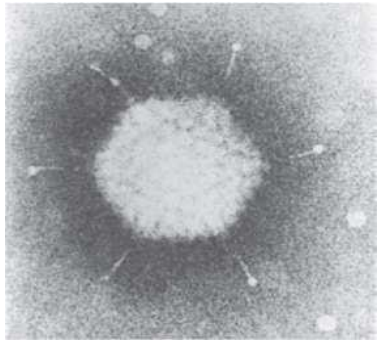
بسم الله الرحمن الرحيم، اللهم افتح لي أبواب حكمتك، وانشر عليّ
رحمتك، وامنحني قوة الفهم، وسرعة الحفظ، وصفاء الذهن، اللهم اجعل
هذا العلم حجةً لي لا حجةً عليّ، ووفّقني لما تحب وترضى.

# Introduction

- Adenoviruses were first isolated from adenoids(**that's why we called them adenoviruses)** surgically removed from children in 1953
- It can replicate and produce disease **mainly** in epithelial cells (the respiratory, gastrointestinal, and urinary tracts and in the eye) **So it has a wide range of effects**
- Many adenovirus infections are subclinical, and the virus may persist in the host for months.
- Adenoviruses are valuable systems for molecular and biochemical studies of eukaryotic cell processes. They are also useful vectors for gene therapy approaches + the induction of tumors in animals for research or therapeutic purposes
- Some adenoviruses strains are oncogenic (to animals) but are not important in human cancer causation

**Adenoids** are lymphoid tissues, a collection of tissue similar to lymph nodes and tonsils. They are located in the upper respiratory tract, specifically in the back of the nose.

# Structure



- Size 70-90 nm in diameter

It is relatively small to medium in size.

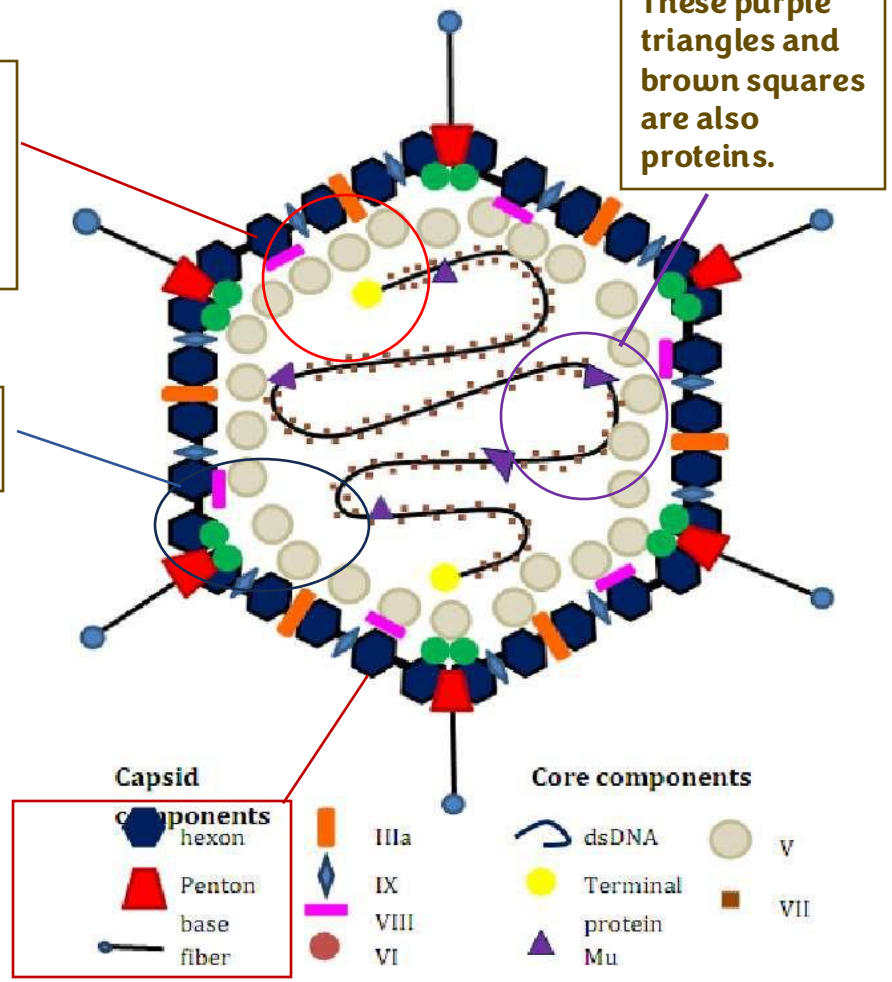
- The viral genome is linear ds-DNA
- A virus-encoded protein is covalently linked to the end of the linear genome (terminal protein)
- Core proteins
- Icosahedral with 252 capsomeres , **consists of :**
- The hexons (240), pentons (12), and fibers (12) at each vertex
- Unenveloped (naked)

One of The structures of adenoviruses is that it has a protein at the end of its genome which has certain role in replication

These purple triangles and brown squares are also proteins.

Core protein for protection

The fibers are unique structures on the capsid, they play a crucial role in attachment to host cells, similar to how glycoproteins function in the envelope of other viruses, At each penton base , there is one fiber projection



- The DNA can be isolated in an infectious form, and the relative infectivity of that DNA is reduced at least 100-fold if the terminal protein is removed by proteolysis.
- The hexons, pentons, and fibers constitute the major adenovirus antigens important in viral classification **(through their distribution, shapes , type)**
- The penton base **(Despite the small amount)** carries a toxin-like activity that causes rapid appearance of cytopathic effect **( the change in morphology)**
- **In some strains of Adenovirus** Fibers are associated with hemagglutinating activity. Because the hemagglutinin is type specific (can be used for viral typing)

✓ When DNA or RNA viruses enter a host cell, they undergo uncoating, which releases the genome alone. This step is crucial for replication, but it makes the virus non-infective during what we call the eclipse period. During this period, the virus cannot infect new host cells because it has lost its protein coat. However, in adenoviruses, this is different. The presence of a terminal protein attached to the end of the genome preserves the genome's infectivity, allowing it to remain functional and infectious even without the other viral components.

✓ Hemagglutinating activity refers to the ability of certain viruses, such as influenza viruses and parainfluenza viruses, to cause red blood cells to clump together (agglutinate) when mixed with a virus suspension

# Classification

- At least 57 distinct antigenic types have been isolated from humans and various animals. About one-third of the 57 known human serotypes are responsible for most cases of human disease.
- Human adenoviruses are divided into seven groups (A–G) on the basis of their genetic, physical, chemical, and biologic properties ,

1- Hemagglutination(None , partial , complete)

2-the percentage of guanine (G) and cytosine (C) in the DNA shows little variation between strain.

3-Oncogenic potential refers to the ability of adenovirus strains to induce tumors in vivo. This means that if we introduce adenoviruses into an animal, we assess whether they can form tumors and, if so, to what degree–high, moderate, low, or none at all. Additionally, it includes the ability to transform normal cells into tumor cells i , Some strains have this ability + , while others do not - , or unknown

| | | Hemagglutination | | | Oncogenic Potential | |
|---|---|---|---|---|---|---|
| Group | Serotypes | Group | Result | Percentage of G + C[a] in DNA | Tumorigenicity in Vivo[b] | Transformation of Cells |
| A | 12, 18, 31 | IV | None | 48–49 | High | + |
| B | 3, 7, 11, 14, 16, 21, 34, 35, 50, 55 | I | Monkey (complete) | 50–52 | Moderate | + |
| C | 1, 2, 5, 6, 57 | III | Rat (partial) | 57–59 | Low or none | + |
| D | 8–10, 13, 15, 17, 19, 20, 22–30, 32, 33, 36–39, 42–49, 51, 53, 54, 56 | II | Rat (complete) | 57–61 | Low or none[c] | + |
| E | 4 | III | Rat (partial) | 57 | Low or none | + |
| F | 40, 41 | III | Rat (partial) | 57–59 | Low or none | + |
| G | 52 | Unknown | | 55 | Unknown | Unknown |

The most important aspect in the clinical role of adenovirus strains is that each group of strains tends to infect specific organs or cells. For example, some strains infect the respiratory tract, while others target the gastrointestinal tract or the eyes( so it also reflected certain diseases )

# Replication and pathogenesis

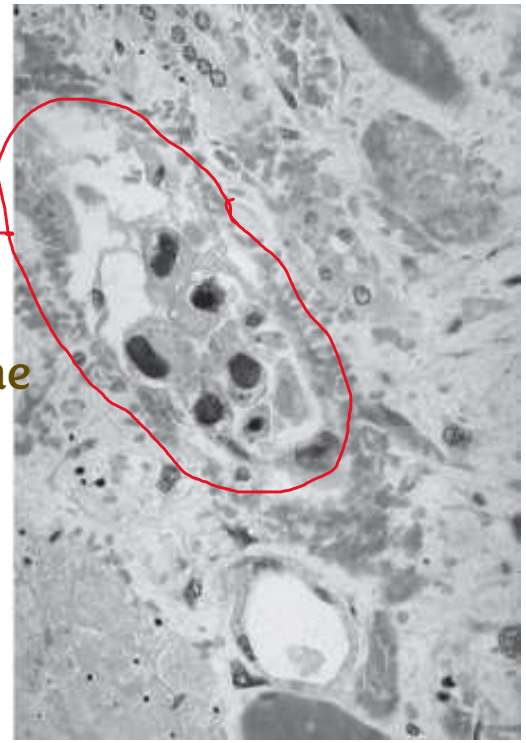
- Adenoviruses replicate well only in cells of epithelial origin (respiratory tract, eye, gastrointestinal tract, and urinary tract)
- The virus attaches to cells via the fiber structures
- The host cell receptor for some serotypes is CAR (coxsackie—adenovirus receptor), a member of the immunoglobulin gene superfamily

exists on epithelial cells associated with the virus

- Adenoviruses are cytopathic for human cell cultures, particularly epithelial cell lines. The cytopathic effect usually consists of marked **rounding**, **enlargement**, and **aggregation** of affected cells into **grape-like clusters**

From pentons part on capsid

Epithelial cells after introduction of the virus



Typical cytopathic effect of the virus

## TABLE 32-1 Important Properties of Adenoviruses

| |
|---|
| **Virion:** Icosahedral, 70–90 nm in diameter, 252 capsomeres; fiber projects from each vertex |
| **Composition:** DNA (13%), protein (87%) |
| **Genome:** Double-stranded DNA, linear, 26–45 kbp, protein bound to termini, infectious* |
| **Proteins:** Important antigens (hexon, penton base, fiber) are associated with the major outer capsid proteins |
| **Envelope:** None |
| **Replication:** Nucleus DNA virus -> replication in the nucleus |
| **Outstanding characteristic:** Excellent models for molecular studies of eukaryotic cell processes |

# Epidemiology

- Adenoviruses exist all over the world and are present year- round; community outbreaks of disease are unusual.
- Transmission: Depends on the location of injury

1. Respiratory infection
   - by inhalation of respiratory droplets.
   - Through contaminated hands.
   - Direct contact with contaminated surfaces.
2. Intestinal tract infection:
   - By the fecal-oral route. The virus enters food and then transmitted to human
3. Eye infection:
   - Through contaminated hands.
   - Using contaminated towels.
   - Using contaminated eye drops, ophthalmic instruments.

# Clinical Manifestation

- Diseases associated with adenoviruses:
  - Keratoconjunctivitis.الالتهاب الجاف للقرنية والملتحمة بالعين
  - Pharyngo -conjunctival fever.
  - Acute respiratory diseases.
  - Gastroenteritis.
  - Urinary tract infection.
  - Meningitis.

# 1- Respiratory Diseases

Respiratory diseases caused by adenoviruses are classified as group C.

- Group C, serotypes 1-7 (Serotypes that affect respiratory system)
- Infants and children: Characteristic symptoms include fever, malaise, sore throat, hoarseness and cough.
- Pneumonia develops in around 10% of cases and can be fatal. In some cases, the virus may descend into the lower respiratory tract and cause more severe infection "pneumonia"
- Adenoviruses are the cause of an acute respiratory disease syndrome among military recruits. This syndrome is characterized by fever, sore throat, nasal congestion, cough, and malaise, sometimes leading to pneumonia.

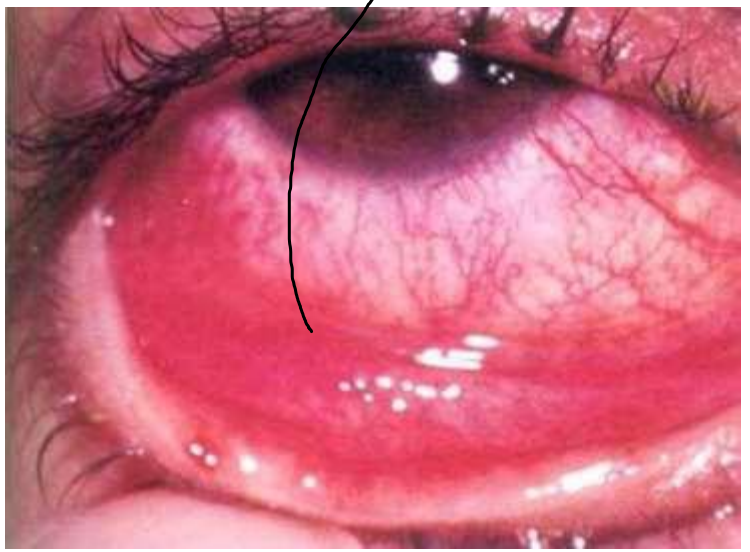
Adenoviruses rarely infect adults due to immunity but can cause acute respiratory disease outbreaks in military personnel due to specific strains.

They are hard to distinguish clinically and require laboratory diagnosis.

upper respiratory tract infections are **indistinguishable** from other viruses.

# 2- Keratoconjunctivitis

Redness ,swelling , tearing ,pain



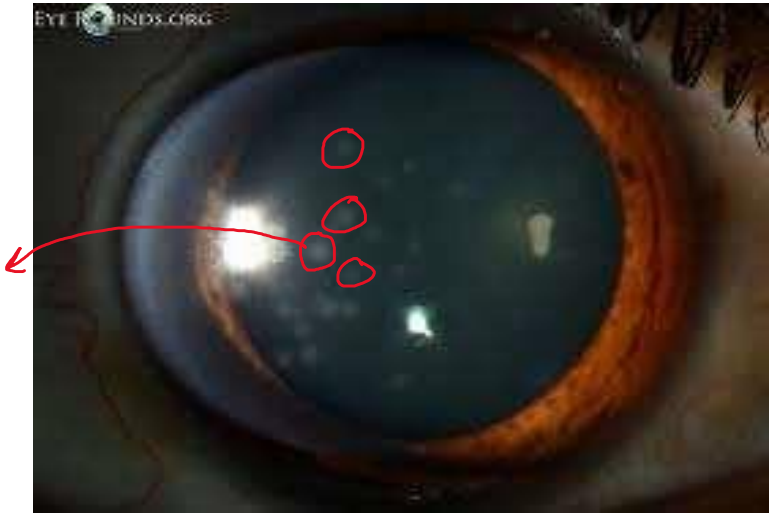
Fear of light occurs because it irritates the eye, worsening symptoms like pain and irritation.

- Group D, Serotypes 8, 19, and 37
- This syndrome is characterized by **aggressive** conjunctivitis, pain, photophobia, and lymphadenopathy followed by the development of superficial punctate keratitis.

enlargement lymph node around the eye

If the infection is prolonged and severe, it can cause superficial punctate keratitis, leading to frequent eye scratching and permanent corneal damage, resulting in white spots.

White spots block light, making the patient see spots when looking at objects.



# 3- Gastroenteritis

- Group F serotypes 40 and 41

Each serotype causes a different disease.

- Associated with cases of endemic gastroenteritis, usually in **young children and neonates**. Can cause occasional outbreaks.

* Viral infections in the GI tract are very common in children, and the younger they are, the more likely they are to develop.

The first cause was rotavirus

- Possibly the second most common viral cause of gastroenteritis **or diarrhea** (7-15% of all endemic cases).
- Similar disease to rotaviruses

mild fever, diarrhea, abdominal pain

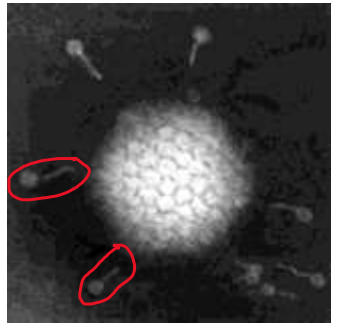
- Most people have antibodies against enteric adenoviruses by the age of three.

they have already get the infection earlier and develop immunity

So we can't distinguish the type of viruses
(Laboratory diagnosis identifies the virus type)

# Lab Diagnosis

Respiratory and GI infections are indistinguishable from other viruses, so laboratory diagnosis of pneumonia and keratoconjunctivitis is helpful.



We can use an electron microscope (fiber projection) help distinguish the virus from other viruses.

- **Virus Isolation:** Adenovirus may be isolated from most body fluids and secretions; eye swabs, throat swabs, urine, feces, and CSF. It can be grown on: Human embryonic kidney cells, Hep-2 cells, and primary monkey kidney cells

Serotype 40 , 41

Their culture is more difficult, but antigen testing may be more useful.

- **Antigens:** fastidious <u>enteric adenovirus</u> antigens can be detected by direct examination of fecal samples by ELISA or latex agglutination tests or Immunofluorescence

IgG and IgM help diagnose acute infection or determine past exposure and immunity development.

- **PCR**
- **Serology:** Infection of humans with any adenovirus type stimulates a rise in complement-fixing antibodies to adenovirus group antigens shared by all types. A four-fold or greater rise in these antibodies between acute phase and convalescent phase sera indicates recent infection.

Explanation in the next slide

**Serology:** Infection of humans with any adenovirus type stimulates a rise in complement-fixing antibodies to adenovirus group antigens shared by all types

When a specific serotype of adenovirus enters the body, antibodies are formed. These antibodies may not always be serotype-specific but can be group-specific, meaning immunity could extend to other serotypes within the same group with similar structural characteristics. For example, if infected with serotype 40 of group F, you are likely to have immunity to serotype 41 as well.

A four-fold or greater rise in these antibodies between acute phase and convalescent phase sera indicates recent infection.

An increase in IgM or a four-fold rise in IgG from the start to the end of the disease, at least two weeks after onset, indicates an acute infection. If IgG levels are elevated but remain constant ( they do not change over time), it typically indicates that the person was previously infected or vaccinated against the virus, meaning the immune system has developed immunity to the disease.

# Treatment and Prevention

- There is no anti-viral drug therapy
  The virus's capsid is complex, and its serotypes and groups are diverse, making it difficult to create a general target for adenovirus, which is why a treatment has not been developed.
- Treatment is supportive
  Only treats symptoms
- Live adenovirus vaccine for military use only infrequently used
  Its use is limited due to its lack of effectiveness, the presence of many strains, and safety concerns, making it uncommon.
- Swimming pool-associated conjunctivitis can be prevented with adequate levels of chlorine in the water
- Prognosis:
  - Self-limiting disease
  - Recovery is usual
  - Disseminated infection in immunocompromised
    The virus can reach unexpected areas, such as causing meningitis.

# For any feedback, scan the code or click on it.

Corrections from previous versions:

| Versions | Slide # and Place of Error | Before Correction | After Correction |
|---|---|---|---|
| V0 → V1 | Slide 7<br><br>Slide 15 | **Pentose**<br><br>**if infected with serotype 4O of group D** | **Pentons**<br><br>**if infected with serotype 4O of group F** |
| V1 → V2 | | | |

# Additional Resources:

# رسالة من الفريق العلمي:

وَأَن لَّيْسَ لِلإِنسَانِ إِلاَّ مَا سَعَى، وَأَنَّ سَعْيَهُ سَوْفَ يُرَى

قَالَ رَسُولُ اللَّهِ ﷺ: المُؤْمِنُ الْقَوِيُّ خَيْرٌ وأَحَبُّ إِلَى اللَّهِ مِنَ الْمُؤْمِنِ الضَّعِيفِ، وفِي كُلٍّ خَيْرٌ، احْرِصْ عَلَى مَا يَنْفَعُكَ، واسْتَعِنْ بِاللَّهِ، ولَا تَعْجَزْ، وإِنْ أَصَابَكَ شَيْءٌ فَلَا تَقُلْ: لَوْ أَنِّي فَعَلْتُ كَذَا كَانَ كَذَا وكَذَا، ولَكِنْ قُلْ: قَدَّرَ اللَّهُ، ومَا شَاءَ الله فَعَلَ؛ فَإِنَّ لَوْ تَفْتَحُ عَمَلَ الشَّيْطَانِ.