5- Adenoviruses

Mohammad Altamimi, MD, PhD
Faculty of Medicine, Jordan University, 2024

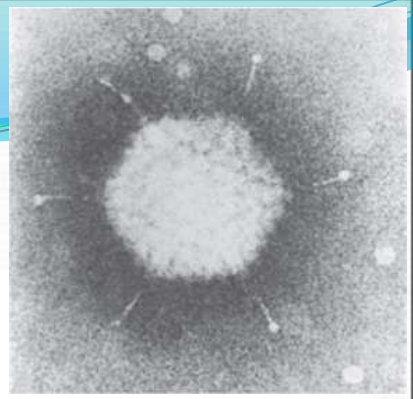
Objectives

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

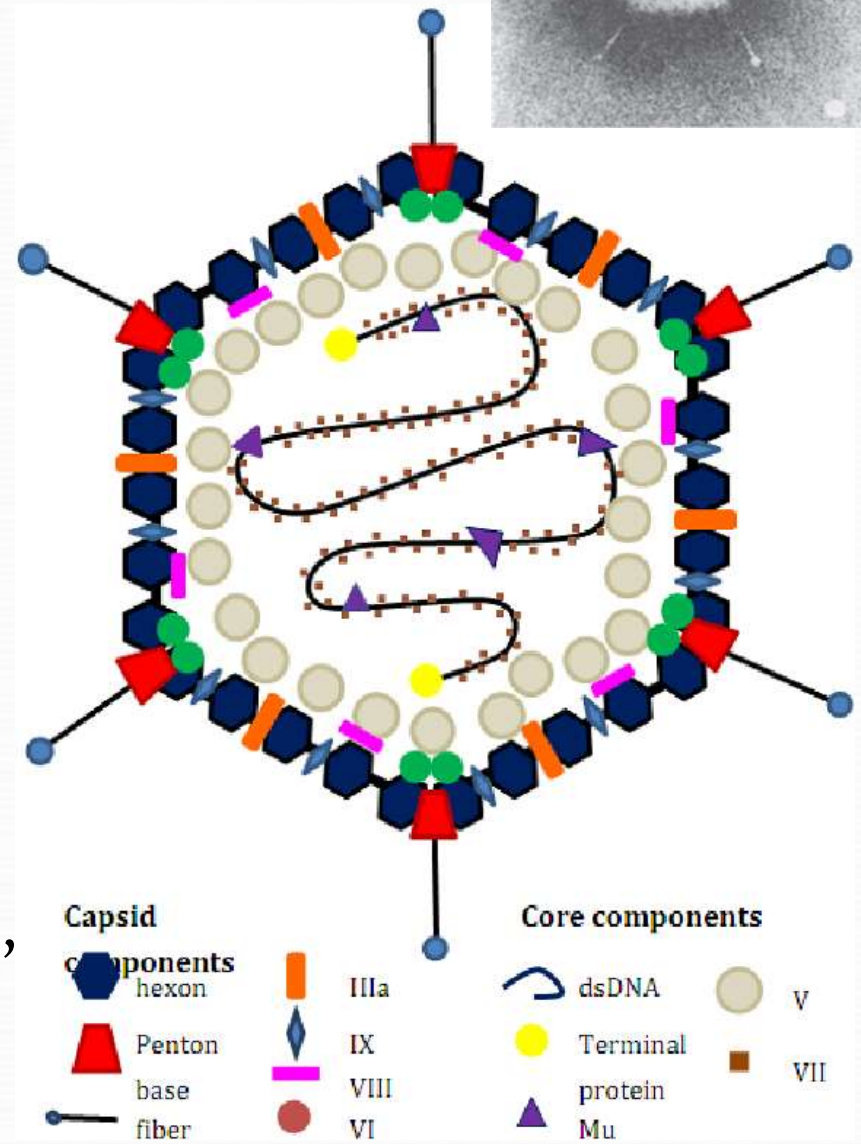
Introduction

- Adenoviruses were first isolated from adenoids surgically removed from children in 1953
- It can replicate and produce disease in epithelial cells (the respiratory, gastrointestinal, and urinary tracts and in the eye)
- 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
- Some adenoviruses strains are oncogenic (to animals) but are not important in human cancer causation

Structure



- Size 70-90 nm in diameter
- 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
- The hexons (240), pentons (12), and fibers (12) at each vertex
- Unenveloped (naked)



- 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
- The penton base carries a toxin-like activity that causes rapid appearance of cytopathic effect
- Fibers are associated with hemagglutinating activity. Because the hemagglutinin is type specific (can be used for viral typing)

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

		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

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
- 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

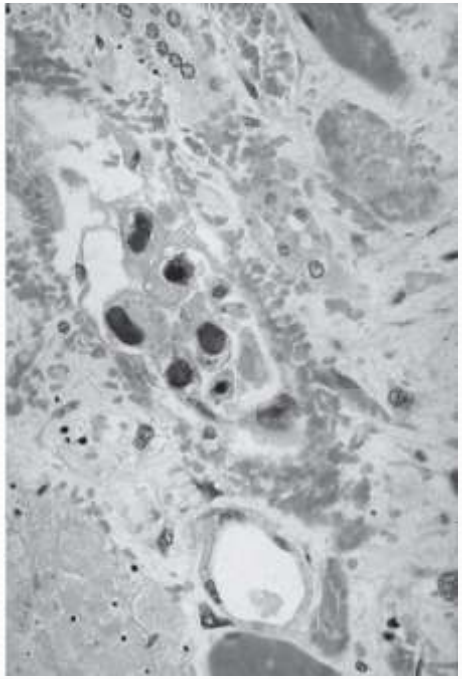


TABLE 32-1 Important Properties of Adenoviruses

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
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:

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.
3. Eye infection:
   - Through contaminated hands.
   - Using contaminated towels.
   - Using contaminated eye drops, ophthalmic instruments.

Clinical Manifestation

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

1- Respiratory Diseases

- Group C, serotypes 1-7
- Infants and children: Characteristic symptoms include fever, malaise, sore throat, hoarseness and cough.
- Pneumonia develops in around 10% of cases and can be fatal.
- 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.

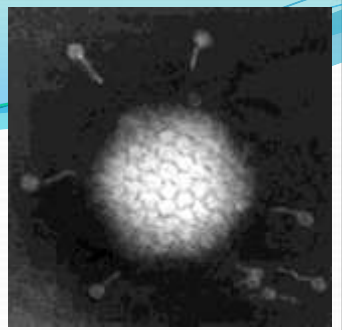
2- Keratoconjunctivitis

- 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.

3- Gastroenteritis

- Group F serotypes 40 and 41
- Associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- Possibly the second most common viral cause of gastroenteritis (7-15% of all endemic cases).
- Similar disease to rotaviruses
- Most people have antibodies against enteric adenoviruses by the age of three.

Lab Diagnosis



- **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
- **Antigens:** fastidious enteric adenovirus antigens can be detected by direct examination of fecal samples by ELISA or latex agglutination tests or Immunofluorescence,
- **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.

Treatment and Prevention

- There is no anti-viral drug therapy
- Treatment is supportive
- Live adenovirus vaccine for military use only infrequently used
- 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