

Adenoviridae family

Introduction

They are medium-sized (70 – 90nm), non-enveloped, icosahedral (252 capsomeres, 240 hexameres, 12 pentameres) viruses with a linear double-stranded DNA. Each pentamere of the virus has a protein fiber with a knob on it. This fiber determines the tropism of that adenovirus and determines what kinds of cells will be affected because this fiber has attachment proteins for different organs in our body systems.

There are many serotypes and groups of adenoviruses with a broad spectrum of clinical manifestations. In the adenovirus family we are concerned with the genus *Mastadenovirus* which cause human infections. This virus has been accidentally isolated from adenoid tissue in 1953. The family of adenoviridae has been divided into six **subgroups** (A-F) according to the *hemagglutination* characteristic feature of the virus. In every subgroup we have different **serotypes** according to the *antigenic determinant* of the virus. The subgroup F (serotypes 40, 41) is called *enteric adenoviruses* that cause gastroenteritis.

Pathogenesis

- According to the cell tropism the virus can infect mucoepithelial cells of the:
 - Respiratory tract (like herpes simplex and varicella zoster)
 - GI tract
 - GU tract
- It enters via epithelium, replicates and spreads to lymphoid tissue
- It can go latent like herpes virus
- Viremia occurs
- We will have secondary involvement of viscera

Replication cycle

The viral DNA enters the nucleus and replicates and we have two stages in the replication cycle of adenoviruses

- **Primary (early) replication cycle:** early transcription and translation of mRNA occurs to form structural and non-structural proteins.
- **Late replication cycle:** late transcription and translation of mRNA occurs to form structural proteins (capsomeres, hexameres, pentameres, and the fiber protein)
- During the replication we have the formation of *inclusion bodies* (like herpes virus) which represent the excess amount of protein that has been formed during the replication cycle. This excess protein does not encapsidate a genome to form a virus particle but it accumulates in the nucleus to form *inclusion bodies*. These inclusion bodies can be stained with special stains and visualized with ordinary microscopes.

Types of infection

- **Lytic infection:** leads to lysis of the cell because it is a non-enveloped virus.
- **Latent infection:** the virus remains in the host cells in the lymphoid tissue (especially subgroup B, C) and it will be reactivated when there is immune-suppression.
- **Oncogenic transformation:** some strains cause cancers in lab animals (e.g. hamsters) and not human-beings

NOTE: Adenovirus can be used as a vector in gene therapy. The desired gene which is deficient in the patient is transferred into the core of the adenovirus. After that they infect the human-being with the virus, so the deficient gene will be easily expressed (*replaced*) after replication of the virus.

Physiochemical properties

- They are stable in the environment
- Relatively resistant to various disinfectants (e.g. Alcohol, detergents, chlorhexidine) because they don't contain lipid envelope
- Stable in GI tract- can withstand low pH, bile acids and proteolytic enzymes
- Incubation period is 2-14 days, varies according to the strain of the virus
- Infectivity of the virus will continue for weeks, even after recovery
- We may have secondary attack due to presence of so many different serotypes. So if we are infected with one serotype, we will be infected with other serotypes.
- We may have endemic, epidemic, sporadic or subclinical infections, highest percentage being *subclinical*
- Epidemics occur in crowded conditions e.g. schools, institutions, military, swimming pools, hospitals

Transmission

- Person-to-person, aerosols, fomites
- Respiratory secretions, tears, fecal/oral
- Under-chlorinated swimming pools, shared towels
- Under-sterilized medical equipment (eye exam equipment, etc.)

Clinical syndromes

Broad spectrum syndrome; it can be respiratory, eye, GIT, GUT infections

- **Respiratory** (serotypes 4, 7): fever, tracheobronchitis, pneumonia
- **Eye:**
 - **Pharyngoconjunctival fever:** headache, fever, malaise → epidemic in summer from contaminated swimming pools
 - **Keratoconjunctivitis:** pink or red eyes, irritation, tearing, foreign body sensation, ocular pain, photophobia, fever, malaise → maybe epidemic, from contaminated swimming pools and ophthalmic solutions
 - **Acute follicular conjunctivitis**
- **Gastroenteritis:** especially in children, by subgroup F (40, 41), maybe co-infection with Rota virus, incubation period is 3-10 days, diarrhea for 10-14 days, fever, intussusception, mesenteric adenitis, appendicitis
- **GU tract:**
 - Acute hemorrhagic cystitis associated with fever, dysuria, and hematuria. More common in males than females.
 - Orchitis, nephritis, cervicitis, urethritis
- **Others:** Myocarditis, pericarditis, meningitis, rash, arthritis

Infections in immunocompromised patients

- Disseminated, severe and often fatal infections
- Due to new infection or reactivation of latent virus
- Prolonged infections with prolonged viremia and viral shedding
- Necrotizing pneumonia, hepatitis, rash, DIC, CNS involvement

Diagnosis: depends on the clinical picture

- **Respiratory infection:** nasopharyngeal swab
- **Eye infection:** conjunctival swab
- **GIT infection:** stool specimen
 - The specimen should be transported by a special transport medium in a test tube to keep the virus viable until it reaches the lab for processing
 - The specimen can be cultured in HeLa cells *tissue-culture*, human embryonic kidney cells *tissue-culture*, and shell vial *tissue-culture*
 - We can stain these cultures with **DFA** (Direct Fluorescent Antibody technique)
- **PCR**
- **Immune Electron Microscopy:** especially for stool specimens
- **ELISA:** for *antibody* detection in serum, or *antigen* detection in the specimen

Prevention

- **Hygiene** (good hand washing, contact precaution, water chlorination, sterilization of ophthalmic equipment)
- **Vaccine:** previously there was a vaccine but now it is halted due to side effects such as intussusception and reactivation because it was a live attenuated vaccine