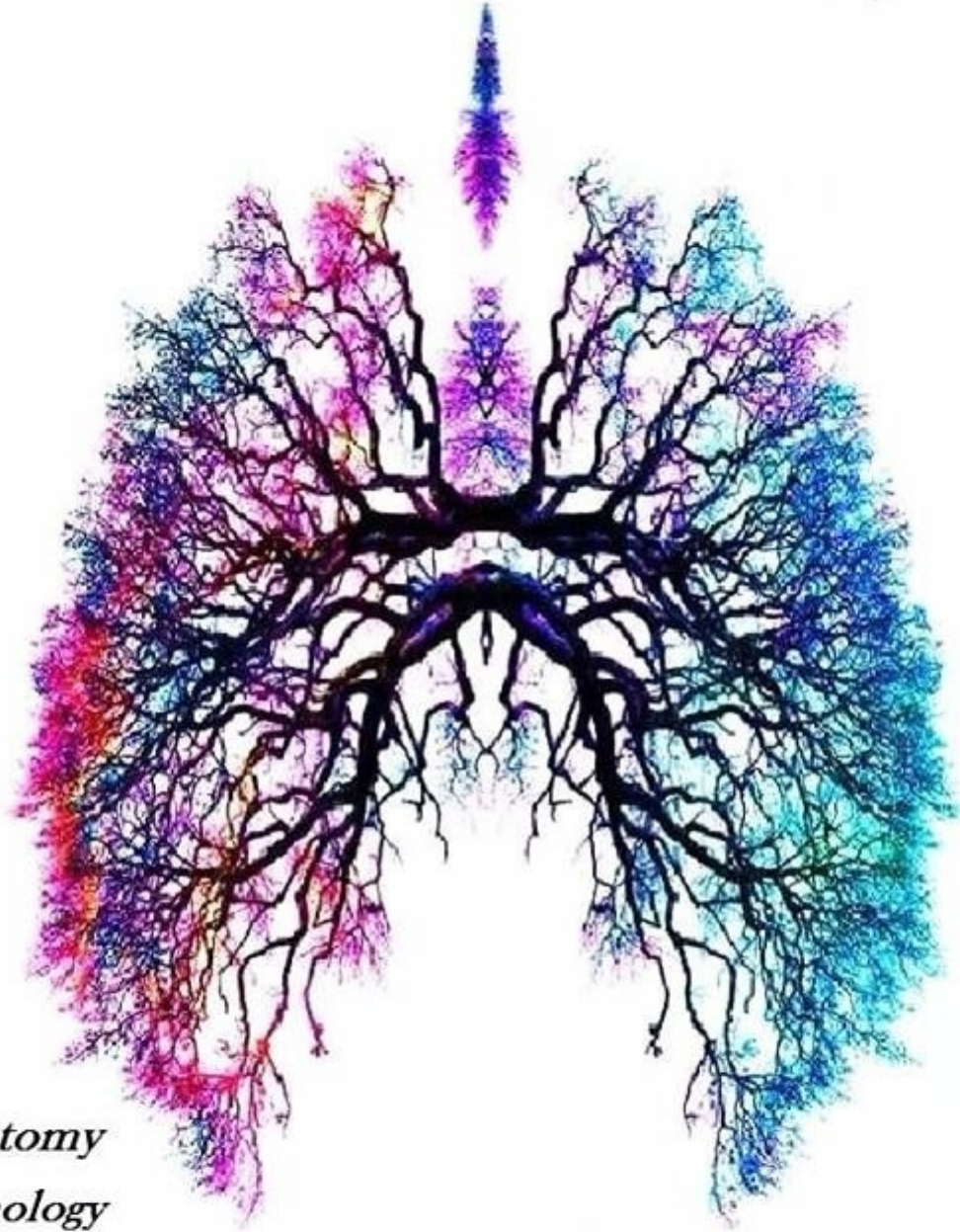


RESPIRATORY SYSTEM

Cover by: *Aseel Khatib*



- Anatomy*
- Pathology*
- Physiology*
- Pharmacology*
- Microbiology*
- PBL*

Dr Name: Dr. Ashraf Khasawneh
Lecture # 2 (VIROLOGY)

Sheet

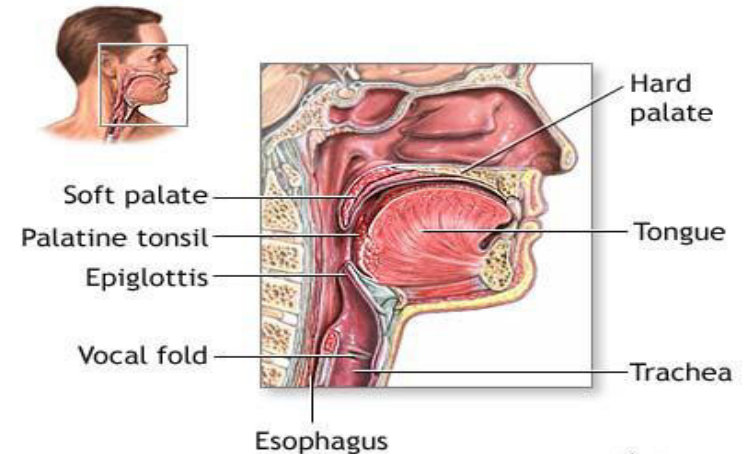
Slide

Other

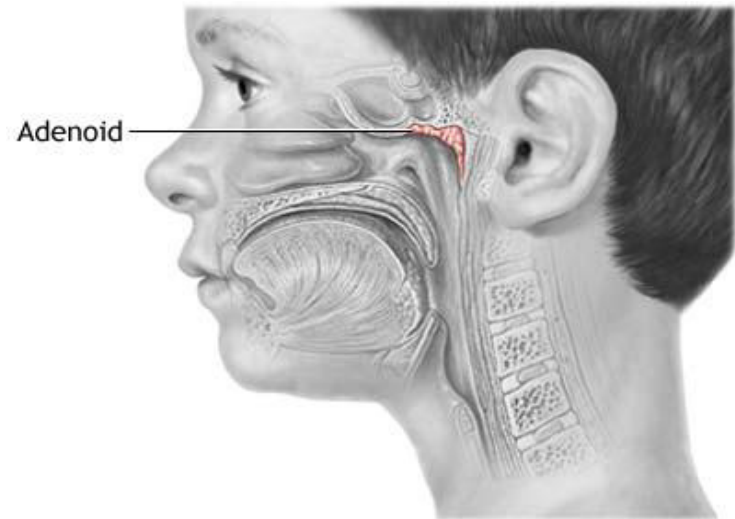
PHARYNGITIS

- What is it?

- Inflammation of the Pharynx secondary to an infectious agent
- Most common infectious agents are Group A Streptococcus and various viral agents
- Often co-exists with tonsillitis



ADAM.



ADAM.

Etiology

- Rhinovirus
- Coronavirus
- Adenovirus
- CMV
- EBV
- HSV
- Enterovirus
- HIV
- Strep.A
- Mycoplasma
- Strep.G
- Strep.C
- Corynebacterium diphtheriae
- Toxoplasmosis
- Gonorrhoea
- Tularemia

Acute Pharyngitis

- Etiology
 - Viral >90%
 - Rhinovirus – common cold
 - Coronavirus – common cold
 - Adenovirus – pharyngoconjunctival fever; acute respiratory illness
 - Parainfluenza virus – common cold; croup
 - Coxsackievirus - herpangina
 - EBV – infectious mononucleosis
 - HIV

Acute Pharyngitis

- Etiology
 - Bacterial
 - Group A beta-hemolytic streptococci (*S. pyogenes*)*
 - most common bacterial cause of pharyngitis
 - accounts for 15-30% of cases in children and 5-10% in adults.
 - *Mycoplasma pneumoniae*
 - *Arcanobacterium haemolyticum*
 - *Neisseria gonorrhoea*
 - *Chlamydia pneumoniae*

PHARYNGITIS

- HISTORY

- Classic symptoms → *Fever, throat pain, dysphagia*

- *VIRAL* → Most likely concurrent URI symptoms of rhinorrhea, cough, hoarseness, conjunctivitis & ulcerative lesions

- *STREP* → Look for associated headache, and/or abdominal pain

- *Fever and throat pain are usually acute in onset*

PHARYNGITIS

- Physical Exam

- *VIRAL*

- EBV – White exudate covering erythematous pharynx and tonsils, cervical adenopathy,

- *Subacute/chronic symptoms (fatigue/myalgias)*

- *transmitted via infected saliva*

- Adenovirus/Coxsackie – vesicles/ulcerative lesions present on pharynx or posterior soft palate

- Also look for conjunctivitis

Epidemiology of Streptococcal Pharyngitis

- Spread by contact with respiratory secretions
- Peaks in winter and spring
- School age child (5-15 y)
- Communicability highest during acute infection
- Patient no longer contagious after 24 hours of antibiotics
- If hospitalized, droplet precautions needed until no longer contagious

PHARYNGITIS

- Physical Exam

- *Bacterial*

- GAS – look for whitish exudate covering pharynx and tonsils

- tender anterior cervical adenopathy

- palatal/uvular petechiae

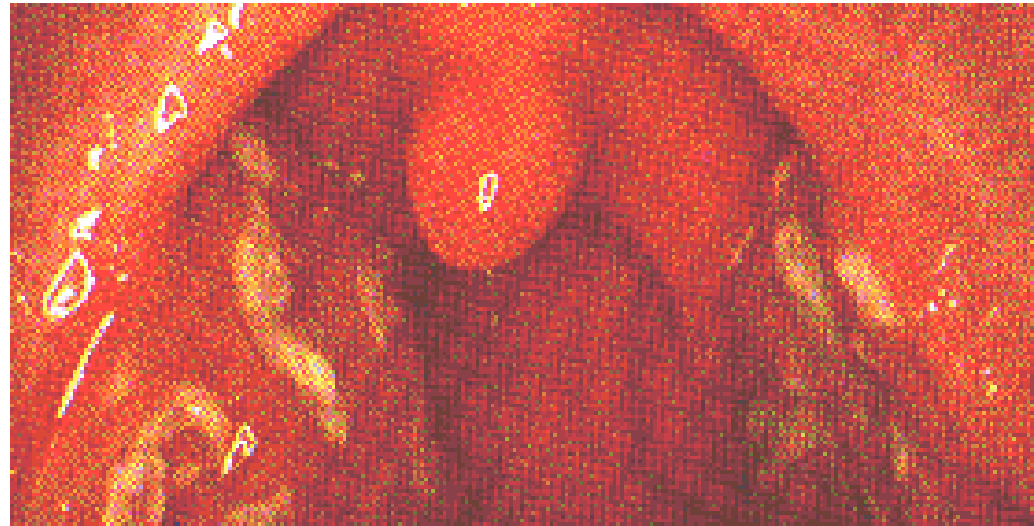
- scarlatiniform rash covering torso and upper arms

- Spread via respiratory particle droplets – NO school attendance until 24 hours after initiation of appropriate antibiotic therapy

- Absence of viral symptoms (rhinorrhea, cough, hoarseness)

Differential diagnosis of pharyngitis

- Pharyngeal exudates:
 - *S. pyogenes*
 - *C. diphtheriae*
 - EBV
 - Adenovirus
 - Oral Candidiasis



Differential diagnosis of pharyngitis

- Skin rash:
 - *S. pyogenes*
 - *HIV*
 - *EBV*



Differential diagnosis of pharyngitis

- Conjunctivitis:
 - *Adenovirus*



Nonsuppurative Complications of Group A Streptococcus

- Acute rheumatic fever
 - follows only streptococcal pharyngitis (not group A strep skin infections)
- Acute glomerulonephritis
 - May follow pharyngitis or skin infection (pyoderma)
 - Nephritogenic strains

Infectious Mononucleosis



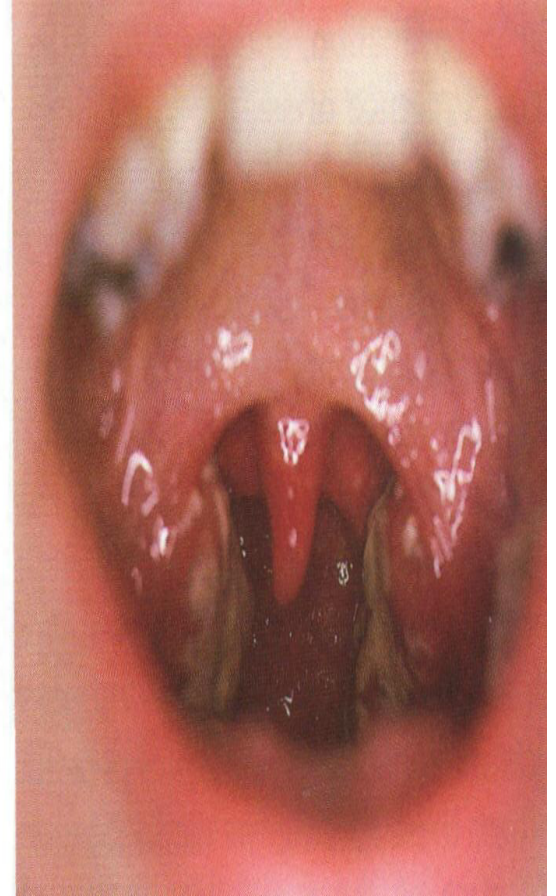
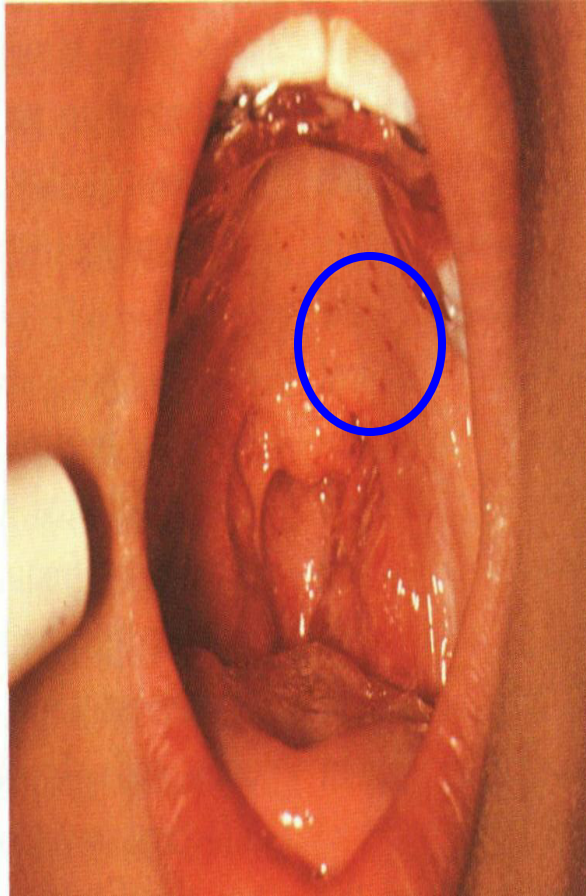
Herpangina



PHARYNGITIS



PHARYNGITIS



pharyngitis



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Scarlatiniform Rash



Clinical manifestation (Strep.)

- Rapid onset
- Headache
- GI Symptoms
- Sore throat
- Erythma
- Exudates
- Palatine petechiae
- Enlarged tonsils
- Anterior cervical adenopathy & Tender
- Red & swollen uvula

Clinical manifestation (Viral)

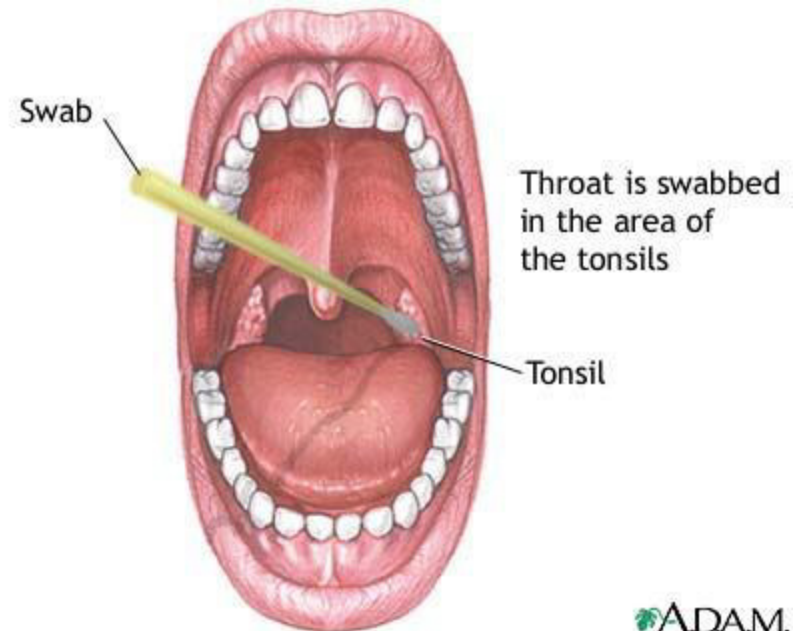
- Gradual onset
- Rhinorrhea
- Cough
- Diarrhea
- Fever

Clinical manifestation

- Vesiculation & Ulceration
Gingivostomatitis → **HSV**
Coxsackievirus
- Conjunctivitis → Adenovirus
- Gray-white fibrinous pseudomembrane
With marked cervical lymphadenopathy → Diphtheria
- Macular rash → Scarlet fever
- Hepatosplenomegally & Rash
& Fatigue & Cervical lymphadenitis → EBV

Diagnosis

- Strep:
 - Throat culture(Gold standard)
 - Rapid Strep. Antigen kits
- Infectious Mono.:
 - CBC(Atypical lymphocytes)
 - Spot test (Positive slide agglutination)
- Mycoplasma:
 - Cold agglutination test



Treatment

(Antibiotic ,Acetaminophen ,Warm salt gargling)

- Strep: *Penicillin* ,Erythromycin , Azithromycin
- 1-Prevention of ARF if treatment started within 9 days of illness
- 2-Reduce symptoms
- 3-Prevent local suppurative complications

BUT

Does not prevent the development of the post streptococcal sequel of acute glomerulonephritis

PHARYNGITIS

- LAB AIDS

- Rapid strep antigen → detects GAS antigen

- Tonsillar swab → 3-5 minutes to perform

- 95% specificity, 90-93% sensitivity

- GAS Throat culture → “gold standard”

- >95% sensitivity

- Mono Spot → serologic test for EBV heterophile Ab

- EBV Ab titers → detect serum levels of EBV IgM/IgG

PHARYNGITIS

- Treatment

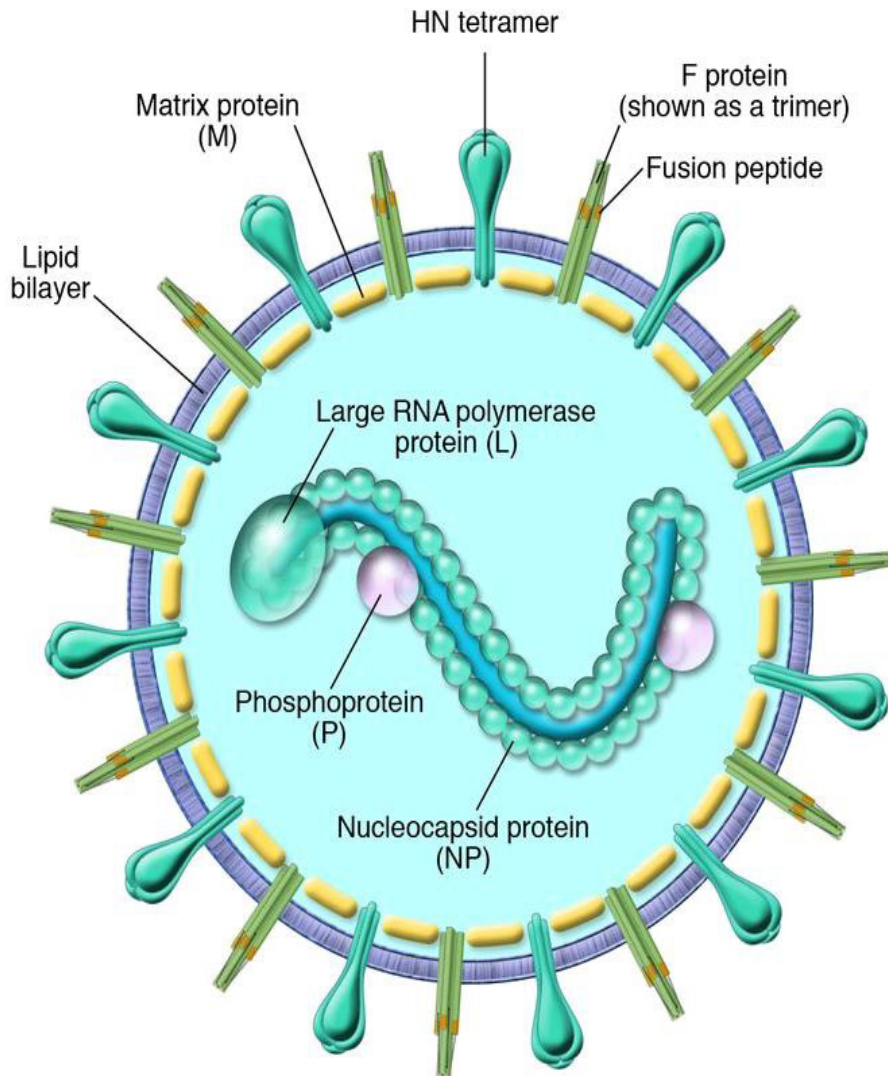
- *VIRAL* – Supportive care only – Analgesics, Antipyretics, Fluids
- No strong evidence supporting use of oral or intramuscular corticosteroids for pain relief → few studies show transient relief within first 12–24 hrs after administration
 - EBV – infectious mononucleosis
 - activity restrictions – mortality in these pts most commonly associated with abdominal trauma and splenic rupture

Parainfluenza Virus



- ssRNA virus
- enveloped, pleomorphic morphology
- 4 serotypes: 1, 2, 3, 4 and 2 subtypes 4a and 4b
- No common group antigen
- Closely related to Mumps virus

Morphology - Parainfluenza



- HPIVs are negative-sense, single-stranded RNA viruses
- They possess **fusion** and **hemagglutinin-neuraminidase** glycoprotein "spikes" on their surface.
- There are four serotypes types of HPIV (1 through 4).

Viral adoption and pathogenesis.

- 150-300 nm in size.
- Envelope Two Glycoprotein
- HN protein attachment to cell surfaces and entry
- F protein causes cell to cell fusion.
- M protein plays a role in assembly
- Grows in Human cell cultures Hela and Hep-2.

Mechanism of pathogenesis in Paramyxoviridae

- HPIV infection in the respiratory tract leads to secretion of high levels of inflammatory cytokines such as interferon (IFN)-alpha, interleukin (IL)-2, IL-6, and tumor necrosis factor (TNF)-alpha.
- The peak duration of secretion is 7-10 days after initial exposure.
- Increasing levels of certain chemokines such as RANTES (regulated upon activation, normal T-cell expressed and secreted), macrophage inflammatory protein (MIP)-K are detected in the nasal secretion of paediatric patients

Para Influenza Viruses types

- Four Types are present.
- Type 1 Acute croup, pharyngitis and tracheobronchitis. Fall months
- Type 2 Acute Laryngo tracheo bronchitis. Fall months
- Type 3 Lower Respiratory infection in children (Bronchitis, pneumonia and croup)
- Type 4 Upper Respiratory infection. Least common

Clinical Manifestations

- Croup (laryngotracheobronchitis) - most common manifestation of parainfluenza virus infection. However other viruses may induce croup e.g. influenza and RSV.
- Other conditions that may be caused by parainfluenza viruses include Bronchiolitis, Pneumonia, Flu-like tracheobronchitis, and Coryza-like illnesses.

Laboratory Diagnosis

- **Detection of Antigen** - a rapid diagnosis can be made by the detection of parainfluenza antigen from nasopharyngeal aspirates and throat washings.
- **Virus Isolation** - virus may be readily isolated from nasopharyngeal aspirates and throat swabs. Monkey kidney cell cultures
- **Serology** - a retrospective diagnosis may be made by serology. EIA and IF.
- PCR

Management

- No specific antiviral chemotherapy available.
- Severe cases of croup should be admitted to hospital and placed in oxygen tents.
- No vaccine is available.

Respiratory Syncytial Virus (RSV)

- ssRNA enveloped virus.
- belong to the genus Pneumovirus of the Paramyxovirus family.
- Considerable strain variation exists, may be classified into subgroups A and B by monoclonal sera.
- Both subgroups circulate in the community at any one time.
- Causes a sizable epidemic each year.
- Genome codes for 10 m RNAs, each codes for a specific protein.

RSV: Epidemiology

- Present world wide, yearly epidemics.
- Appears in Nov. or Dec. persists till Apr. or May.
- A strain predominant , the two strains circulate.
- Strain variation does not significantly affect the clinical severity.
- Peak incidence 2-5 months.
- In the 1st two years of life : one or more RSV infections
- More severe : Boys , lower socioeconomic classes.
- Reinfection throughout life is common.
- Milder than primary infection.

RSV : Pathogenesis & Immunity

- Incubation period :2-8 days.
- Ocular, nasal contact with infected secretions.
- Upper airway : cough & rhinorrhea.
- 50% primary infection spreads to lower tract.
- Bronchiolitis: lymphocyte infiltrate & epithelial proliferation.
- Obstruction: mucus & epithelium .
- Hyperinflation.
- Interstitial infiltrates: Pneumonia.

RSV: Immunity

- Immune response : not well understood.
- Different parts of immune system are involved.
- Antibodies:
 - Higher levels of maternal Abs , lower infection rates.
 - Prophylactic Abs reduce but do not eliminate severe disease.
 - No level of serum Abs provides protection.

Clinical Manifestations

- Most common cause of severe lower respiratory tract disease in infants, responsible for 50-90% of Bronchiolitis and 5-40% of Bronchopneumonia
- Other manifestations include croup (10% of all cases).
- In older children and adults, the symptoms are much milder: it may cause a coryza-like illness or bronchitis.

Infants at Risk of Severe Infection

1. **Infants with congenital heart disease** - infants who were hospitalized within the first few days of life with congenital disease are particularly at risk.
2. **Infants with underlying pulmonary disease** - infants with underlying pulmonary disease, especially bronchopulmonary dysplasia, are at risk of developing prolonged infection with RSV.
3. **Immunocompromized infants** - children who are immunosuppressed or have a congenital immunodeficiency disease may develop lower respiratory tract disease at any age.

Mortality rate 0.5-1%. In the above group might reach 15%

Diagnosis:

- Young Children:
 - Season
 - Typical history: cough, wheezing and respiratory distress +/- fever
 - Physical examination
 - Clinical findings: hyperexpansion, hypoxemia, hypercapnia
- Children & Adults:
 - Signs & Symptoms are less specific.
 - Chest x-ray nonspecific
- Chest X-rays:
 - Hyperinflation
 - Increased interstitial markings

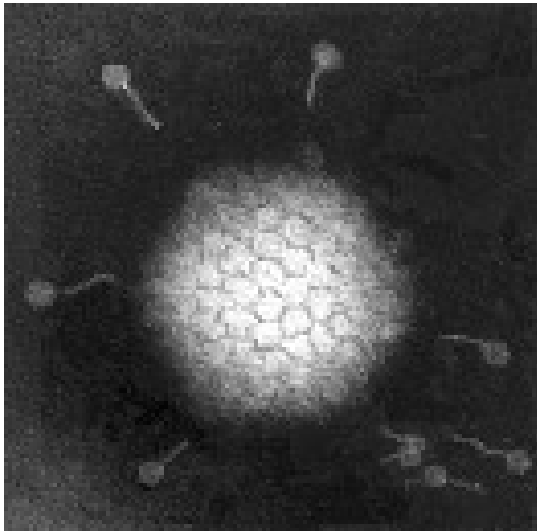
RSV: Diagnosis

- Infants:
 - Nasal wash
- Children & adults:
 - Swab from nasal turbinates+pharynx
 - or bronchoalveolar lavage are the most likely to be positive Specimens obtained by endotracheal tube
 - Specimens for culture should be placed in viral culture media & kept cold during transport.
 - RSV grows in multiple cell lines (Hep-2 & HeLa)
 - Typical pattern: syncytial & giant cell , 3-7
 - Fluorescein-labeled Ab are applied to cultures.

Treatment and Prevention

- Adequate oxygenation, ventilatory support and close observation for bacterial superinfection.
- Aerosolised ribavirin can be used for infants with severe infection, and for those at risk of severe disease.
- There is no vaccine available.
- RSV immunoglobulin (against F protein) can be used to protect infants at risk of severe RSV disease. Expensive.

Adenovirus



(Linda Stannard, University of Cape Town, S.A.)

- Virion:
 - Icosahedral, non-enveloped, 70-90 nm in diameter, 252 capsomeres; fibers project from each other
 - 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
 - Replication: Nucleus
 - Virus classification: Group I: ds DNA; Family: Adenoviridae; Genus: Mastadenovirus; Species: Human adenovirus (H Ad)
- At least 54 serotypes are known
- classified into 7 subgenera: A to G

Adenovirus

- Outstanding characteristics
 - virion has unique **"spike" or fiber associated with each penton base** of the capsid that aids in attachment to the host cell via the coxsackie-adenovirus receptor on the surface of the host cell
 - Adenovirus has tropism for **cells of epithelial origin**
 - Replicative cycle is sharply divided into EARLY & LATE events
 - Different types/serotypes are associated with different conditions:
 - respiratory disease (mainly species HAdV-B and C)
 - conjunctivitis (HAdV-B and D)
 - gastroenteritis (HAdV-A & F serotypes 40 and 41)
 - Severe respiratory + PCF (HAdV-E)

Clinical Syndromes

1. Pharyngitis 1, 2, 3, 5, 7
2. Pharyngoconjunctival fever 3, 7
3. Acute respiratory disease of recruits 4, 7, 14, 21
4. Pneumonia 1, 2, 3, 7
5. Follicular conjunctivitis 3, 4, 11
6. Epidemic keratoconjunctivitis 8, 19, 37
7. Pertussis-like syndrome 5
8. Acute haemorrhagic cystitis 11, 21
9. Acute infantile gastroenteritis 40, 41
10. Intussusception 1, 2, 5
11. Severe disease in AIDS and other immunocompromized patients 5, 34, 35
12. Meningitis 3, 7

Laboratory Diagnosis

- In addition to a complete medical history and physical examination, diagnostic tests for adenoviruses may include:
 - blood work
 - culture of respiratory secretions by nasal swab
 - stool culture
 - chest x-ray
- Antigen detection, PCR, virus isolation, and serology can be used to identify adenovirus infections.

Prevention & Management

- There is **no specific antiviral therapy**; **cidofovir** might be effective.
- There are currently **no vaccines** available to protect against the adenovirus.
- A vaccine is available against Adult Respiratory Distress Syndrome. It consists of live adenovirus 4, 7, and 21 in enterically coated capsules. It is given to new recruits into various arm forces around the world.
- **Good hygiene**
 - Handwashing: still the best way to avoid picking up the adenovirus from an infected person.
 - wear **special isolation apparel**, such as gowns and gloves
 - **Heat and bleach** will kill adenoviruses on objects.
 - Adenoviruses are unusually stable to chemical or physical agents and adverse pH conditions, allowing for prolonged survival outside of the body.