



UNIwersytet Medyczny
IM. PIASTÓW ŚLĄSKICH WE WROCLAWIU

Subject: Faculty Lectures of Virology

Topic: Viruses of Respiratory Tract Infections

Academic Year 2024/2025

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Faculty: Medicine
Field of study: Virology
Level of study (uniform MA):
Form of study (full time):
Year of study: III

Academic title/professional title: professor
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Position of person conducting classes: teacher
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Viral respiratory tract infections

Two-thirds of patients with viral infection are treated with antibiotics

Viral RTI

URTI and LRTI

Symptoms: runny or stuffy nose,
cough,
low-grade fever, sore throat,
headaches

In Children may last longer than in
adults (up to 14 days) and occur more
frequently

Patients present sooner to their GPs

Bacterial RTI

URTI and LRTI (sinusitis, otitis media,
pneumonia)

Symptoms: rather stuffy nose, cough,
higher fever, sore throat, headaches

Symptoms may persist longer than in
viral

The average duration of illness is similar

The differences are not significant enough to allow doctors to differentiate
between these infections

ca. 80% of
RTIs are viral

Seasonality

Short incubation
period

Pose a risk of bacterial superinfections
and co-infections

Diagnostic markers

- **Complement Receptors and Clinical Infection Score (CIS)**

measuring the expression of complement receptors, particularly CR1 (CD35), on neutrophils (high sensitivity (98%) and specificity (97%) in distinguishing between bacterial and viral infections

- **C-Reactive Protein (CRP) and Estimated CRP Velocity (eCRPv)**

C-reactive protein (CRP) levels are commonly used to differentiate between bacterial and viral infections

Bacterial infections typically present with higher CRP levels compared to viral infections.

The estimated CRP velocity (eCRPv), which considers the CRP level relative to the time from symptom onset, further enhances diagnostic accuracy. Bacterial infections show significantly higher eCRPv values compared to viral infections, making this a useful tool for rapid differentiation, especially in cases with intermediate CRP levels

- **Host-Protein Based Assay: ImmunoXpert** assay combines three proteins (TNF-related apoptosis-inducing ligand (TRAIL), interferon γ -induced protein-10 (IP-10), and CRP) = high diagnostic accuracy in distinguishing bacterial from viral infections in children

Machine learning models utilizing routine blood test values, CRP levels, biological sex, and age have shown promise in differentiating between bacterial and viral infections (high accuracy (82.2%)), can significantly improve diagnostic decision-making, particularly in cases where CRP alone is insufficient

LRTI (acute bronchitis, bronchiolitis, tracheitis, pneumonia)

Influenza (T,P)
Parainfluenza
Coronavirus
COVID-19 (P)
Adenoviruses
RSV (P)
Rhinoviruses
Hantaviruses

URTI (common cold, laryngitis, tonsillitis, acute rhinitis, and rhinosinusitis, acute otitis media)

Rhinoviruses
Coronaviruses
Influenza (T,P)
Parainfluenza
Adenoviruses
Enteroviruses
(EV-D68)

PNEUMONIA

Primary
Influenza
COVID-19
RSV
Adenoviruses
Parainfluenza

Secondary
Measles
Herpes viruses
(VZV, CMV,
EBV, HSV)

Red=RNA; **green**=DNA

T=specific treatment
available
P=specific prophylaxis
available (vaccines)



Spread of viruses

Transmission

Direct

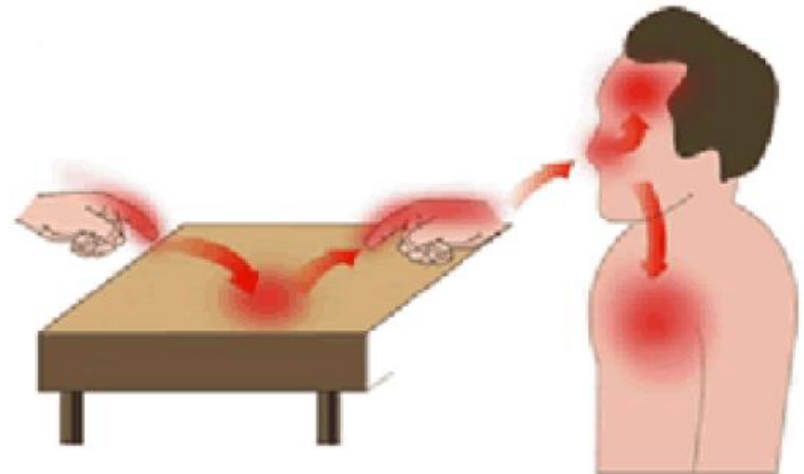
infectious
droplet nuclei
aerosols

5 μm

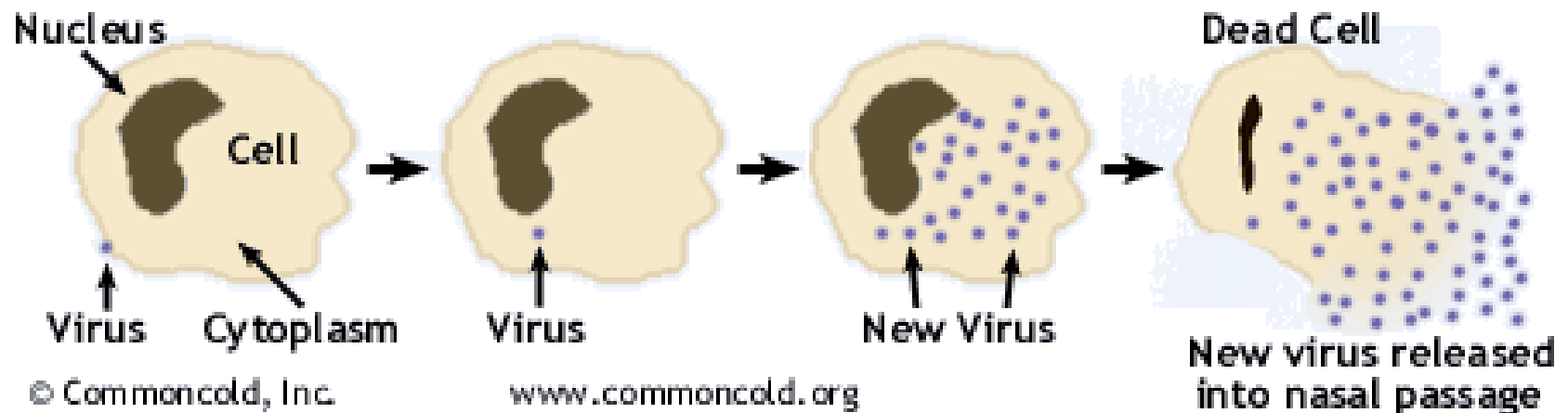
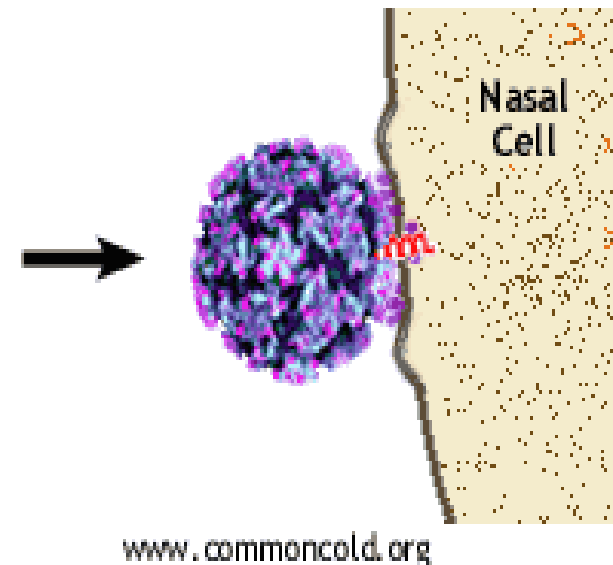
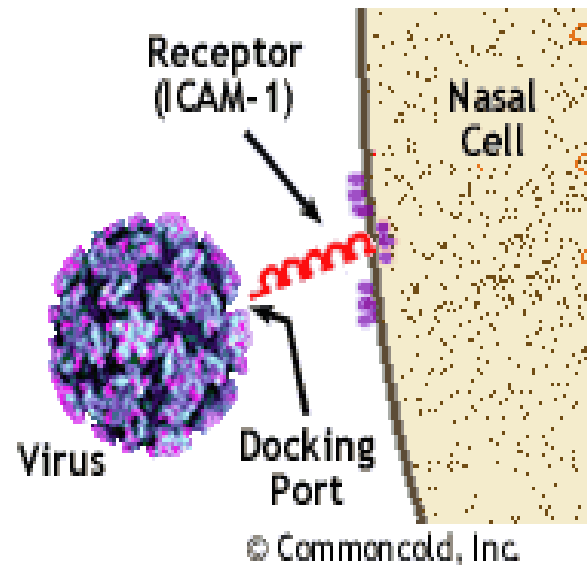
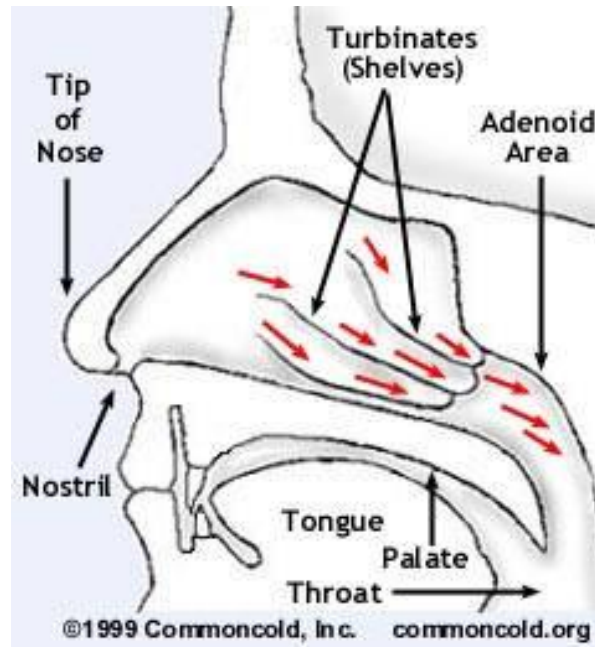
Size of droplets

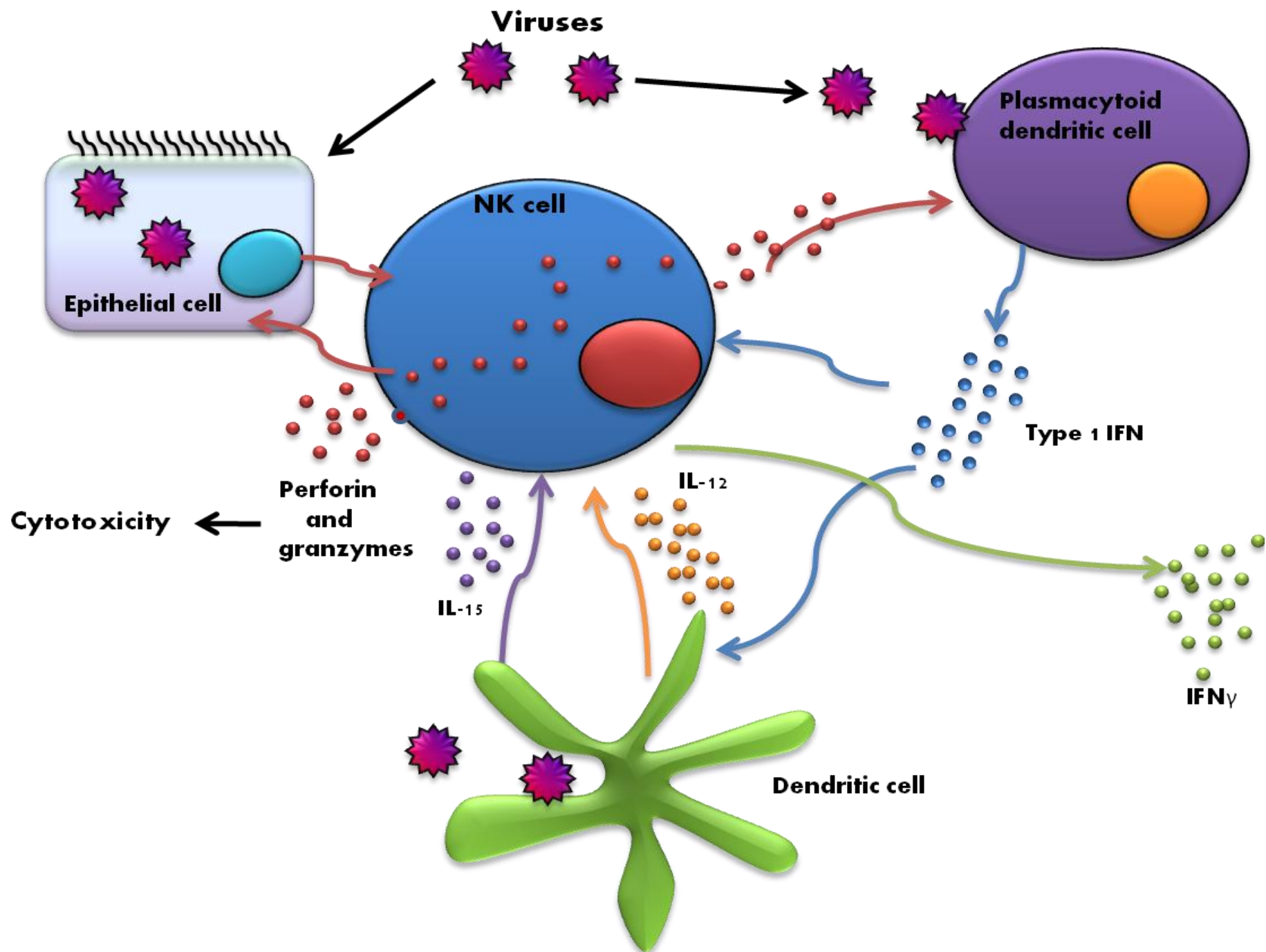
Indirect

Transmission



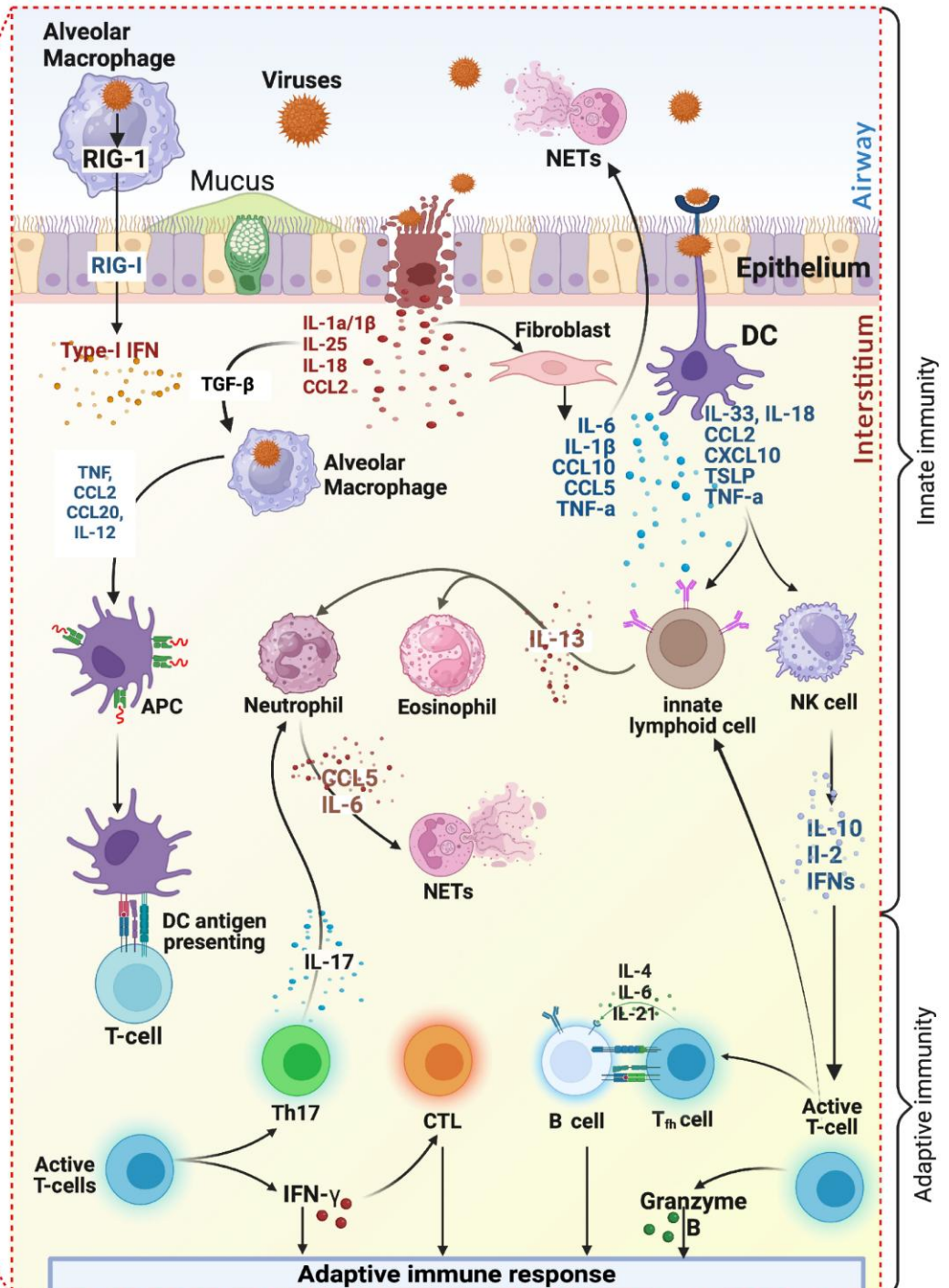
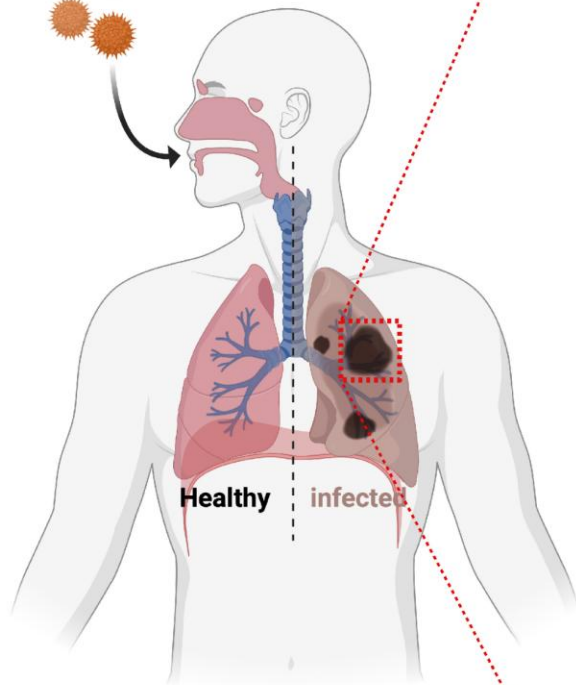
Common cold virus infection

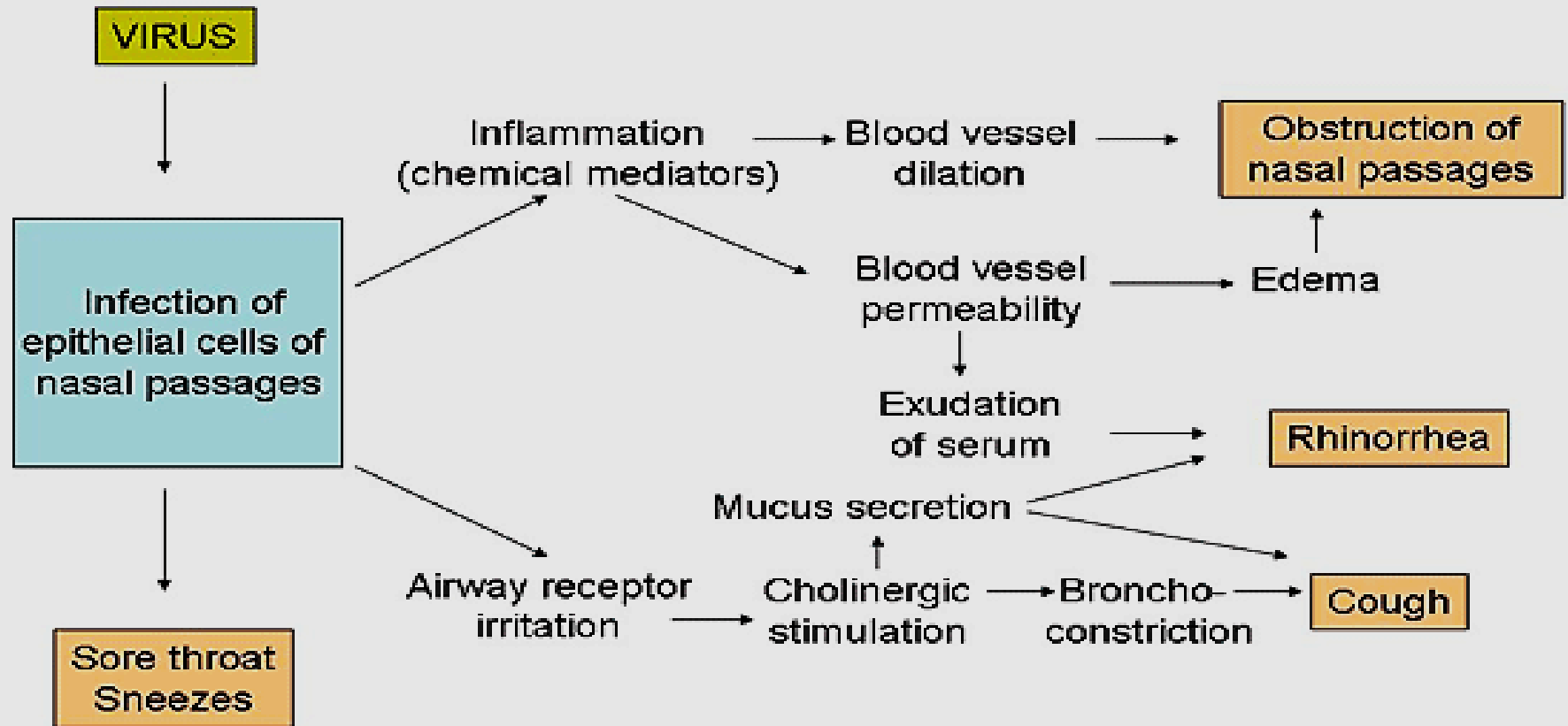




Et tu Brute contra me?!

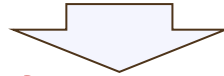
Respiratory virus infection





Pathomechanism of upper and lower respiratory tract infections

Virus infection



Inflammation

Decreased ciliary activity = Increased amount of mucus production, destruction of epithelial cells, swollen mucous membrane



Nasopharyngeal flora



Bacterial co-infections or superinfections: otitis media, sinusitis, bronchitis, pneumonia

Viruses of respiratory tract infections

Syndrome	Common viruses	Less common viruses
Coryza	Rhinoviruses, Coronaviruses	Influenza, Parainfluenza Enteroviruses, Adenoviruses
Influenza	Influenza viruses	Parainfluenza, Adenoviruses
Croup	Parainfluenza viruses	Influenza virus, RSV, Adenoviruses
Bronchiolitis	RSV	Influenza, Parainfluenza, Adenoviruses
Bronchopneumonia	Influenza virus RSV, Adenoviruses	Parainfluenza viruses Measles, VZV, CMV

Common cold viruses

- Common colds account for one-third to one-half of all acute respiratory infections in humans
- **Rhinoviruses** 30-50% and **Coronaviruses** 10-30% cases
- The remaining cases - **Adenoviruses, Enteroviruses, RSV, Influenza, and Parainfluenza viruses**
- Clinical symptoms identical independently of virus

Rhinovirus **RNA** virus without an envelope, > 200 serotypes; stable out of the body for 2 h

No specific treatment, no vaccine)

Reservoir: diseased humans



DIRECT, indirect routes
of transmission

URTI epithelium (nasal ICAM-1
molecules = viral receptor)

Inflammation
(1-day incubation)

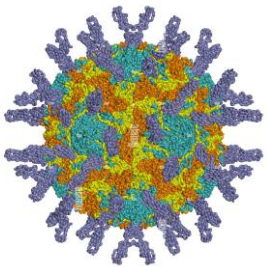
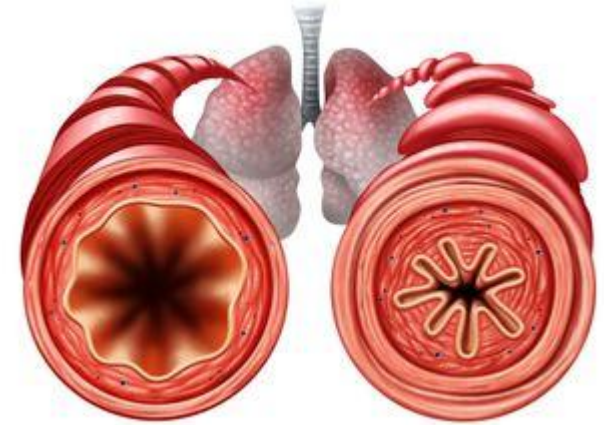
Symptoms (rhinorrhoea, nasal congestion, sneezing,
cough, slight fever, and systemic reaction)

Recovery
(4-7 days)

Complications (<1%): sinusitis,
otitis media, bronchiolitis,
bronchopneumonia =
co-infection with bacteria

BUT
Elderly - longer duration; >60% LRTI symptoms
Asthma exacerbation

Pleconaril - treatment asthmatic persons with RV
infection



Parainfluenza virus **RNA** virus with an envelope, 5 serotypes

stable out of the body for 6 h

No vaccine, treatment (supportive)

Reservoir: diseased humans

Ca. 80% of children seropositive against HP1, 2, 3 by age 5

DIRECT, RESPIRATORY, and indirect routes of transmission

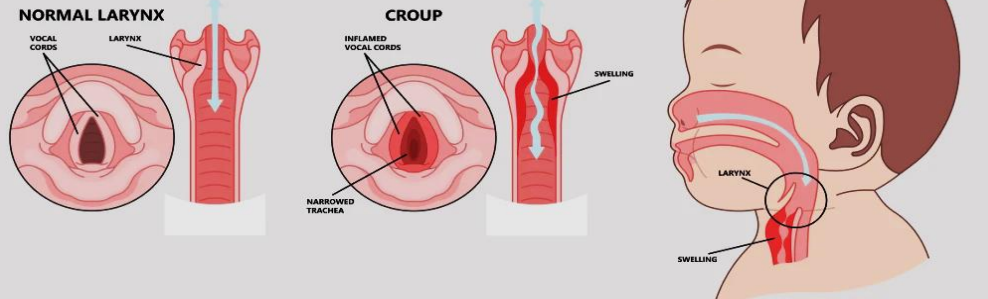
Seasonal infection with rates that increase in the fall, and **peak in winter** **No lasting immunity**

Inflammation
(2-6 days incubation)

Symptoms (rhinorrhoea, nasal congestion, sneezing, cough, slight fever, ear aches) - **recovery**

Diseases: **croup** (laryngotracheobronchitis: barking cough, hoarseness, stridor, wheezing), bronchitis, bronchiolitis, pneumonia

Croup



BUT:

In adults: URTI and bronchitis are the most common

In older adults and persons with weakened immune system - pneumonia

In immunosuppressed - persistent infection, severe LRTI, and often death

Respiratory syncytial virus (RSV) RNA virus with an envelope, A & B group
stable out of the body for 3-30 h. No specific treatment, no vaccine, treatment (symptomatic)

Reservoir: diseased humans

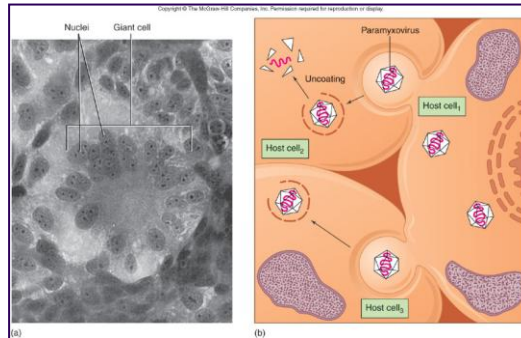
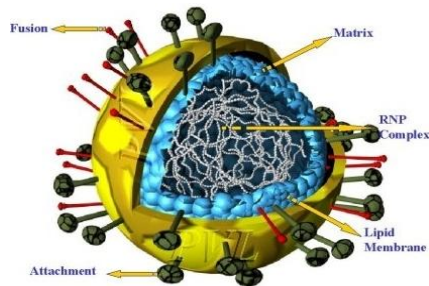
DIRECT, RESPIRATORY, and indirect routes of transmission

Inflammation
(4-7 days incubation)

Each year, 3.6 mln RSV-associated hospitalizations and 100,000 RSV-attributable deaths in children under 5 years worldwide

Most common cause of severe LRTI in infants:
50-90% of bronchiolitis
5-40% of bronchopneumonia
croup 10% of all cases
Common cold is the most common manifestation of the infection in children and adults

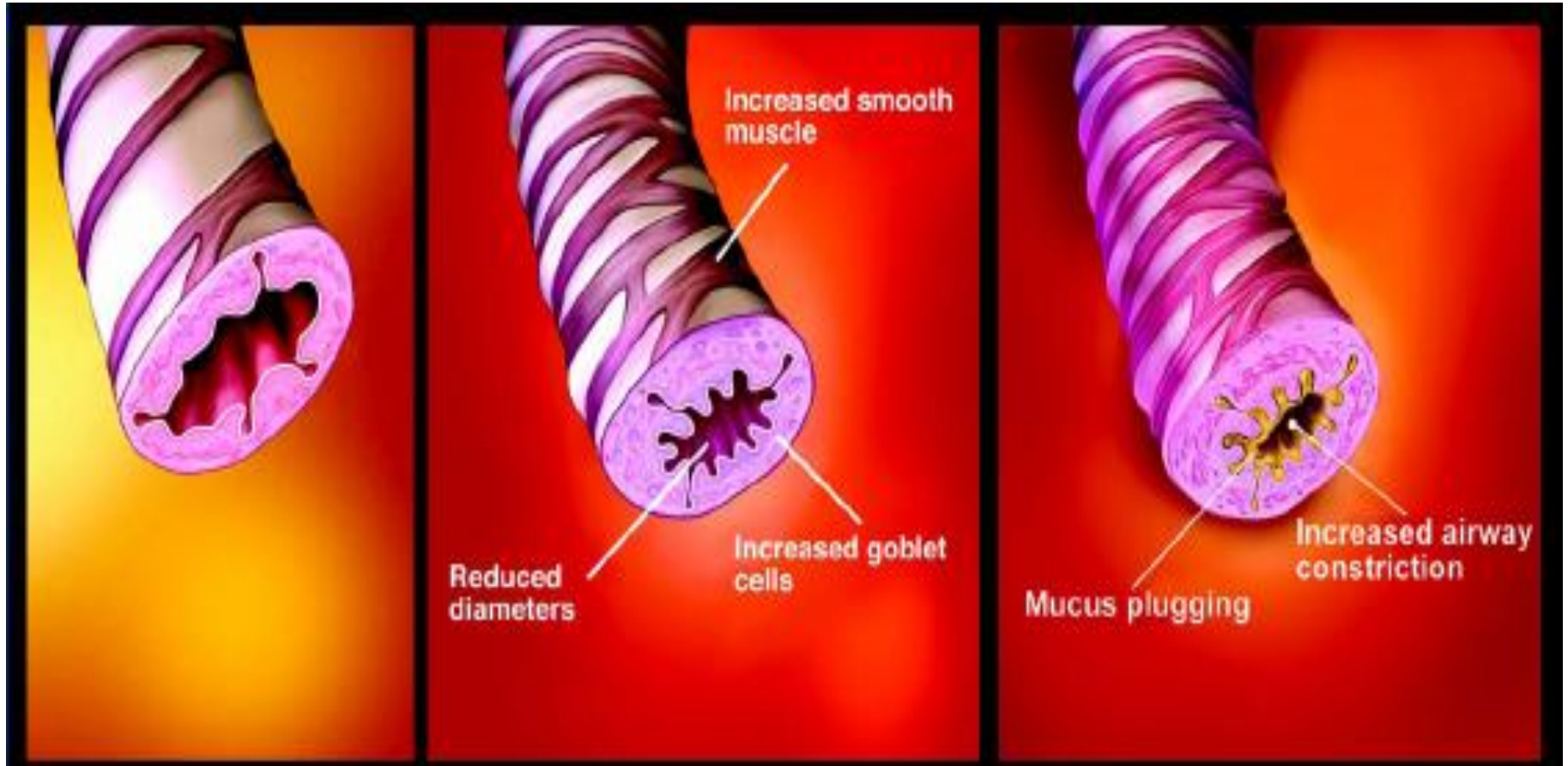
Highest incidence in infants of all virus RTI resulting in hospitalization



Aerosolized ribavirin approved for use against RSV in the USA

BUT severe complications:
BRAIN (apneas, status epilepticus)
HEART (ventricular tachycardia or fibrillation, cardiogenic shock, complete heart block, pericardial tamponade)
BRAIN, LIVER, KIDNEY (Reye's syndrome)

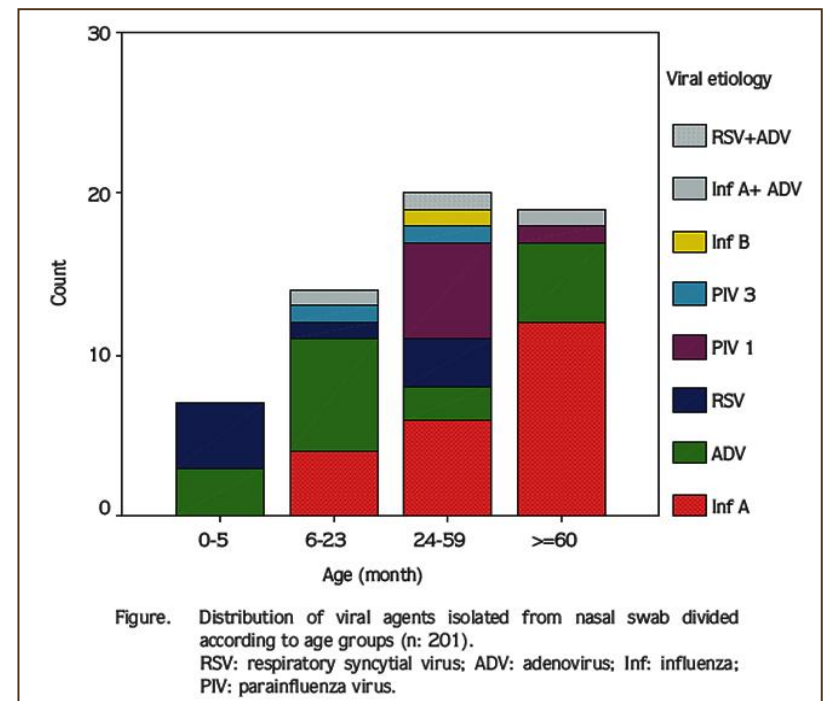
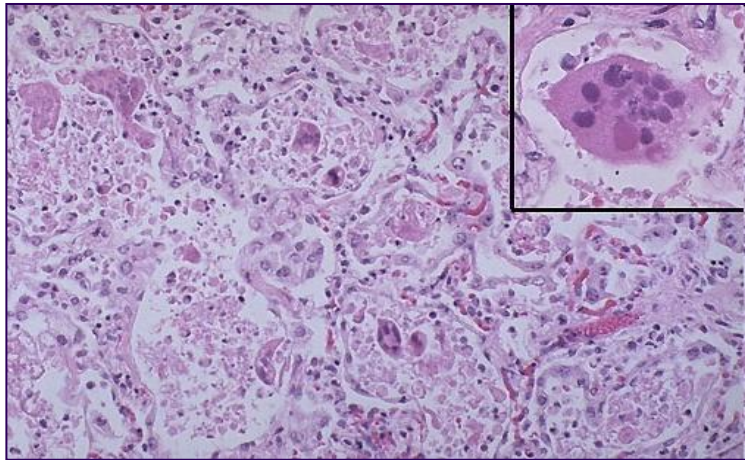
RSV pathomechanism



Immunologic mechanisms (inflammatory cytokine production, peribronchial lymphocyte infiltrations) - Mucous edema - Increased mucous secretion
Cell necrosis that leads to sloughing of debris - Bronchioles become plugged with debris and mucus - Bronchoconstriction

RSV: risk factors

1. Infants with congenital heart disease
2. Infants with underlying pulmonary disease, especially bronchopulmonary dysplasia, are at risk of developing prolonged infection with RSV
3. Premature infants
4. Immunocompromised infants



Specific prophylaxis

Abrysvo vaccine = maternal RSV vaccine
Nirsevimab, Palivizumab = monoclonal antibodies against RSV (lower the chance of hospitalization in infants by >80%)

BUT:

RSV has become an increasingly important pathogen in the elderly population

Currently, RSV is **the second most commonly identified cause of pneumonia in elderly persons**







COVID-19, Flu, RSV or a Cold?



Check your child's symptoms

How To Tell Them Apart

Common symptoms of all four illnesses include fever, cough, fatigue, stuffy, runny nose and congestion. Some symptoms that may be different include:

Illness	Sudden loss of taste or smell	Headache	Loss of appetite	Sore throat	Sneezing
 COVID-19	✓	✓	✓	✓	
 Flu		✓	✓	✓	✓
 Cold				✓	✓
 Respiratory syncytial virus (RSV)					✓

Call your pediatrician if your child has any of the following symptoms:

- Rapid breathing, flaring nostrils, wheezing and grunting
- Shortness of breath/difficulty breathing
- Chest caving in with each breath
- Very ill or drowsy
- Poor feeding
- Dehydration
- Vomiting for more than 24 hours
- Bloody diarrhea
- Fever:
 - above 104°F in any child
 - above 100.4°F if child is under 2 months old
 - above 103°F for more than 24 hours

Adenoviruses **DNA** non-enveloped, 47 serotypes within 6 subgroups A-F

stable out of the body for 7 days to 3 mo.

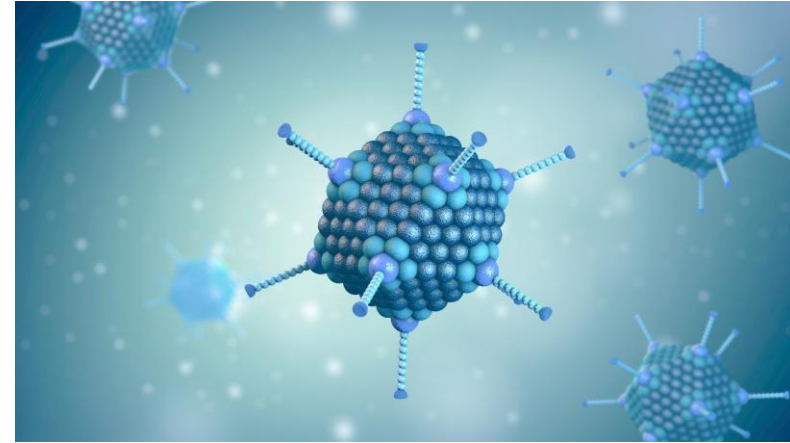
No specific treatment, no vaccine, treatment (supportive)

Reservoir: diseased humans

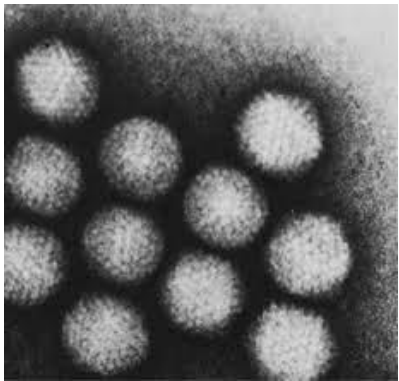
DIRECT, aerosolized droplets, and indirect routes of transmission

Inflammation
(2-14 days incubation RTI
and 3-10 incubation GITI)

Diseases: upper and lower respiratory tract infections
2-5% of all respiratory infections globally
10% of cases of pneumonia in children



Multiply in different cells: airway epithelial cells, lymphocytes

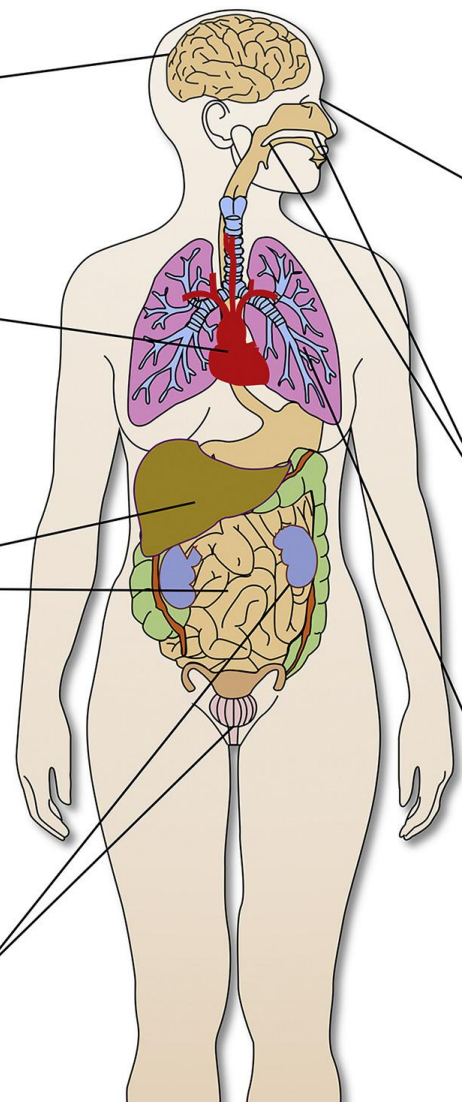


Unsusceptible to interferons

Treatment: **cidofovir** applied locally
(in immunocompromised individuals like hematopoietic stem cell transplant recipients)

Latency - B2 & C subgroups in lymphoid tissue of pharyngeal ring, mesenteric lymph nodes

Endogenous recurrences of acute infection & chronic dysplasia of infected lymphoid tissue



Central Nervous System

- Meningoencephalitis – 1, 2, 3, 4, 5, 6, 7, 11, 12, 26, 32, 41

Cardiovascular System

- Myocarditis – 7, 21
- Dilated cardiomyopathy

Gastrointestinal Tract

- Gastroenteritis – 1, 2, 3, 5, 7, 11, 12, 15, 17, 31, 32, 33, 40, 41
- Childhood diarrhea – 12, 31, 40, 41
- Intussusception – 1, 2, 3, 5, 6, 7, 40, 41
- Appendicitis – 1, 2, 7
- Mesenteric lymphadenitis – 1, 2, 3, 5, 7
- Hepatitis – 1, 2, 3, 5, 7

Urinary Tract

- Hemorrhagic cystitis – 7, 11, 21, 34, 35
- Nephritis – 3, 4, 7a, 11

Eye

- Follicular conjunctivitis – 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 15, 16, 17, 19, 20, 22, 31, 34, 37
- Pharyngoconjunctival fever – 1, 2, 3, 4, 5, 6, 7, 7a, 8, 14, 37
- Epidemic keratoconjunctivitis – 2, 3, 4, 5, 7, 8, 10, 11, 13, 14, 15, 16, 17, 19, 23, 29, 37, 54, 56
- Hemorrhagic conjunctivitis – 11

Upper Respiratory Tract

- Upper respiratory tract infection(s) – 1, 2, 3, 5, 6, 7

Lower Respiratory Tract

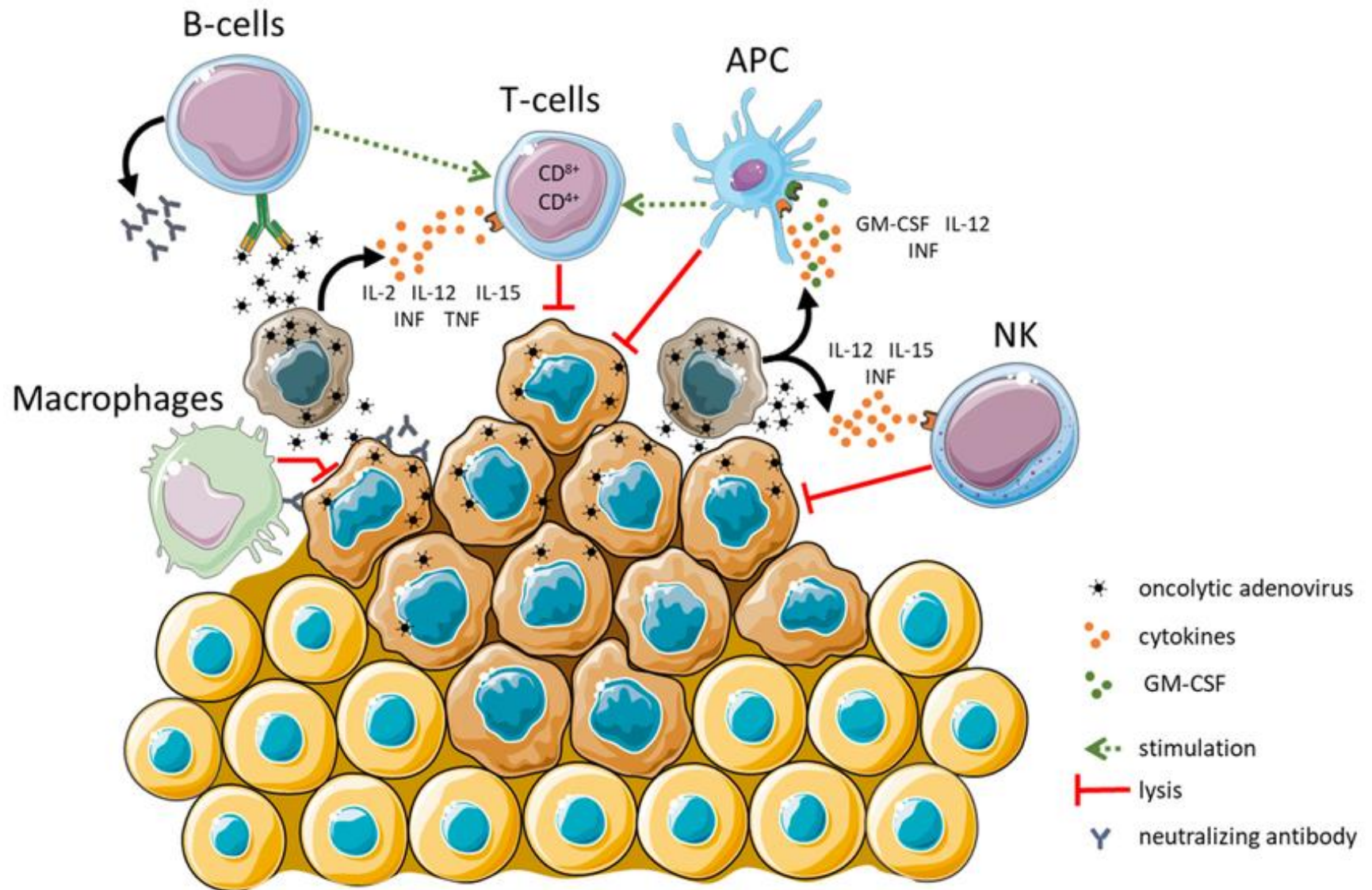
- Acute Bronchiolitis – 3, 7, 21, 60
- Bronchiolitis obliterans – 2, 3, 7, 21
- Pneumonia – 1, 2, 3, 4, 5, 7, 7a, 8, 11, 14, 14p1, 21, 35, 55, 56

Other Organ Systems

- Arthritis – 7
- Thyroiditis – unknown

Clinical manifestations	Serotype
Acute respiratory diseases	1, 7, 14, 21
Viral pneumonia	1, 3, 4, 7, 55
Conjunctivitis	3, 7, 8, 10, 14, 19, 37
Gastroenteritis	9, 11, 31, 40, 41
Meningoencephalitis	2, 6, 7, 12, 32

Oncolytic adenoviruses (OAdS) are engineered to selectively replicate in and destroy cancer cells, while also stimulating the immune system to fight cancer



Enterovirus D68 **DNA virus** non-enveloped,

No specific treatment, no vaccine, treatment (supportive)

Reservoir: diseased humans

DIRECT, aerosolized droplets, and indirect routes of transmission

Inflammation
(2-14 days incubation)

Diseases: upper and lower respiratory tract infections

Neurologic sequele:

AFM (acute flaccid myelitis; poli-like paralysis) lower motor neurosn in the spinal cord grey matter - muscle weakness (arms, legs) - may lead to severe respiratory failure

cranial nerve dysfuction, encephalitis, meningoencephalitis - after febrille illness (respiratory and gastrointestinal symptoms)

Unknown receptor - ICAM-5 present on neurons, but absent in respiratory tract and spinal cord

Answer questions

Preventable by vaccine are viral respiratory tract infections caused by:

- a) Adenovirus**
- b) Influenza virus**
- c) RSV**
- d) Rhinovirus**

Infection with which respiratory virus causes the most hospitalizations and deaths among children?

- a) Rhinovirus**
- b) RSV**
- c) Parainfluenza virus**
- d) Adenoviruses causing pneumonia**

Viral RTIs most commonly are caused by DNA or RNA viruses?

Which viruses can produce primary pneumonia?

What does maternal vaccine mean?



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