



Lecture Five

Mechanisms of Virus Infection and Spread

A- Virus Entry

By

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Learning outcomes

By the end of this lecture students should

- **Recognize the sequential steps of virus infection and spread.**
- **Recognize different portals of virus entry into human body.**
- **Define viremia and its sources and types.**
- **Recognize different portals of virus shedding.**



The Sequential Steps in Viral Infection

1 ➤ Virus Entry

1.1. Entry via Skin and mucous membranes

1.2. Urogenital tract.

1.3. Oropharynx and gastrointestinal tract.

1.4. Gastrointestinal tract.

1.5. Respiratory Tract.

2 ➤ Virus Spread.

3 ➤ Virus Shedding.

4 ➤ Virus Transmission

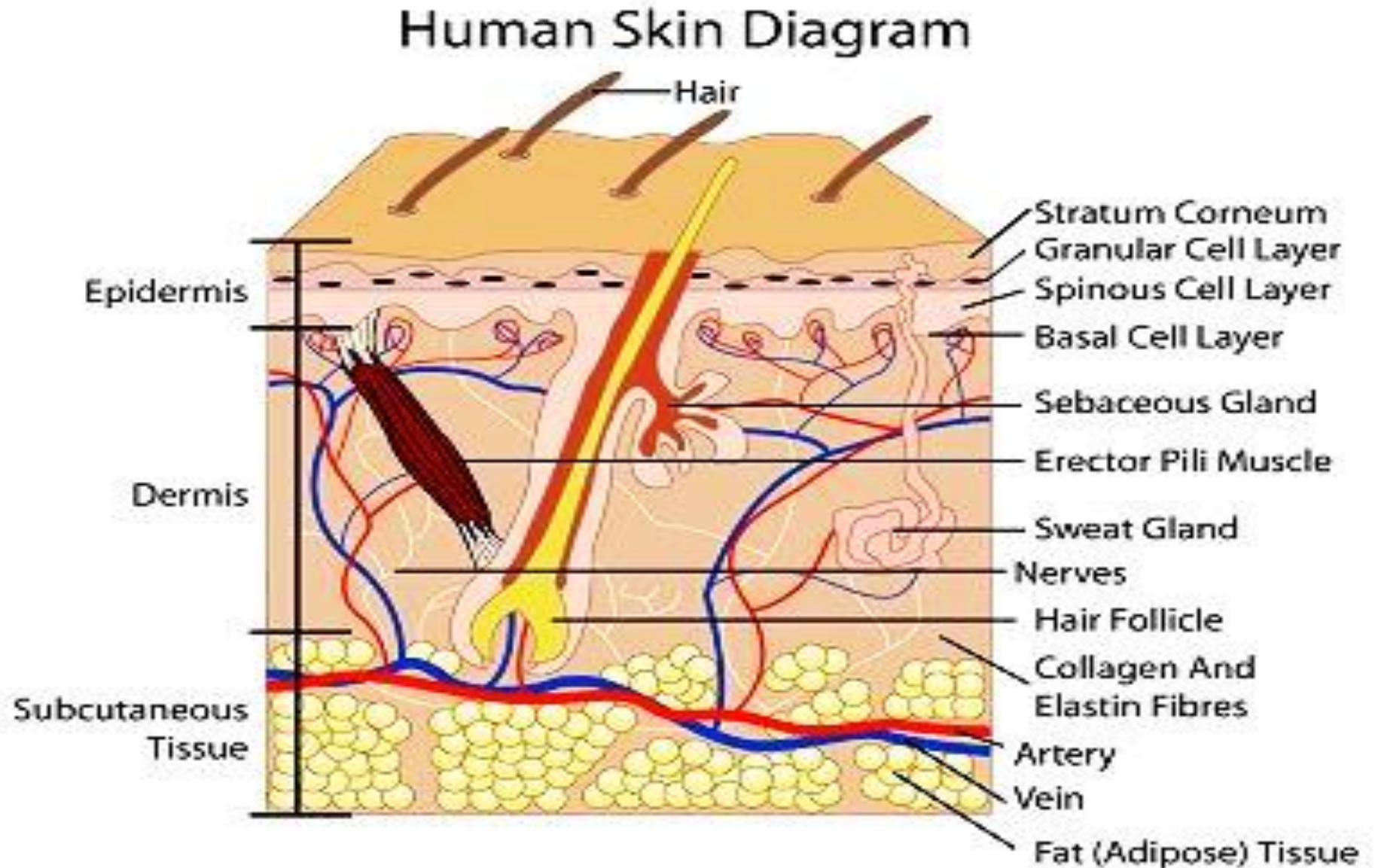


The Sequential Steps in Viral Infection

- Infection of an animal host that has many specialized organs and tissues is a complex multistep process.
- In each step of virus infection, the virus must **overcome** natural barriers to dissemination, such as the anatomic boundaries that separate organs and tissues.
- Some viruses are confined to the site of initial infection and spread only locally (**Local infection**), while others disseminate widely (**Systematic infection**).
- **Blood-borne viruses** may invade almost any organ or cell type, while **neurotropic viruses** are usually confined to the peripheral and central nervous system and replicate in relatively few peripheral tissues.

Step 1: Entry

1.1. Entry via Skin and mucous membranes





Step 1: Entry

1.1. Entry via Skin and mucous membranes

- Many different viruses replicate in cells of the skin or mucous membranes.
- Not all viruses can invade the intact skin since there are no viable cells directly on the surface.
- The exterior of the skin constitutes a relatively **hostile** environment due to its dryness, acidity and bacterial flora.
- Virus invades through a break in the barrier that allows contact with living cells.



Step 1: Entry

1.1. Entry via Skin and mucous membranes

- For instance, both **herpes simplex** virus and **poxviruses** replicate in germinal cells of the epidermis as well as macrophages and fibroblasts of the dermis.
- **Papillomaviruses** initially infect the germinal cells of the epidermis and complete their replication cycle in the stratum granulosum.
- **The conjunctiva of the eye**, a specialized mucous membrane, is the primary site of entry of a few viruses, such as **certain adenovirus** types and selected **enteroviruses** that can cause conjunctivitis.



Step 1: Entry

1.1. Entry via Skin and mucous membranes

Transcutaneous injection – *Insect and Animal bites*

- **Some viruses breach the cutaneous barrier by injection.**
- **A wide variety of viruses are arthropod-borne (arboviruses) and have a life cycle that alternates between an insect vector and a vertebrate host.**
- **Several medically important viruses (hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV)) are frequently transmitted by blood or blood products or by contaminated needles.**



Step 1: Entry

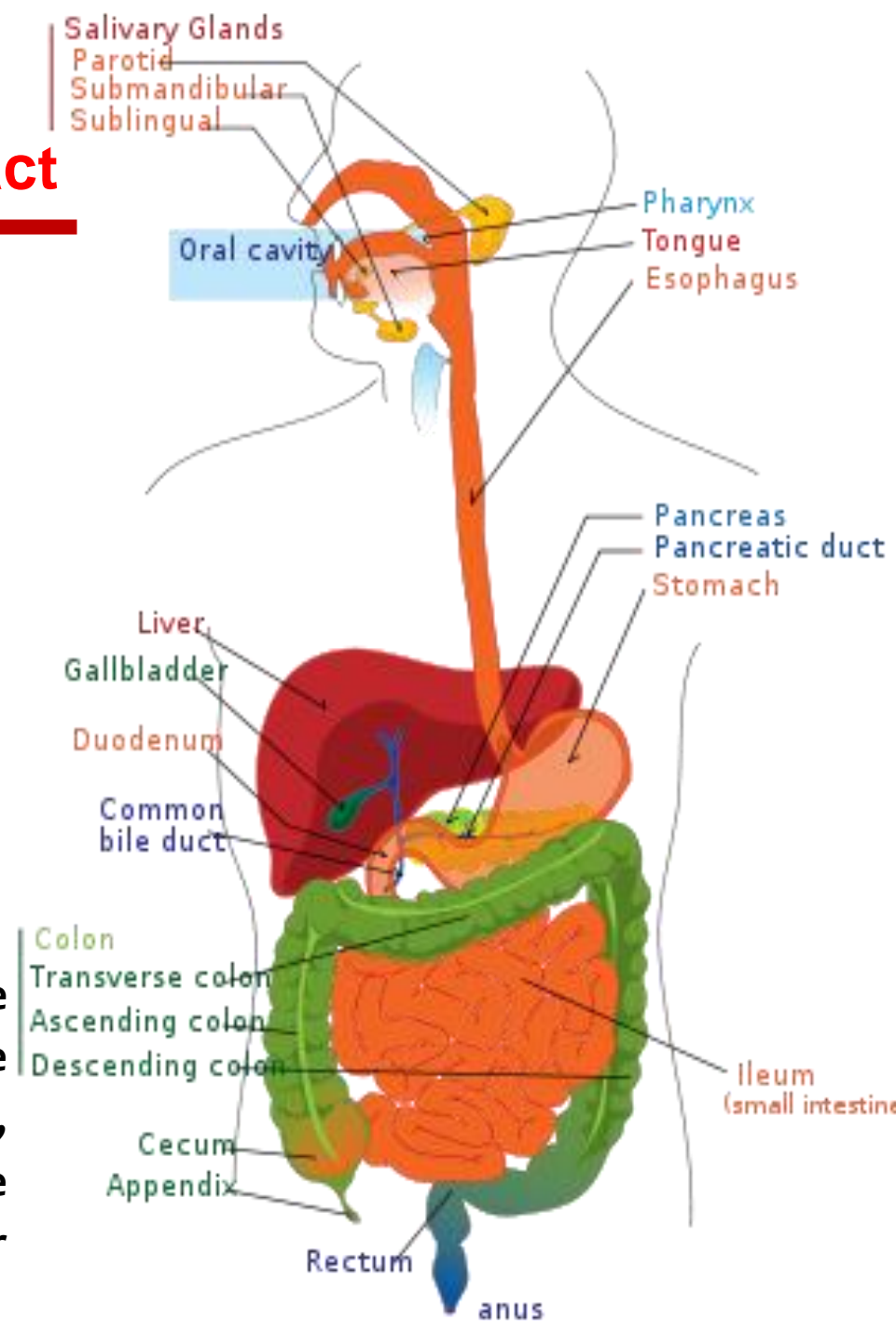
1.2. Urogenital tract

- **Herpes simplex virus type 2** and **papillomaviruses**, replicate in mucous membranes of the genital tract.
- **HBV** and **HIV**, which do not replicate in epithelial cells, are associated with persistent viremia and may be transmitted via minute ‘injections’ of blood during sexual contact.
- **HBV** may transit mucous membranes directly to invade the circulation through surface capillaries.
- **HIV** infects CD4 T lymphocytes, macrophages and dendritic cells in the skin and submucosal tissues and is then carried to draining lymph nodes.

Step 1: Entry

1.3. Oropharynx and gastrointestinal tract

- The oropharynx and gastrointestinal tract are the portal of entry for many viruses; particular viruses may invade at specific sites ranging from the tonsils to the colon.
- Some enteric invaders remain confined to the intestinal tract, while others spread via the blood to produce systemic infection.
- Although most enteric viruses replicate only in the intestinal tract, some, such as poliovirus, also infect the tonsils.
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Step 1: Entry

1.4. Gastrointestinal tract – Barriers to infection

- Invading virus may remain sequestered within the intestinal contents or fail to penetrate surface mucus.
 - * The acidity of the stomach.
 - * Alkalinity of the intestine.
 - * The proteolytic enzymes secreted by the pancreas.
 - * The lipolytic activity of bile.
 - * The neutralizing action of secreted IgA.
 - * Scavenging macrophages.
- Viruses must resist this hostile environment or exploit it by activation into an infectious particle, as in the case of **reovirus**.
- **Coronavirus** is susceptible to this harsh environment, however, virus ingestion with milk or food protects the virus and can initiate infection.

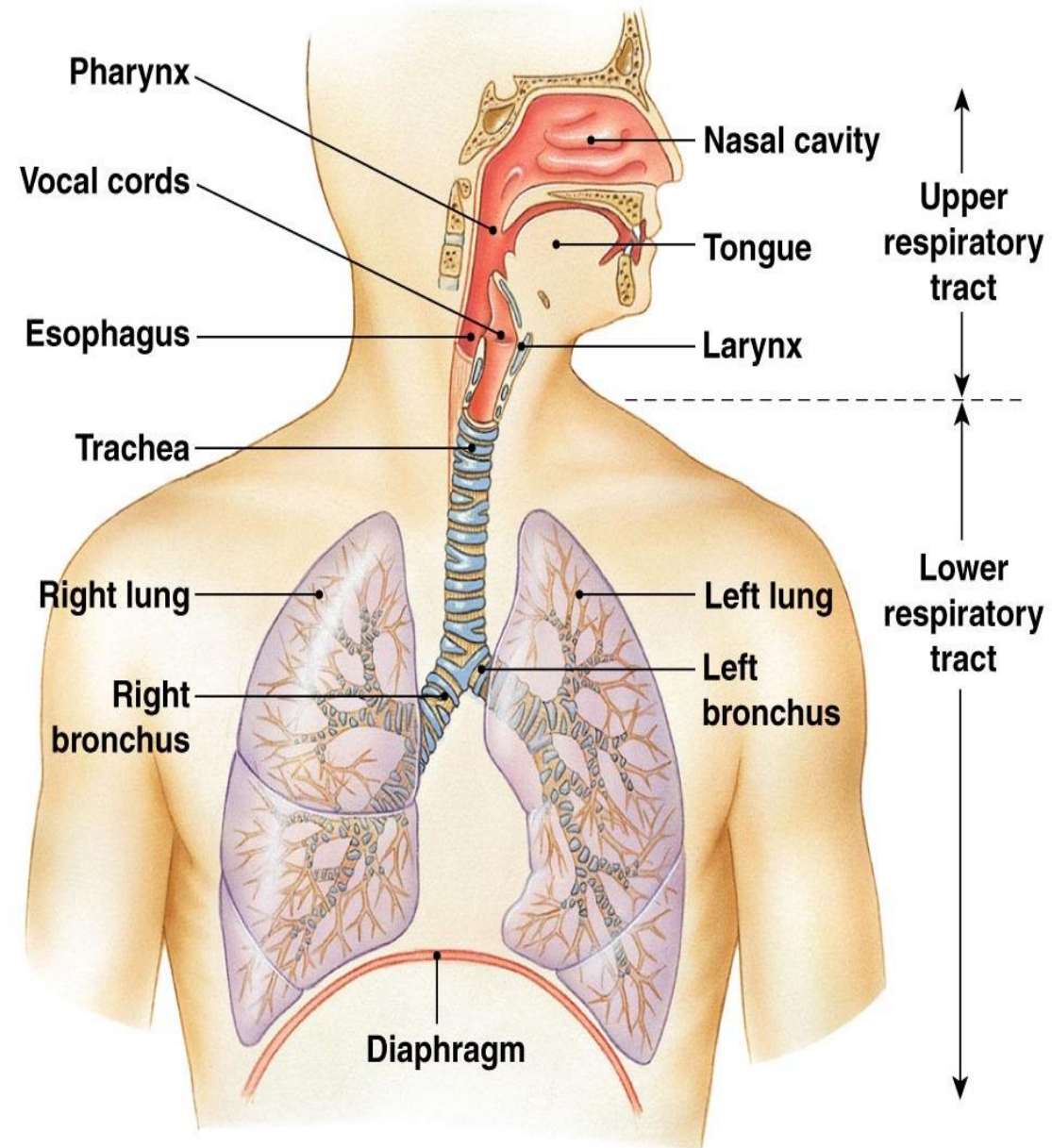
Step 1: Entry

1.5. Respiratory tract

- Viruses get access to the respiratory tract via aerosol inhalation or by mechanical transmission of infected nasopharyngeal secretions.

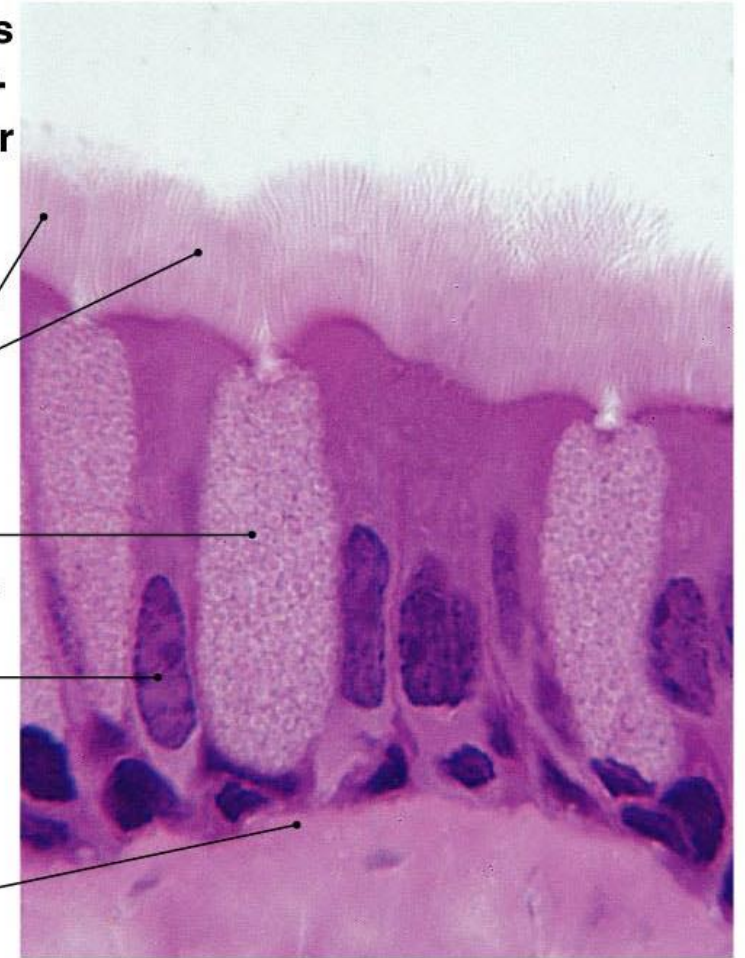
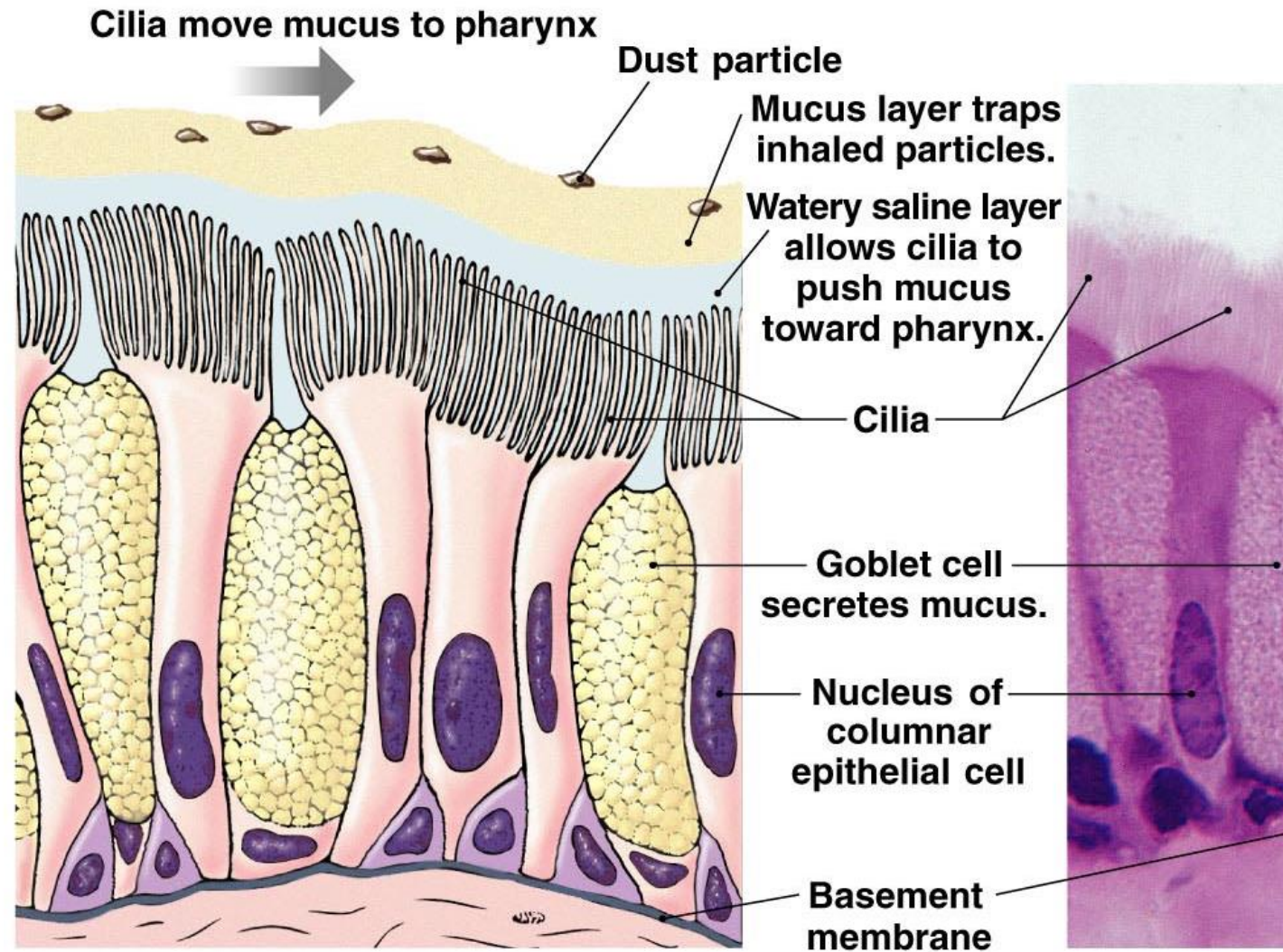
Droplets size

- > 10 μm in diameter lodge in the nose,
- 5–10 μm in diameter lodge in the airways.
- < 5 μm reach the alveoli of the lower respiratory tract.



Step 1: Entry

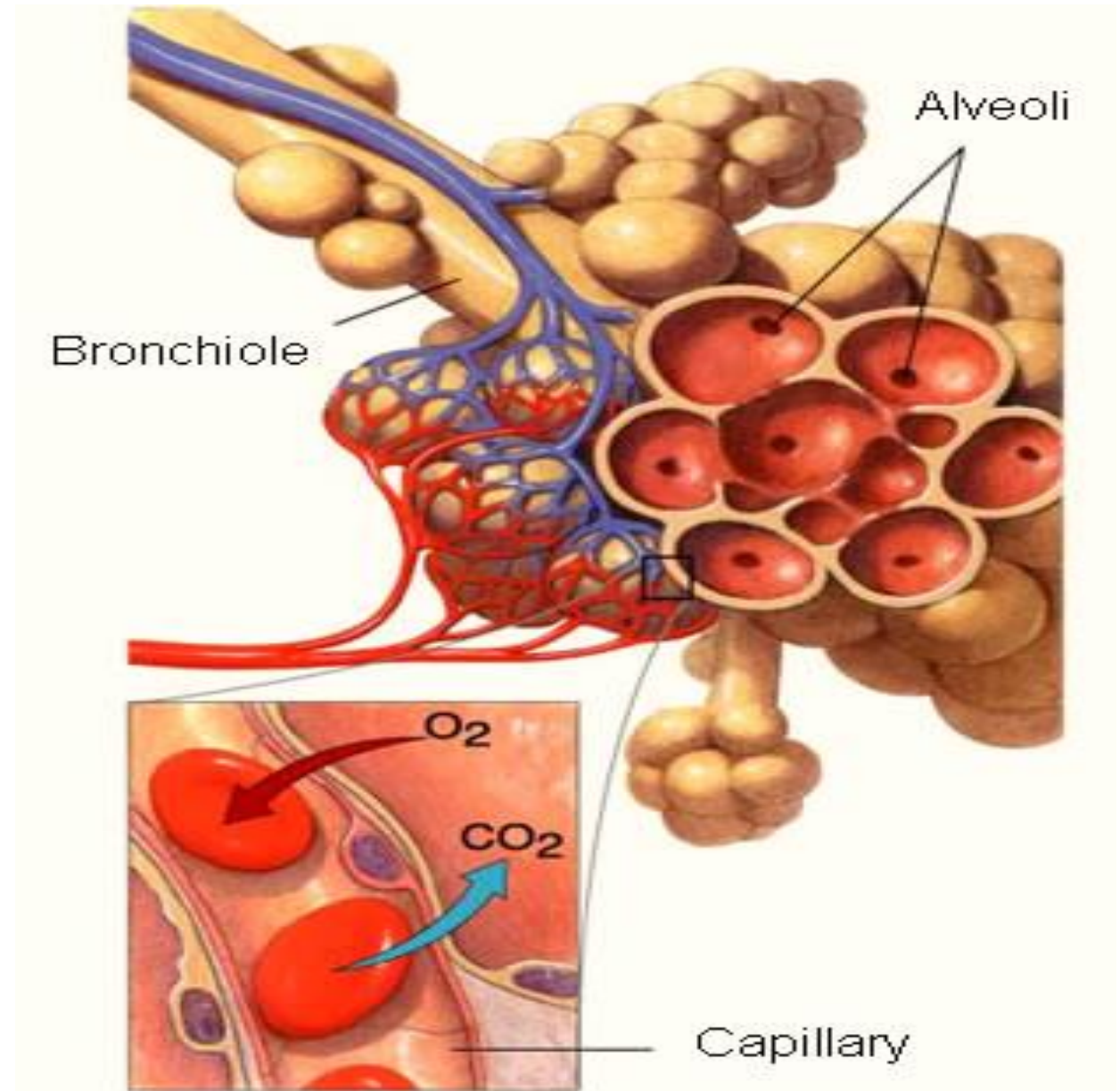
1.5. Respiratory tract



Ciliated epithelium of the trachea

Step 1: Entry

1.5. Respiratory tract





Step 1: Entry

1.5. Respiratory tract – Barriers to infection – Cont.

- * The protective coating action of mucus.
- * The ciliary action of the respiratory epithelium that sweeps particles out of the airways
- * The activity of immunoglobulins and macrophages that engulf foreign particles.
- * Temperature gradient between the nasal passages (33°C) and the alveoli (37°C) that plays an important role in the localization of infection.

Examples:

- **Rhinoviruses**, cause upper respiratory tract infections or the common cold.
Replicate well at 33°C but grow poorly at 37°C.
- **Influenza virus** infects the lower respiratory tract and replicates well at 37°C



Step 1: Entry

1.5. Respiratory tract – Barriers to infection – Cont.

The initial sites of infection for some respiratory viruses.

- 1- **Rhinovirus** has been shown to replicate in the epithelial lining of the nose.
- 2- **Poxviruses**, some of which enter via aerosol transmission, replicate initially in macrophages free in the airways and then in the epithelial lining of small bronchioles.
- 3- Types of **reovirus** that can enter via the respiratory route infect M cells that overlie bronchus-associated lymphoid tissue.

Representative viruses that invade via skin and mucous membranes

Site of entry	Route	Virus family	Representative example
Skin	Minor breaks	Papillomaviridae	Human papilloma virus
		Herpesviridae	Herpes simplex virus 1
		Poxviridae	Ectromelia virus
Conjunctiva	Contact	Picornaviridae	Enterovirus 70
		Adenoviridae	Adenoviruses
Oropharynx	Contact	Herpesviridae	Epstein-Barr virus
Genital Tract	Contact	Retroviridae	HIV
		Papillomaviridae	Human papilloma virus
		Herpesviridae	Herpes simplex virus 2
Rectum	Contact	Retroviridae	HIV

