# Normal Respiratory Tract Flora and Host Defenses

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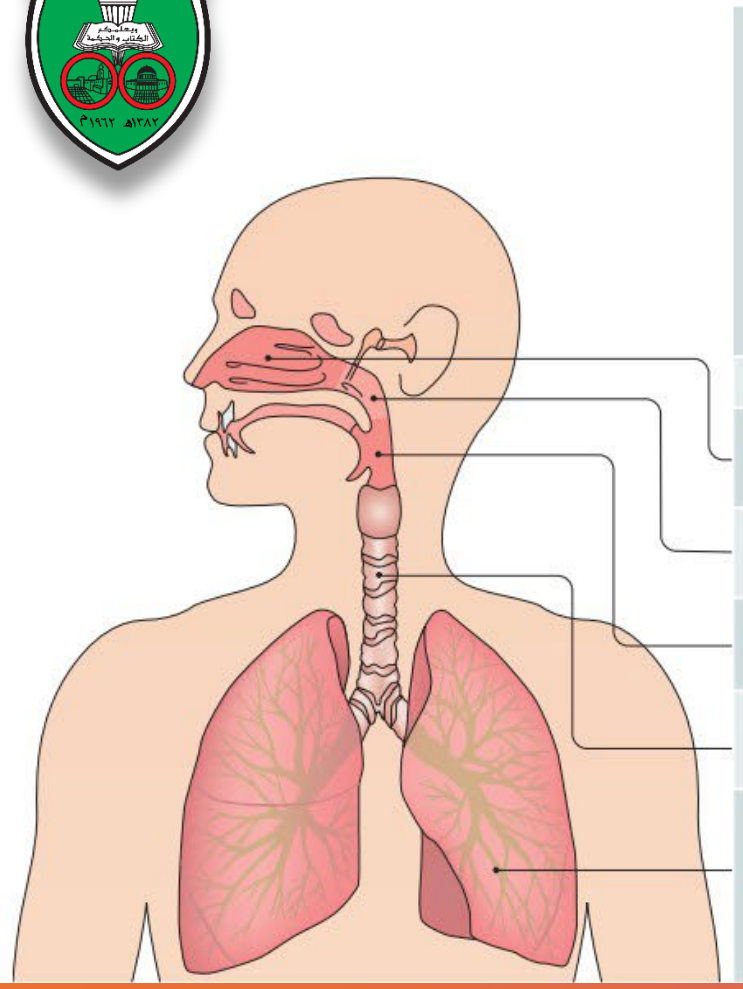
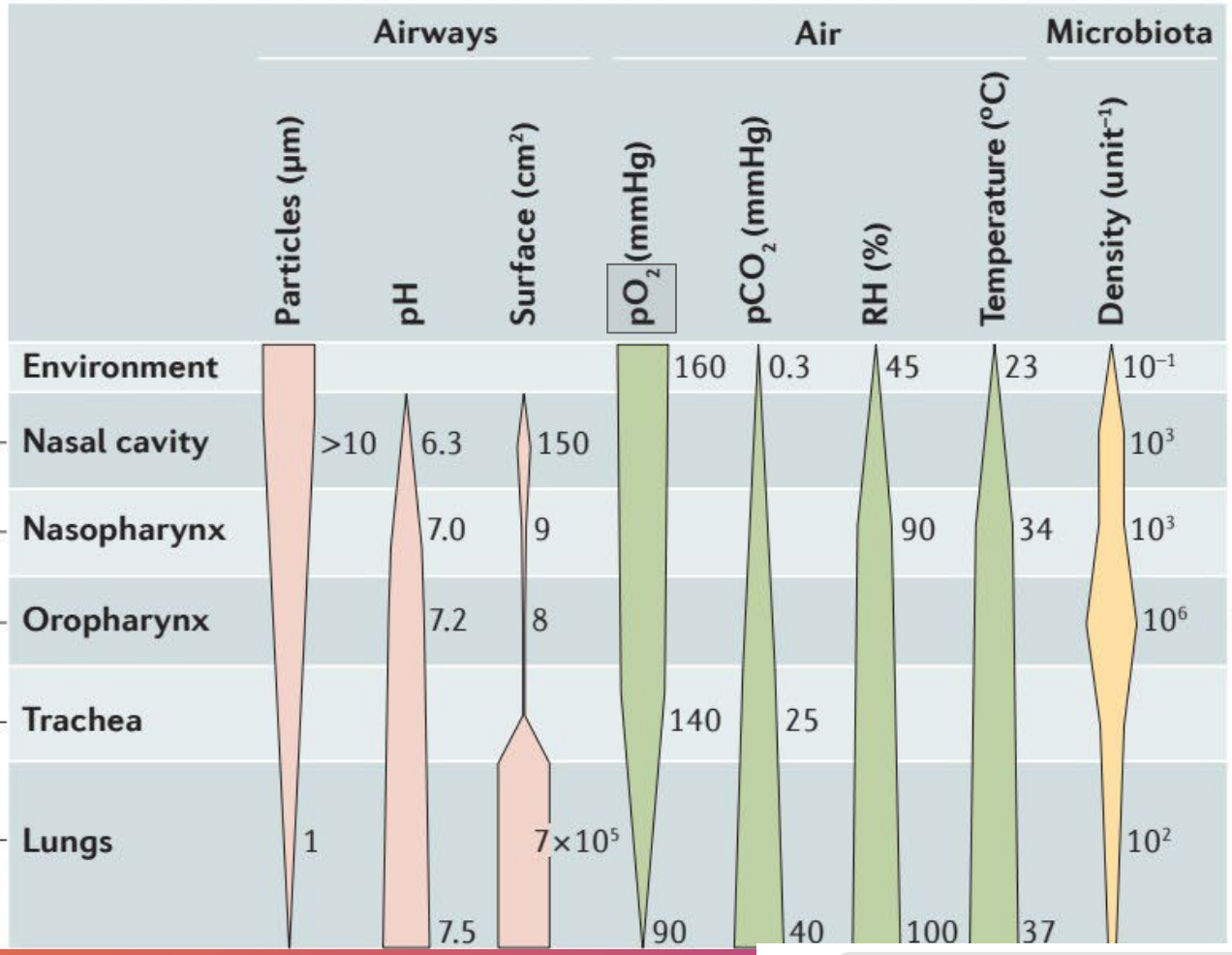
Source: Man, W., de Steenhuijsen Piters, W. & Bogaert, D. The microbiota of the respiratory tract: gatekeeper to respiratory health. Nat Rev Microbiol 15, 259–270 (2017). https://doi.org/10.1038/nrmicro.2017.14






*Staphylococcus* spp., *Propionibacterium* spp., *Corynebacterium* spp., *Moraxella* spp. and *Streptococcus*

*Moraxella* spp., *Staphylococcus* sp *Corynebacterium* spp., *Dolosigranulum* spp., *Haemophilu and Streptococcus* spp.

*Streptococcus* spp., *Rothia* spp., *Veillonella* spp., *Prevotella* spp. an *Leptotrichia* spp.

*Prevotella* spp., *Veillonella* spp., *Streptococcus* spp. and *Tropheryma whipplei*

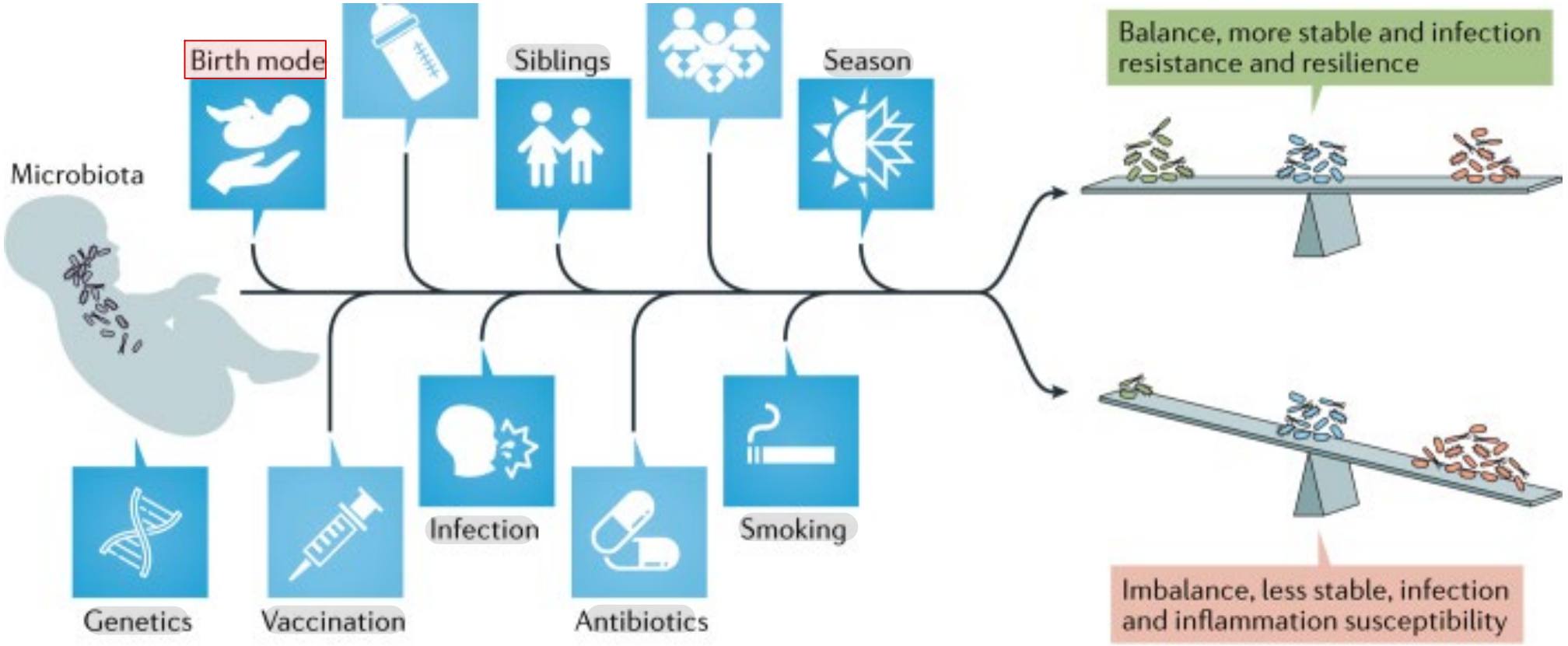
7. Oxygen tension plays a recognizable role in the formation of respiratory microbial communities. TRUE

# Introduction to Respiratory Microbiota

Upper and lower respiratory tracts have distinct microbial communities

Source: Man, W., de Steenhuijsen Piters, W. & Bogaert, D. The microbiota of the respiratory tract: gatekeeper to respiratory health. Nat Rev Microbiol 15, 259–270 (2017). https://doi.org/10.1038/nrmicro.2017.14

19. Many host and environmental factors influence the respiratory microbiota with the exception of the mode of birth. FALSE




# Introduction to Respiratory Microbiota

Many host and environmental factors influence the respiratory microbiota

# Respiratory Microbial Ecology

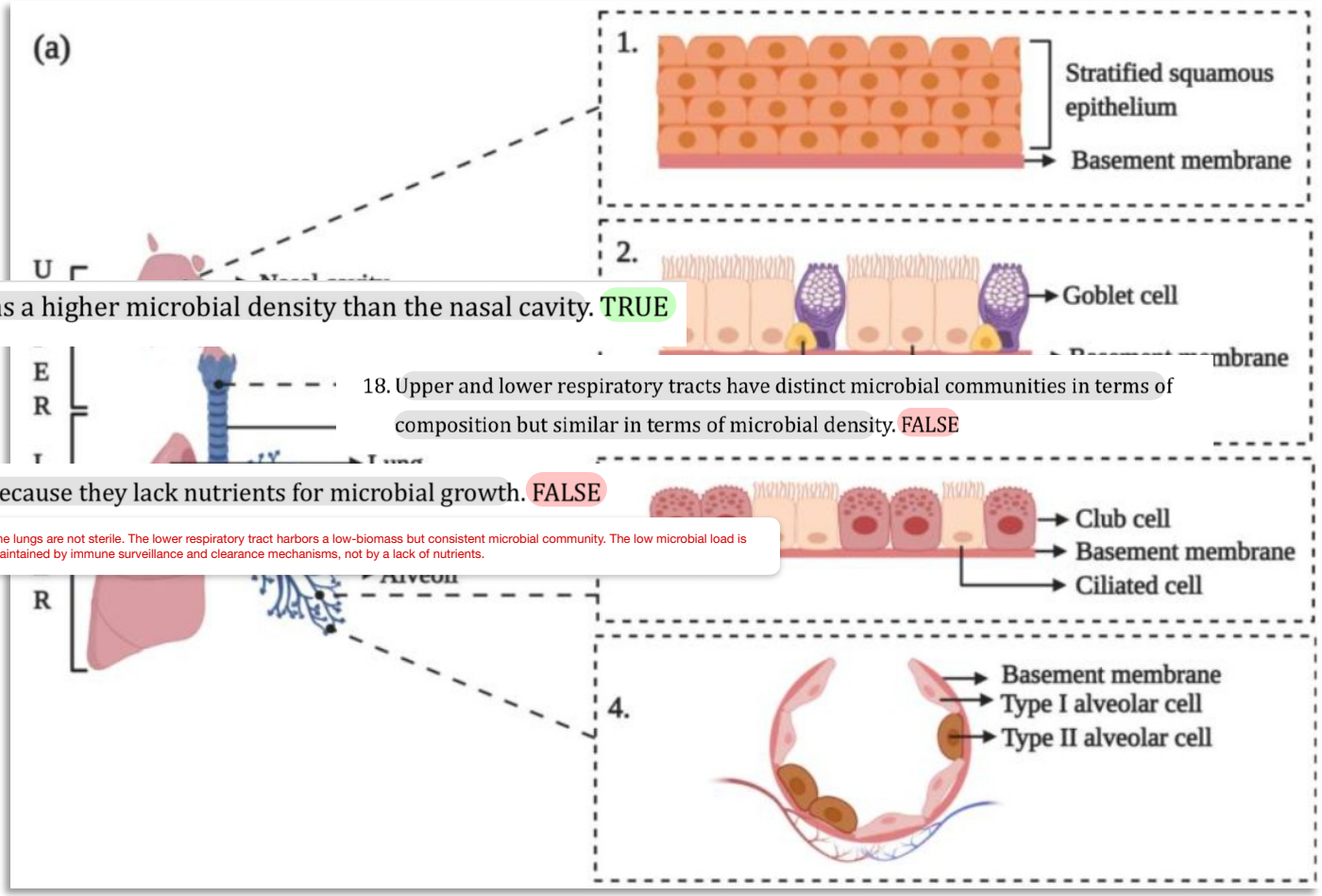
- **From microbiology point of view, the RT is classified into two distinct zones:**
- URT: humid, nutrient-rich, and heavily colonized, controlled by IgA.
- LRT: lower colonization, controlled by immune surveillance.
- **Factors that shape microbial survival:**
- Temperature changes (30-37°C).
- Shear forces from airflow.
- Concentration of antimicrobial peptides.
- Mucociliary transport velocity.

1. The oropharynx has a higher microbial density than the nasal cavity. TRUE

18. Upper and lower respiratory tracts have distinct microbial communities in terms of composition but similar in terms of microbial density. FALSE

8. The lungs are sterile because they lack nutrients for microbial growth. FALSE

The lungs are not sterile. The lower respiratory tract harbors a low-biomass but consistent microbial community. The low microbial load is maintained by immune surveillance and clearance mechanisms, not by a lack of nutrients.




Source: Adivitiya et al. "Mucociliary Respiratory Epithelium Integrity in Molecular Defense and Susceptibility to Pulmonary Viral Infections." Biology vol. 10,2 95. 29 Jan. 2021, doi:10.3390/biology10020095

# URT Microbiota

11. *Staphylococcus epidermidis* is a dominant colonizer of the nasal cavity but rarely persists in the lower respiratory tract. TRUE

- *Streptococcus mitis*, *S. salivarius*, *S. pneumoniae*: Regulate epithelial TLR signaling and induce **baseline TH-17/Treg balance**.
- *Staphylococcus epidermidis*: Produce **serine protease Esp** that inhibits *S. aureus* colonization.

20. *Staphylococcus epidermidis* produces serine protease that inhibits *Staphylococcus aureus* colonization in the upper respiratory tract. TRUE

- *Corynebacterium accolens* and *C. pseudodiphtheriticum*: Release **free fatty acids** toxic to pathogens.

21. *Corynebacterium diphtheriae* release free fatty acids toxic to pathogens to protect the upper respiratory tract. FALSE

- Anaerobes (*Prevotella*, *Veillonella*, *Actinomyces*): Major contributors to **mucin degradation**.

9. The dominance *Prevotella* in the oropharynx is driven by reduced oxygen tension relative to the nasal cavity. TRUE

- *Neisseria* spp.: Maintain respiratory **mucosal immune tolerance**.

# LRT Microbiota

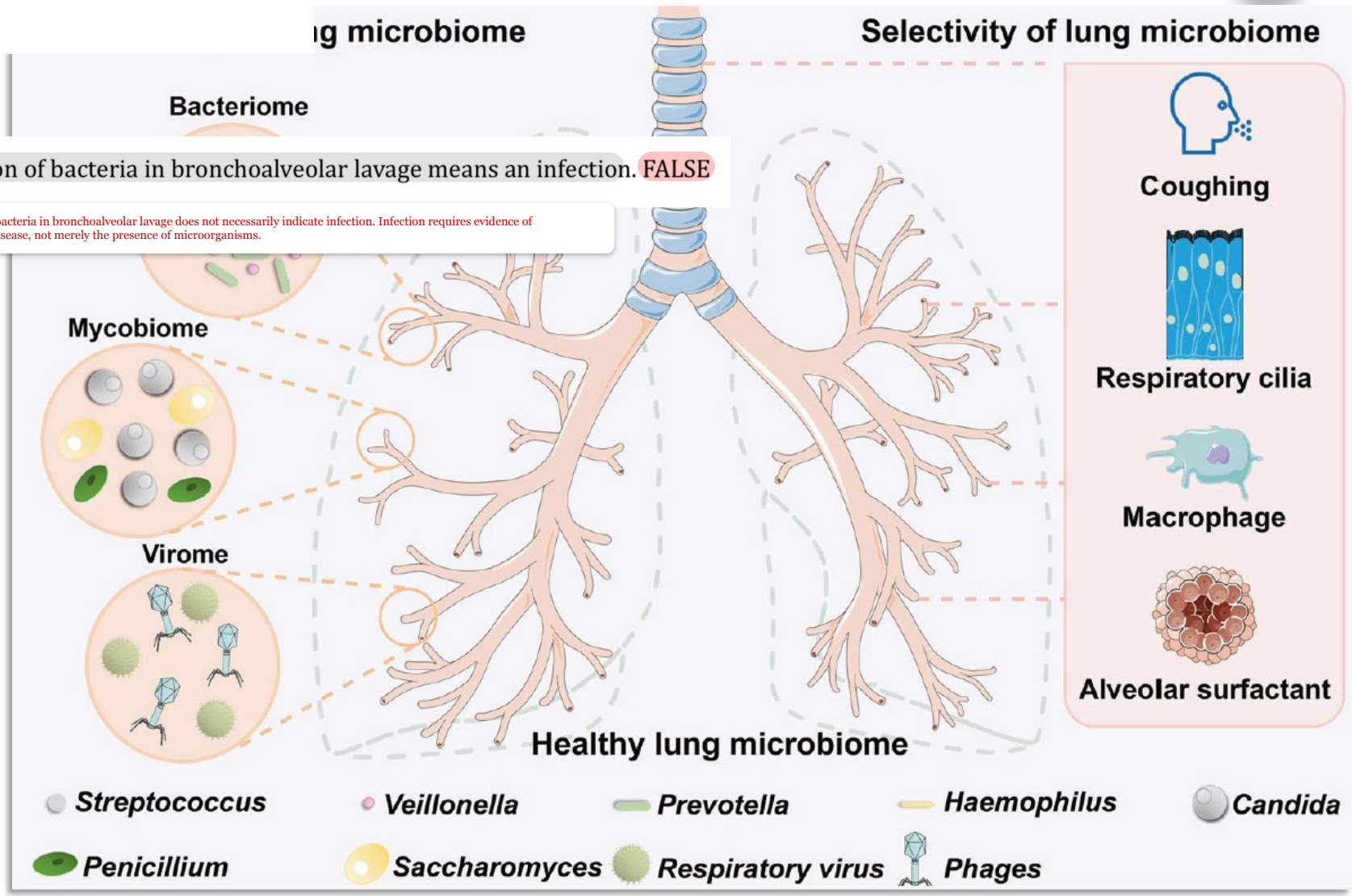
22. The lower respiratory tract contains abundant and consistent microbial population.

FALSE

- The LRT contains rare yet consistent microbial population: *Prevotella, Veillonella, Streptococcus, Fusobacterium, Haemophilus*
- **Composition influenced by:**
  - Micro-aspiration input
  - Mucociliary and cough clearance
  - Immune elimination

2. Detection of bacteria in bronchoalveolar lavage means an infection. FALSE

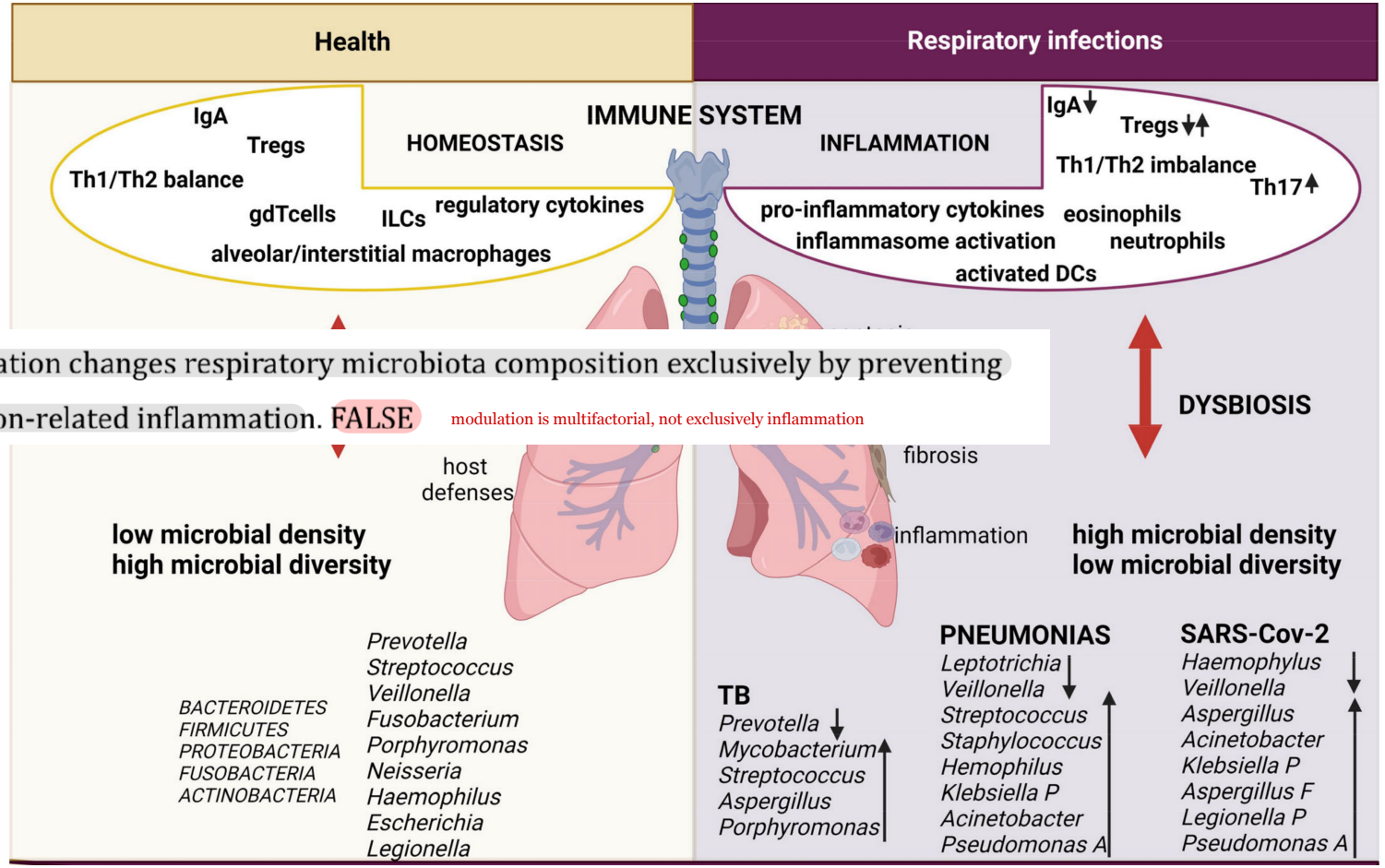
Therefore, the detection of bacteria in bronchoalveolar lavage does not necessarily indicate infection. Infection requires evidence of inflammation and clinical disease, not merely the presence of microorganisms.




Source: Li, R., Li, J. & Zhou, X. Lung microbiome: new insights into the pathogenesis of respiratory diseases. Sig Transduct Target Ther 9, 19 (2024). https://doi.org/10.1038/s41392-023-01722-y

# RT Microbiota Induce Mucosal Immunity

- Induction of secretory IgA.
- Training of alveolar MΦ.
- Modulation of epithelial barrier proteins such as claudins and occludins.
- Production of short-chain fatty acids that enhance Treg activity.
- Competitive inhibition of pathogens via nutrient depletion, receptor blockade, bacteriocin production, and pH modulation.




15. Vaccination changes respiratory microbiota composition exclusively by preventing infection-related inflammation. FALSE modulation is multifactorial, not exclusively inflammation

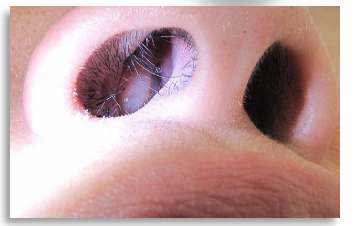
10. Early-life microbial exposure is associated with long-term respiratory infection susceptibility through modulating adaptive mucosal immunity. TRUE

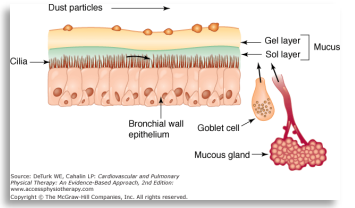
Source: Marrella V, Nicchiotti F, Cassani B. Microbiota and Immunity during Respiratory Infections: Lung and Gut Affair. Int J Mol Sci. 2024 Apr 5;25(7):4051. doi: 10.3390/ijms25074051.

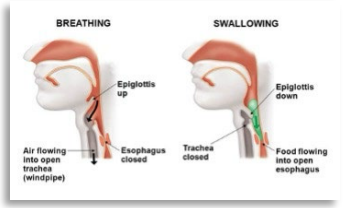
# Mechanical Defenses of the RT

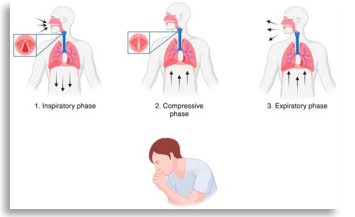
- Nasal hairs: trap large particulates ≥10 μm.
- Turbinate-induced turbulent airflow: increases deposition of microbes onto mucus-coated surfaces.
- Mucociliary escalator: Cilia propel mucus. Smoking reduces ciliary beat frequency by up to 40%.
- Cough reflex: expels aspirated material.
- Sneezing reflex: defense mechanism to expel pathogens.
- Epiglottic and glottic reflexes: prevent aspiration during swallowing.

3. Turbinate-induced turbulent airflow increases deposition of microbes onto mucus-coated surfaces and form a major factor in the mechanical defenses of the respiratory tract. TRUE





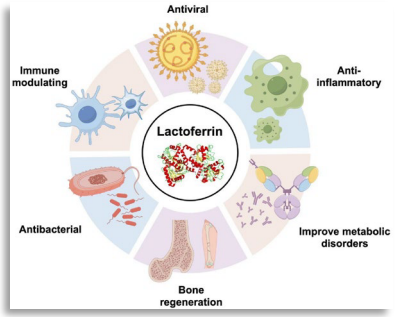



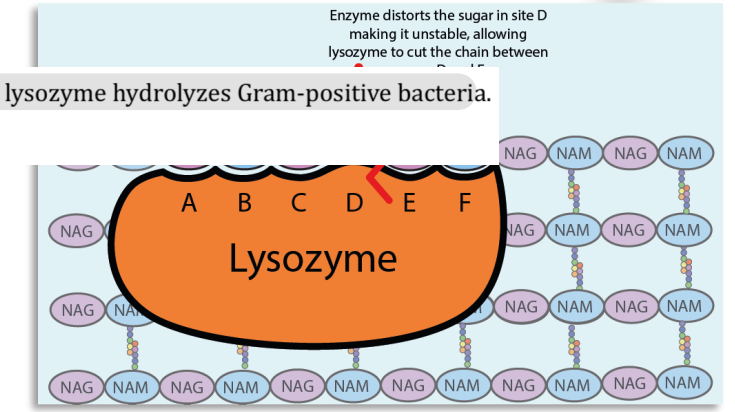



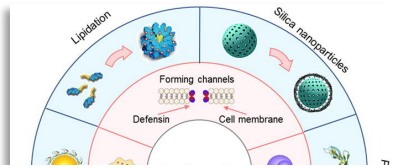

# Chemical Defenses of the RT

- **Lysozyme:** hydrolyzes peptidoglycan, especially effective against Gram-positive bacteria.
- **Lactoferrin:** iron sequestration causes bacteriostatic effect on many pathogens.
- **Defensins and cathelicidin LL-37:** form membrane pores in bacteria and some viruses.
- **Surfactant proteins A and D (SP-A, SP-D):** opsonize bacteria, enhance phagocytosis.
- **Secretory IgA** in large quantities along nasal and bronchial surfaces.

4. In the respiratory tract chemical defence, lysozyme hydrolyzes Gram-positive bacteria. TRUE



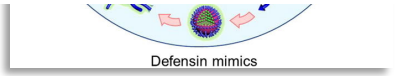



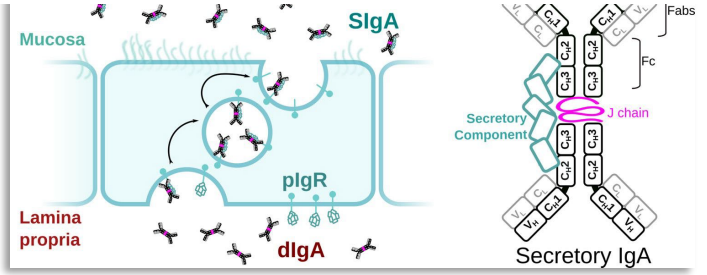




**SP-A and SP-D: Dual Functioning Immune Molecules With Antiviral and Immunomodulatory Properties**

*Alastair Watson[1,2,3*], Jens Madsen[4] and Howard William Clark[4,5]*

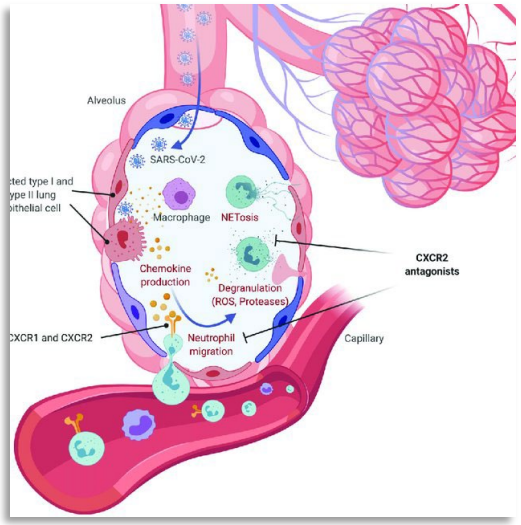
5. Surfactant proteins A and D opsonize bacteria, enhancing phagocytosis in the respiratory tract. TRUE

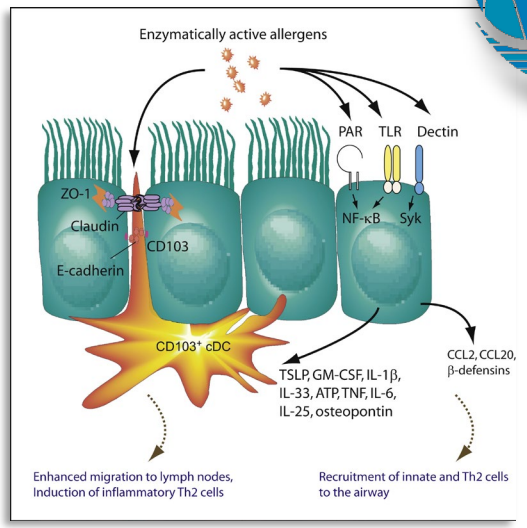


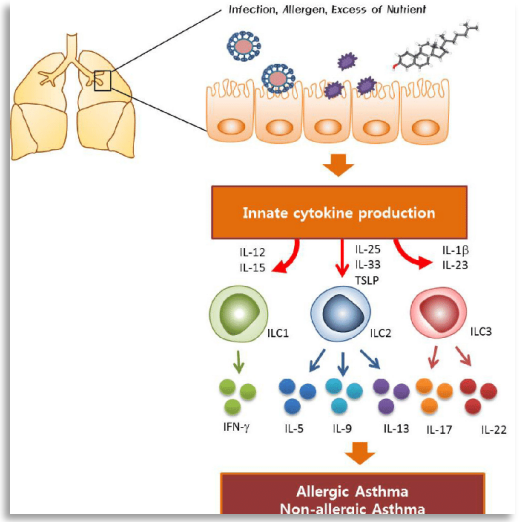
# Cellular Innate Defenses

- **Alveolar MΦ:** Remove particles and microbes at alveolar spaces.
- **Dendritic cells:** Extend dendrites into airway lumen to sample microbial antigens. Bridge innate and adaptive immunity.
- **Neutrophils:** Rare in healthy lungs; explode in number during infection.
- **Innate lymphoid cells:** Regulate mucus production, epithelial repair, and early anti-bacterial responses.





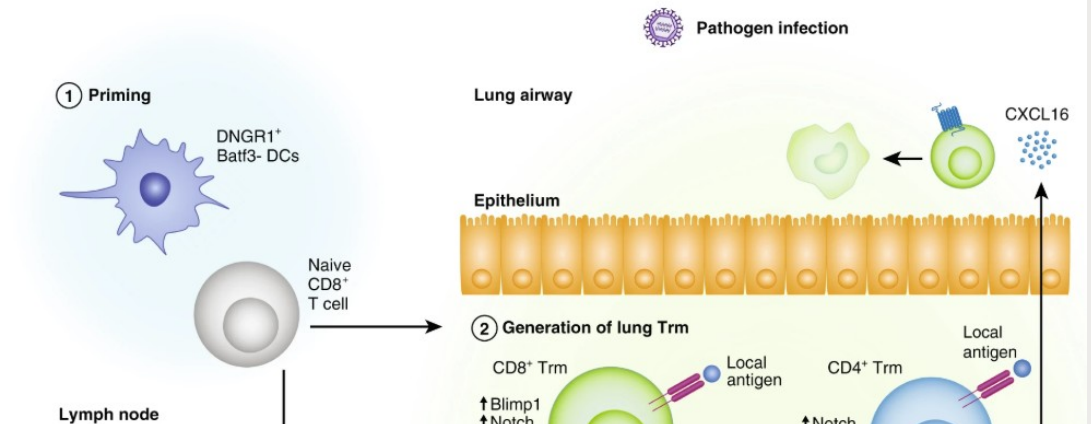


# Adaptive Immunity in the RT

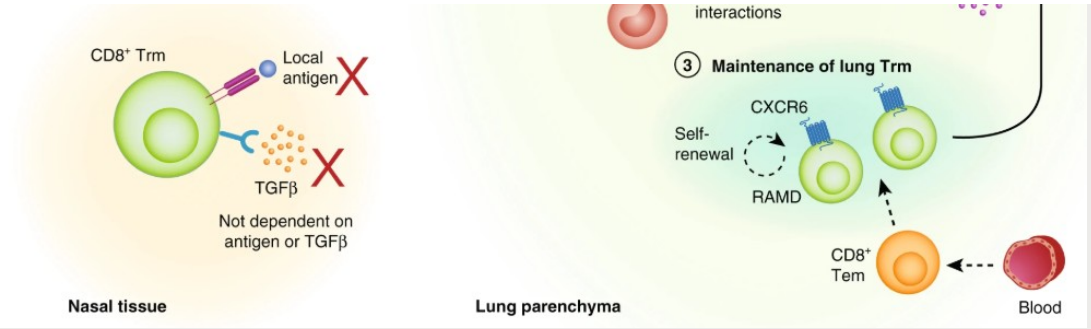
12. Mucosal IgA is preferred in the URT because it neutralizes pathogens without activating complement-mediated inflammation. TRUE

**Fig. 1: Respiratory tract Trm generation and maintenance.**

From: Tissue resident memory T cells in the respiratory tract

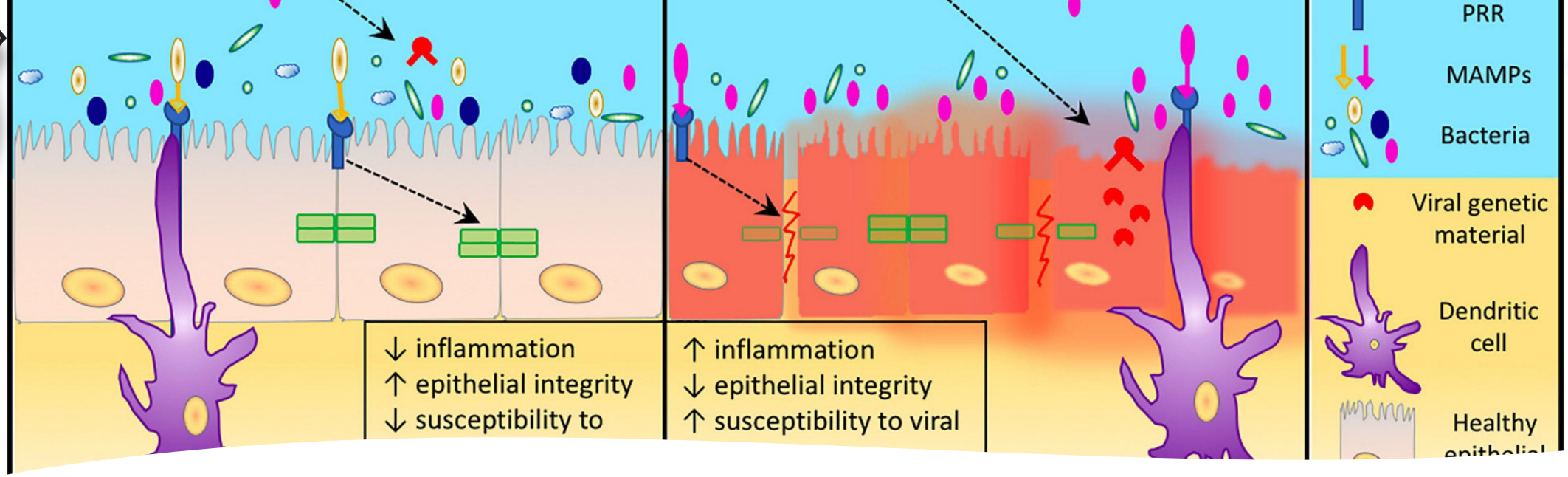



23. Th1 cells are essential for clearing extracellular pathogens from the respiratory tract. FALSE




Source: Zheng, M.Z.M., Wakim, L.M. Tissue resident memory T cells in the respiratory tract. Mucosal Immunol 15, 379–388 (2022).

- **Mucosal IgA:** blocks adhesion of viruses (influenza, RSV), bacteria (*S. pneumoniae*, *N. meningitidis*).
- **IgG in the LRT:** opsonizes encapsulated organisms.
- **Th17 cells:** potent mediators of mucosal defense against extracellular bacteria and fungi.
- **Th1 cells:** essential for clearing intracellular pathogens (e.g., *M. tuberculosis*, viruses).
- **Tissue-resident memory T-cells** in the airway epithelium: Provide rapid protection upon re-exposure.



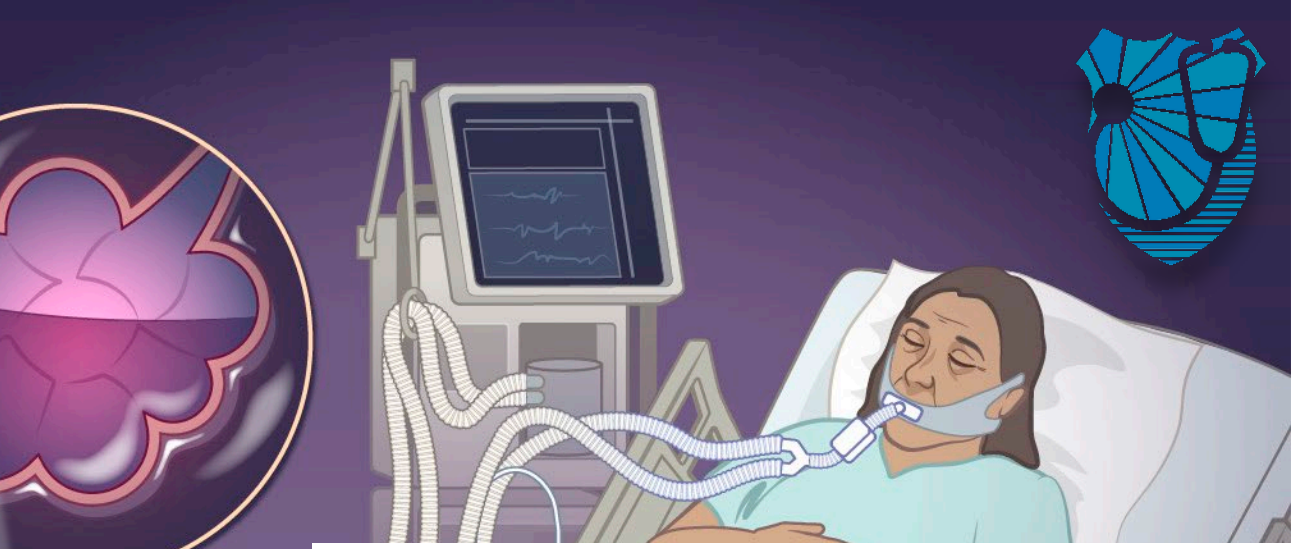

Source: Nesbitt H, Burke C and Haghi M (2021) Manipulation of the Upper Respiratory Microbiota to Reduce Incidence and Severity of Upper Respiratory Viral Infections: A Literature Review. Front. Microbiol. 12:713703. doi: 10.3389/fmicb.2021.713703

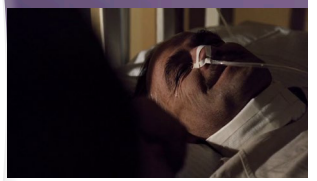
## How RTI Occurs When Host Defenses and Respiratory Microbiota are Impaired

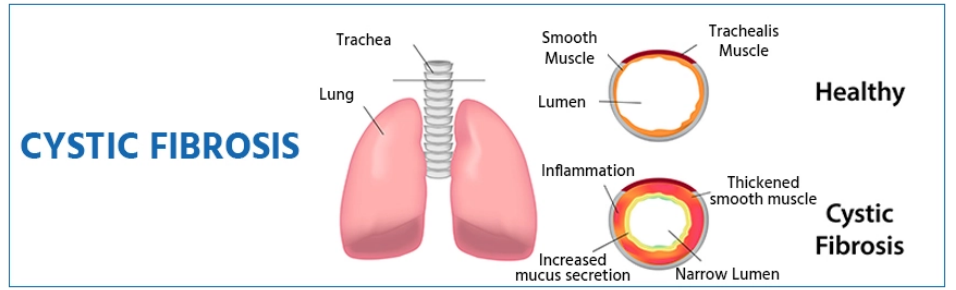
- Viral infections (RSV, influenza): Cause ciliary dyskinesia + Expose adhesion receptors + Reduce MΦ effector functions
- Antibiotics: Reduce microbial diversity → Expand resistant pathogen
- Smoking: Decreases ciliary beat frequency → Alters mucus flow and increases viscosity
- Chronic diseases (COPD, asthma): Promote mucus plugging and biofilm formation
- Aging & immunosuppression impair all levels of defense.
- Dysbiosis + weakened defenses = pathogen overgrowth + invasion.

13. Antibiotics reduce respiratory infection risk by elimination of pathogenic bacteria.
FALSE
Antibiotic use reduces microbial diversity in the respiratory tract, leading to dysbiosis and expansion of resistant pathogens, which may increase rather than decrease the risk of respiratory infections.

# Examples of Microbiota Shifts Leading to RTIs





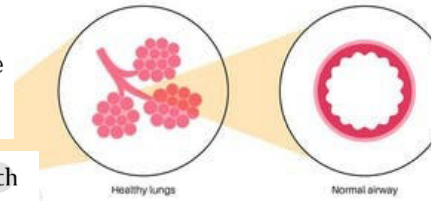



- Pneumococcal pneumonia: URT carriage and enhanced adhesion after viral infection.
- Otitis media in children: microbial imbalance favoring *Moraxella* and *Haemophilus*.
- Cystic fibrosis: viscous mucus → chronic colonization with *Pseudomonas aeruginosa* and *Burkholderia cepacia*.
- Ventilator-associated pneumonia (VAP): bypassed mechanical defenses + biofilm formation on endotracheal tubes.
- Aspiration pneumonia: alcohol and neurologic impairment → loss of epiglottic reflexes.

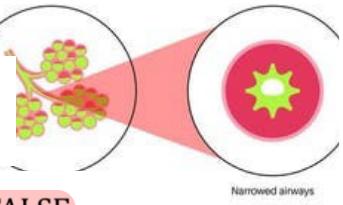
ASPIRATION PNEUMONIA

14. Ventilator-associated pneumonia occurs because intubation bypasses multiple innate mechanical defenses. TRUE

24. Ventilator-associated pneumonia occurs since mechanical defenses are bypassed with biofilm formation by bacteria n endotracheal tubes. TRUE




16. Aspiration pneumonia results from altered host reflexes rather than increased bacterial virulence. TRUE



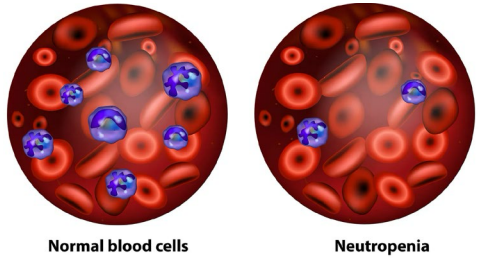

6. Aspiration pneumonia is invasion of environmental bacteria through inhalation. FALSE

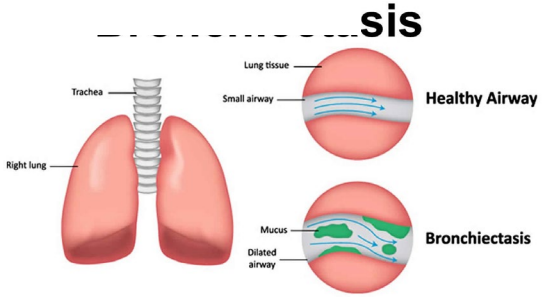
Aspiration pneumonia results from the aspiration of oropharyngeal flora due to impaired protective reflexes (e.g., loss of epiglottic or cough reflexes), not from inhalation of environmental bacteria.

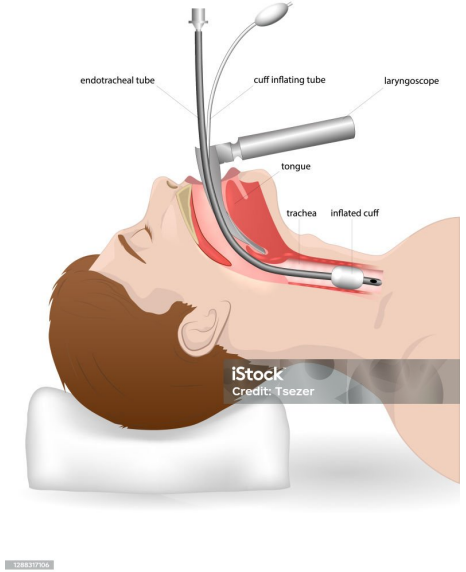
# Examples Impaired Host Defenses Leading to RTIs

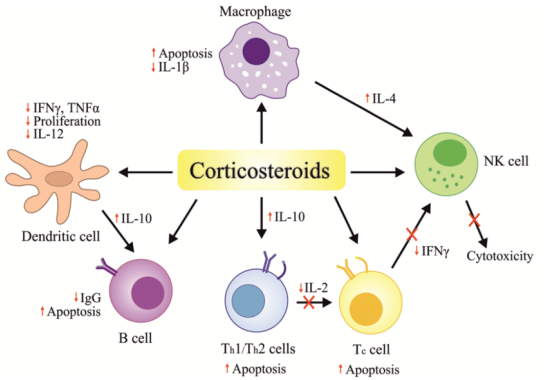
- Corticosteroids → decreased macrophage and neutrophil activation
- Chemotherapy → neutropenia, HIV/AIDS → loss of Th17 and MΦ dysfunction
- Structural abnormalities (bronchiectasis) → impaired clearance
- Intubation and mechanical ventilation → direct breach of first-line barriers

17. Corticosteroids increase respiratory infection risk by suppressing innate immune cell activation. TRUE



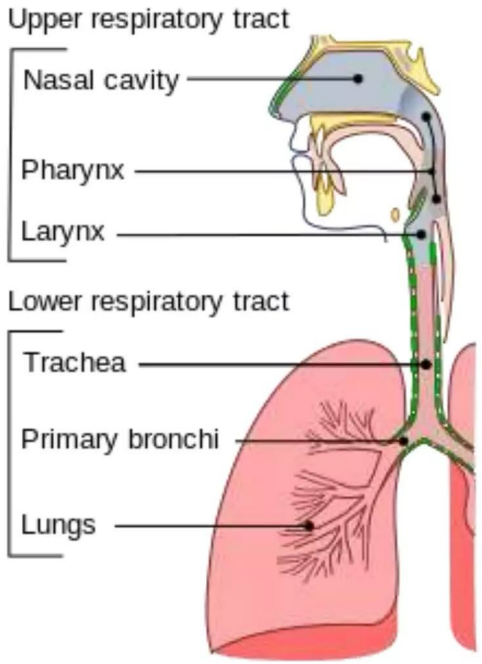



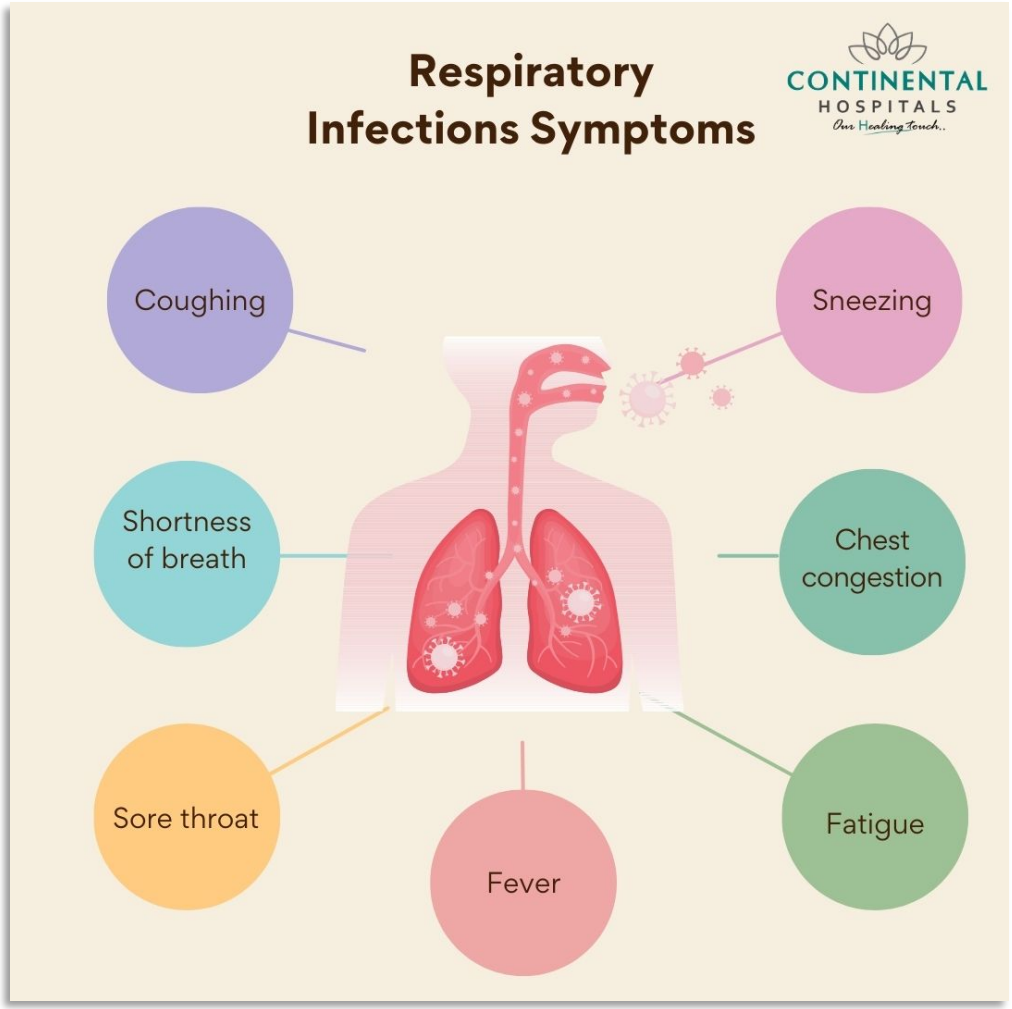
# Spectrum of RTIs and manifestations

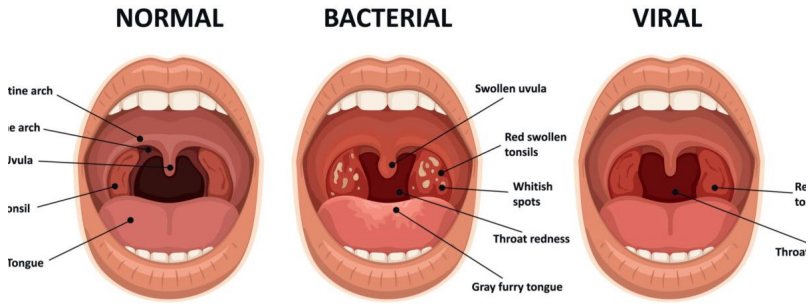
## Spectrum

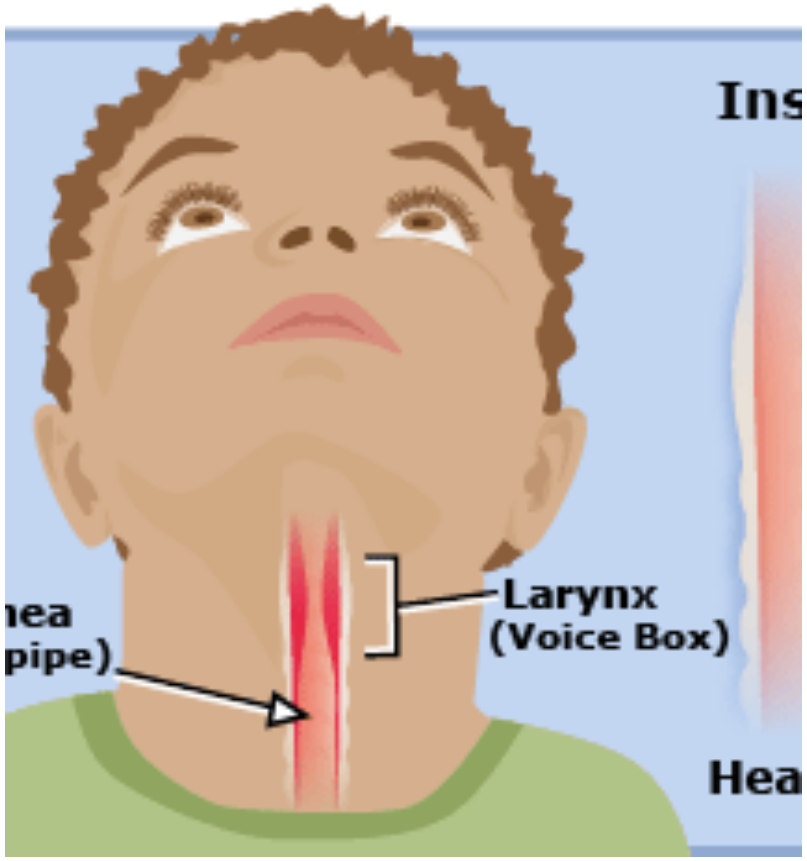
Rhinitis
↓
Tonsillitis
↓
Sinusitis
↓
Otitis media
↓
Pharyngitis
↓
Epiglottitis
↓
Laryngitis

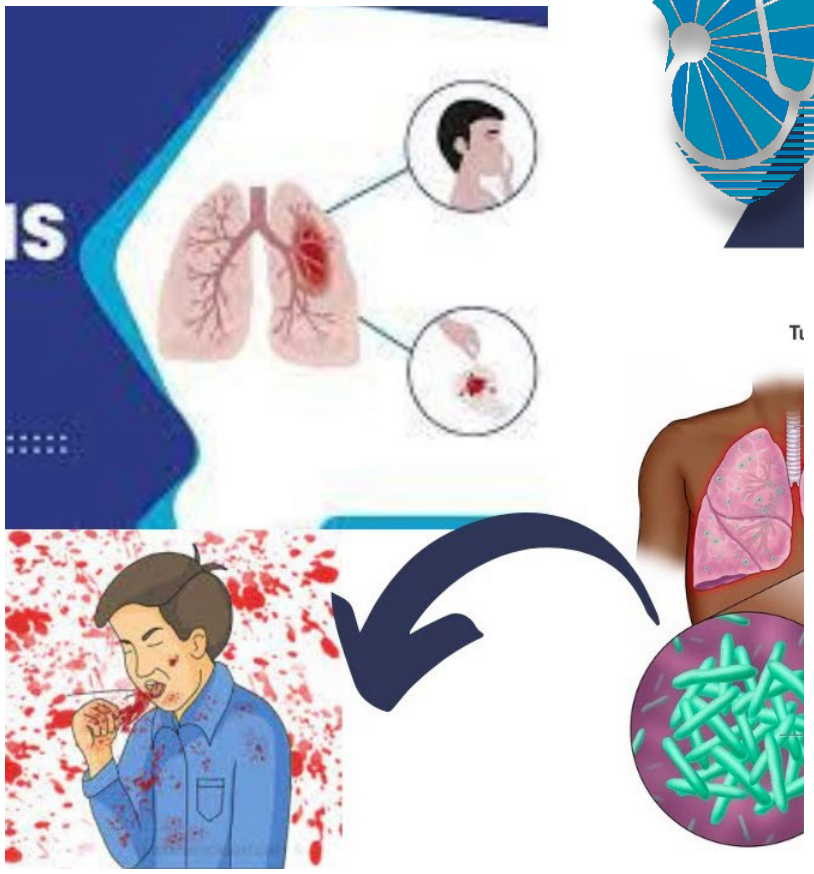


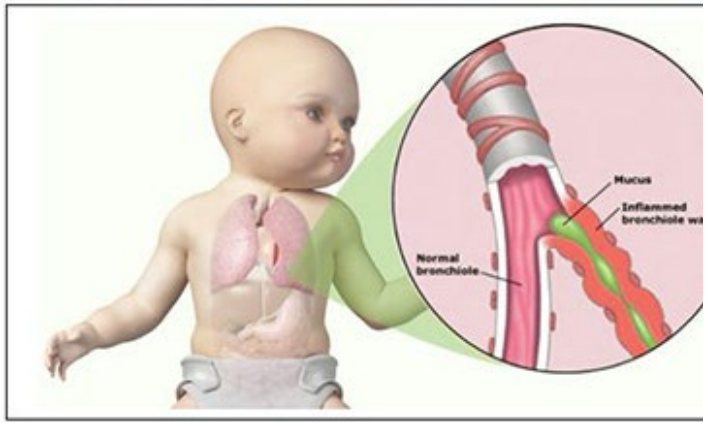

Tracheitis
↓
Bronchitis
↓
Bronchiolitis
↓
Pneumonia
↓
Pleurisy






# Spectrum of RTIs and manifestations

# Thank You…
# Wishing You All the Best!