

Vulnerability of Respiratory Tract

- Aerogenous exposure
 - Extensive surface area exposed (human - 200 m²)
 - Large volume of air (human – 9,000 l/day)
 - High concentration of noxious agents in air
- Bloodborne exposure
 - Entire cardiac output of right ventricle
 - Extensive surface area of capillary bed (human –70 m²)

Particle Deposition and Clearance

- Deposition – particle trapping
 - Impaction
 - $> 10 \mu\text{m}$ - nasal mucosa
 - 2-10 μm - tracheal and bronchial bifurcation
 - Sedimentation/diffusion – $< 2 \mu\text{m}$ – broncho-alveolar region
- Clearance – sneezing, coughing, mucociliary clearance and phagocytosis most important
- Retention = deposition - clearance

Factors Important in Particle Deposition/Clearance

■ Particle characteristics

■ Size

- Infective aerosols – particles $< 2\mu\text{m}$

■ Shape

- Some long slender particles, e.g. asbestos, bypass normal clearance mechanisms

■ Chemical nature e.g. inert vs reactive

■ Host characteristics

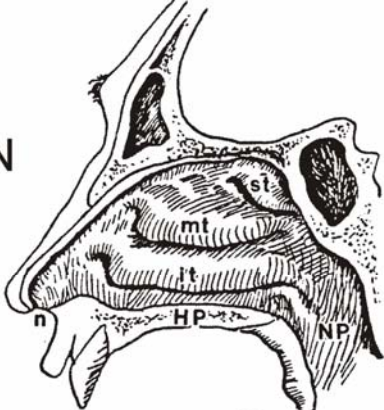



■ Species differences

- Nasal cavity complexity
- Bronchial branching and cells distribution

■ Individual status

- Prior damage
- Immune system

Comparative Nasal Airway Structure and Function

	Human	Monkey	Rat	
<p>HUMAN</p> 	Human	Monkey	Rat	
<p>MONKEY</p> 	Volume (cm ³)	8	0.4	
<p>RABBIT</p> 	Turbinate Anatomy	Simple	Complex	
<p>RAT</p> 	Olfactory Epithelial Surface Area	Small <10%	Moderate 20-30%	Large 50%
	Breathing	Oronasal	Oronasal	Nasal

Normal Flora

- Normal bacterial flora present in extrathoracic respiratory tract
- Varies by species
- Includes those that are considered pathogens e.g. *P. multocida*, *M. haemolytica*, *B. bronchiseptica*
- Pili of normal flora adhere to receptors - prevent colonization by pathogens (competitive inhibition)
- Cleared from intrathoracic respiratory system by defense mechanisms

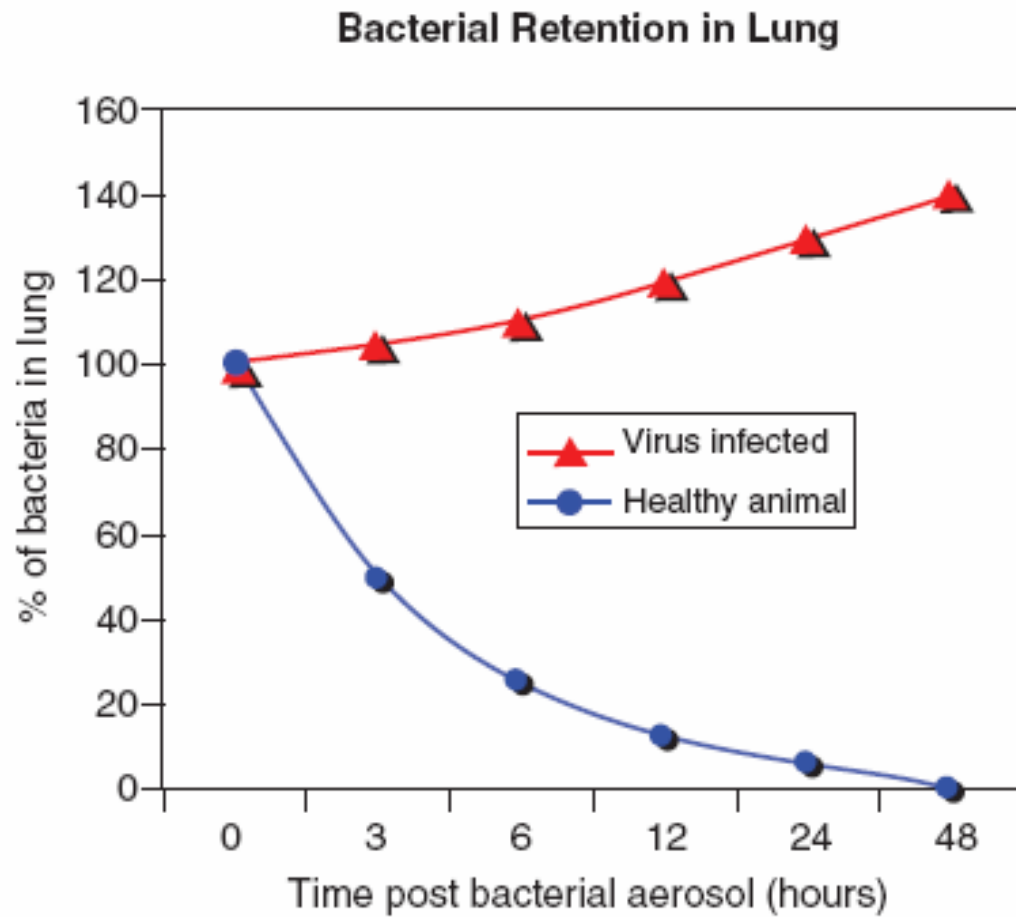


Fig. 9-7 Pulmonary clearance and retention of bacteria following inhalation of an experimental aerosol of bacteria.

Acknowledgment: this and subsequent tables from A. Lopez (2006) Respiratory system. In: *Special Pathology*. 2nd Edn. McGavin and Zachary, Eds, In press.

Main Defense Mechanisms of the Respiratory System

Conducting system (nose, trachea and bronchi)	Mucociliary clearance, antibodies, lysozyme, mucus
Transitional system (bronchioles)	Clara cells, antioxidants, lysozyme, antibodies
Exchange system (alveoli)	Alveolar macrophages (inhaled pathogens), intravascular macrophages (circulating pathogens), opsonizing anti- bodies, surfactant, antioxidants

Defense Mechanisms – Mucociliary Clearance

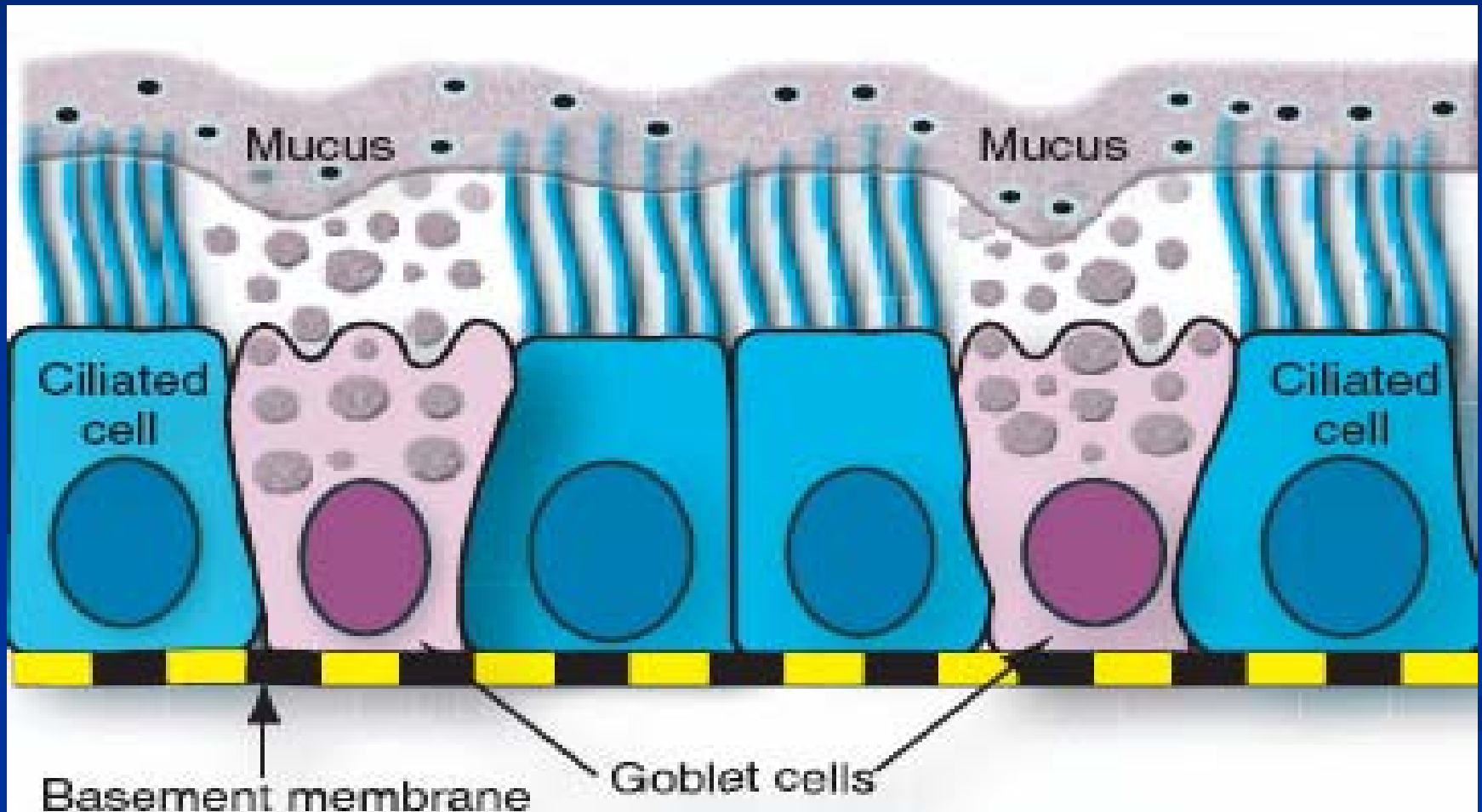


Table 9-2 Defense Mechanisms Provided by Some Cells and Secretory Products Present in the Respiratory System

Cell/Secretory Product	Action
Alveolar macrophage	Phagocytosis, main line of defense against inhaled particles and microbial pathogens in the alveoli
Intravascular macrophage	Phagocytosis, removal of particles, endotoxin, and microbial pathogens in the circulation
Ciliated cells	Expel mucus and inhaled particles and microbial pathogens by ciliary action
Clara cells	Detoxification of xenobiotics (mixed function oxidases) and protective secretions against oxidative stress and inflammation

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Cell/Secretory Product	Action
Mucus	Traps inhaled particles and microbial pathogens and neutralizes soluble gases
Surfactant	Protects alveolar walls and enhances phagocytosis
Lysozyme	Antimicrobial enzyme
Transferrin and lactoferrin	Inhibition and suppression of bacterial growth
α_1 -Antitrypsin	Protects against the noxious effects of proteolytic enzymes release by phagocytic cells; also inhibits inflammation
Interferon	Antiviral agent and modulator of the immune and inflammatory responses