

## Case #1

- Two year old male had an upper respiratory infection for 2 weeks. Ten days after the respiratory infection began, he had anorexia and lethargy. He was seen in the emergency room the next day with a fever of 39.0°C, clear chest, exudative pharyngitis, and bilaterally enlarged cervical lymph nodes. A throat culture was taken, and he was placed on amoxicillin. His course worsened, becoming increasingly lethargic for two more days. Finally, he developed respiratory distress and was admitted to the hospital. The throat culture was negative for *Streptococcus pyogenes*. On admission he was febrile at 38.9°C with an exudate in the posterior pharynx as a yellowish thick membrane which bled when scraped. He eventually developed heart failure and died.

## Case #2

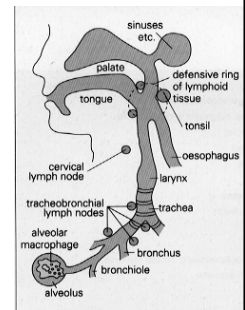
- 5 - week old male was admitted to the hospital with 10 day history of choking spells. Spells began with repetitive coughing, progressing to his turning red and gasping for breath. Lately had been vomiting with coughing. Pulse was 160, respiration 72, clear chest X-ray, fever of 38.0°C. No tracheal abnormalities. WBC 15,500/mm<sup>3</sup> with 70% lymphocytes.

## Questions

- What causes pharyngitis?
- Host defenses involved?
- How does damage occur?
- What caused his heart failure?
- What can we do to save the patient?
- Why antibiotic treatment did not help?

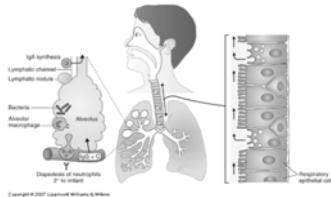
## Respiratory Bacteria: Basic Pathogenesis

- **Upper respiratory tract (URT)**
  - ◆ Sinuses
  - ◆ Middle ear
  - ◆ Oropharynx
  - ◆ Trachea
  - ◆ Bronchi
  - ◆ Bronchioles
- **Lower respiratory tract (LRT)**
  - ◆ Alveoli and bronchoalveoli
  - ◆ alveolar macrophages



## DEFENSES

- **Structural**
  - ◆ Mucus
  - ◆ Ciliated epithelium
- **Mechanical**
  - ◆ Glottal reflex
  - ◆ Coughing
- **Cellular**
  - ◆ Alveolar macrophages (lower)
  - ◆ Neutrophils - with inflammation
- **Fluid**
  - ◆ IgA (upper)
  - ◆ IgG and complement transudation from blood (lower)



## DISEASES

- **Pharyngitis** - sore throat (only 5-10% are bacterial)
  - ◆ *S. pyogenes*, *C. diphtheriae*, etc.
- **Localized URT infection with systemic consequences**
  - ◆ Whooping cough---pertussis toxin
  - ◆ Diphtheria---diphtheria toxin
- **Pneumonias - infection of the LRT and lung parenchyma**
  - ◆ *S. pneumoniae*, *L. pneumophila*, *Mp. pneumoniae*, *Mb. tuberculosis*, *H. influenzae*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *C. pneumoniae*.
- **Otitis media** - middle ear infection
  - ◆ *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*
- **Epiglottitis**
  - ◆ *H. influenzae* type b

## ENCOUNTER

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- Human
  - ◆ *Bordetella pertussis*
  - ◆ *Streptococcus pneumoniae*
  - ◆ *Chlamydia pneumoniae*
  - ◆ *Mycoplasma pneumoniae*
  - ◆ *Mycobacterium tuberculosis*
- Environment
  - ◆ *Legionella pneumophila* (non-contagious)
  - ◆ Atypical *Mycobacteria*
  - ◆ *Pseudomonas aeruginosa*

## ENTRY

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- Infection of URT
  - ◆ *C. diphtheriae*
  - ◆ *B. pertussis*
  - ◆ *Mp. pneumoniae*
- Colonization of URT followed by aspiration into LRT
  - ◆ *S. pneumoniae*
- Inhalation into LRT from droplets
  - ◆ *M. tuberculosis*
  - ◆ *L. pneumophila*
- Hematogenous infection of the lung
  - ◆ viridans streptococci

## DAMAGE

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- Local damage
  - ◆ *S. pneumoniae* (can be systemic)
  - ◆ *Mp. pneumoniae*
- Systemic damage
  - ◆ Diphtheria toxin
  - ◆ Pertussis toxin
- Spreading
  - ◆ Extracellular
    - *S. pneumoniae*
  - ◆ Intracellular
    - *M. tuberculosis*
    - *L. pneumophila*

## MULTIPLICATION

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- Intracellular
  - ◆ Phagosome/phagolysosome
    - *Mycobacterium*
    - *Legionella*
    - *Chlamydia*
- Extracellular
  - ◆ Serous exudates
  - ◆ Fastidious
    - *B. pertussis* - bordet-gengou agar
    - *C. diphtheriae* - serum tellurite

## EVASION OF DEFENSES

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- URT
  - ◆ IgA & ciliated cells
- LRT
  - ◆ Complement, alveolar macrophages & IgG
- Predisposing conditions?
  - ◆ chronic obstructive airway disease
  - ◆ physical obstruction (foreign object)
  - ◆ impairment of glottal/cough reflex
  - ◆ mucociliary elevator (smoking, alcoholism)
  - ◆ viral infection
  - ◆ loss of consciousness

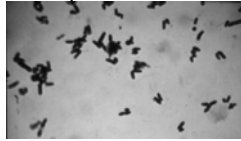
## DAMAGE

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- Host immune response
  - ◆ Inflammation
    - *S. pneumoniae*
    - *H. influenzae*
    - *Mycoplasma*
  - ◆ Cell-mediated immunity
    - *Mycobacteria*
    - *Legionella*
- Toxins
  - ◆ *C. diphtheriae*
  - ◆ *B. pertussis*

## Diphtheria: *Corynebacterium diphtheriae*

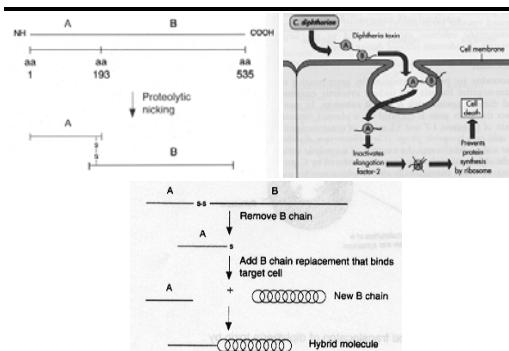
- Gram positive rod
- Encounter -- only from humans by inhalation
- Entry
  - ◆ Restricted to URT
- Spread - none
- Multiplication- fastidious
  - ◆ use serum tellurite
- Evade defenses - not much to deal with in URT
- Damage
  - ◆ Diphtheria toxin



## Diphtheria toxin

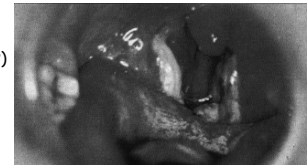
- Encoded on bacteriophage
  - ◆ lysogenic conversion
- A-B type toxin
  - ◆ ADP ribosylates Elongation Factor -2 (EF-2)
  - ◆ Damaging heart, nerve and kidneys, etc.
    - Heparin-binding epidermal growth factor
    - Death from heart/nervous system damage
  - ◆ Potential use of the DT toxin
    - Immunotoxin

## Diphtheria toxin



## Diphtheria

- Symptoms
  - ◆ Pharyngitis
  - ◆ Pseudomembrane
    - Necrosis by toxin, inflammatory cells, fibrin
  - ◆ Fever
- Vaccine
  - ◆ Toxoid induced IgG (DTP)
- Treatment
  - ◆ Antibiotics
  - ◆ Anti-toxin
- Transmission
  - ◆ Respiratory droplet (highly contagious)



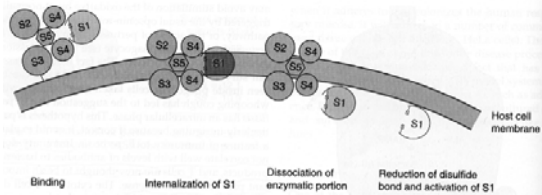
## Whooping cough - *Bordetella pertussis*

- Gram-negative rod
  - ◆ Primarily in infants and children
  - ◆ "Violent cough", "the cough of 100 days"
- Encounter - only from humans by inhalation
- Entry - restricted to URT, adherence to ciliated epithelium - FHA, pili
- Spread - None
- Evade defenses - ?
- Multiplication - fastidious
  - ◆ Bordet-Gengou or other special plates

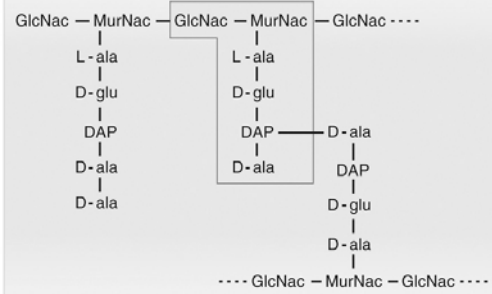
## DAMAGE

- Pertussis toxin
  - ◆ A-B type toxin, ADP-ribosylates G protein increasing cAMP
  - ◆ Localized tissue damage
  - ◆ Systemic toxicity (hypoglycemia, leukocytosis, neurological damage, etc.)
- Tracheal cytotoxin (TCT)
  - ◆ Peptidoglycan building block derivative
  - ◆ Loss of ciliated cells
  - ◆ Stops mucus flow

## Pertussis toxin



## Tracheal cytotoxin (TCT)

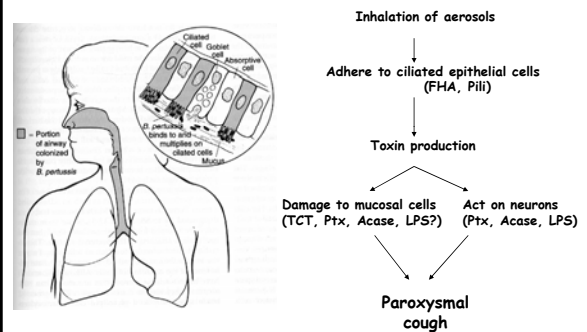


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## Whooping cough

- Symptoms
  - ◆ Severe coughing, spasms, inspiratory whoop
  - ◆ Lymphocytosis
- Stages of disease
  - ◆ Catarrhal → Paroxysmal → Convalescent
- Transmission--highly contagious
  - ◆ Inhalation or direct contact with secretion
- Usually self-limiting
  - ◆ Neurological sequelae
  - ◆ Secondary respiratory infections
  - ◆ Secondary aspiration pneumoniae
    - leading cause of death

## Whooping cough



## Clinical presentation of *B. pertussis* disease

	Incubation	Catarrhal	Paroxysmal	Convalescent
Duration	7-10 days	1-2 weeks	2-4 weeks	3-4 weeks (or longer)
Symptoms	None	Rhinorrhea, malaise, fever, sneezing, anorexia	Repetitive cough with whoops, vomiting, leukocytosis	Diminished paroxysmal cough, development of secondary complications (pneumonia, seizures, encephalopathy)
Bacterial culture				

## Vaccine

- Acellular vaccine
  - ◆ Pertussis toxoid + FHA
  - ◆ NIH sponsored trial in Sweden and Italy (1996):
    - 84% vs. 34% efficacy

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