

1. Professional vs. Opportunistic Pathogens

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Professional: Efficient entry, multiplication and spread.

-Obligate human pathogens;

- many viruses (e.g. Herpes, smallpox)
- some bacteria (e.g. *Chlamydia*, *B. pertussis*, Gonococcus)
- some parasites as part of life-cycle

-Facultative pathogens

- many parasites
- many bacteria (e.g. *V. cholerae*)
- some fungi
- some viruses (e.g. Influenza)

Opportunistic: Entry and multiplication require a breach in immunity; poor or no horizontal spread.

-many viruses, bacteria, parasites and fungi

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2. Bronchiectasis

Chest x-ray (bronchiectasis)



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3. *Pseudomonas aeruginosa*

***Pseudomonas aeruginosa* - an easy bug
to identify**

- A. Gram-negative rod, motile
- B. Aerobic, prototroph (no special growth requirements)
- C. Oxidase-positive (like *Neisseriae*)
- D. Fruity odor, greenish-blue color
- E. Some strains are mucoid (e.g. CF lung)

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4. *P. aeruginosa* - frequent opportunistic pathogen

**Why is *P. aeruginosa* a frequent
opportunistic pathogen?**

- A. Ubiquitous in moist environments
- B. Minimal nutritional requirements
 - can use a variety of organic compounds
 - has been cultured from dH₂O, lotions, disinfectants, sinks, vegetables
- C. Inherent and acquired antibiotic resistances
 - penicillins, cephalosporins, tetracyclines
 - chloramphenicol, vancomycin

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5. Requirements as an opportunist?

Requirements as an opportunist?

Requires a breach of the normal host defenses...

A. Local breaches:

- burn
- cut
- puncture (as from catheter or needle)
- abrasion (as from endotracheal tube, contacts)
- lung mucus defect

B. Systemic breaches:

- neutropenia (chemotherapy or other)
- diabetes

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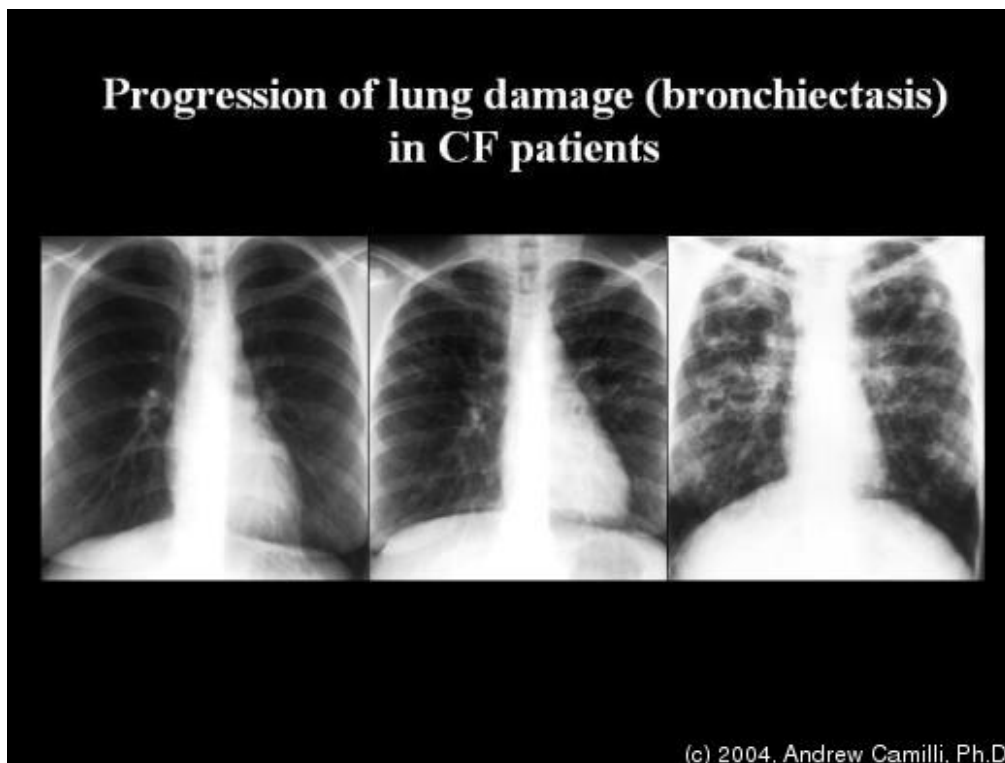
6. Major nosocomial pathogen

P. aeruginosa is a major nosocomial pathogen

- 11% of all nosocomial infections
- Leading cause of nosocomial pneumonia (12%)
- 2nd leading cause of burn wound infections (19%)
- 3rd leading cause of urinary tract infections
- 3rd leading cause of Gram-negative sepsis

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7. Progression of lung damage



8. Chronic lung infection

***P. aeruginosa* causes chronic lung infection in
cystic fibrosis patients**

- A. Opportunity
 - Genetic defect in cystic fibrosis transmembrane conductance regulator (CFTR), a membrane chloride transporter in epithelial cells. Results in a thick dehydrated sticky mucus that interferes with mucociliary action.
- B. Phenotypic conversion of *P. aeruginosa* to mucoid form
 - Constitutive production of alginate, an extracellular polysaccharide.
 - Decrease in motility and expression of toxins and proteases.
- C. Chronic infection acquired between 5 and 18 years, with no advance to sepsis

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9.

Virulence Factors

***P. aeruginosa* virulence factors**

A. Attachment:

Pili attach to damaged epithelium

B. Dissemination and nutrient acquisition:

Proteases: - Elastase; cleaves elastin, collagen, IgG, IgA,
complement, transferrin and α_1 -proteinase inhibitor
- Alkaline protease; interferes with γ -interferon pathway

Hemolysins: - Phospholipase C
- heat-stable hemolysin (a glycolipid)

Toxins: - Exotoxin A, inhibits host protein synthesis by
ADP-ribosylation of elongation factor 2

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10.

Virulence Factors (cont.)

***P. aeruginosa* virulence factors**

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B. Dissemination and nutrient acquisition:

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complement, transferrin and α_1 -proteinase inhibitor
- Alkaline protease; interferes with γ -interferon pathway

Hemolysins: - Phospholipase C
- heat-stable hemolysin (a glycolipid)

Toxins: - Exotoxin A, inhibits host protein synthesis by
ADP-ribosylation of elongation factor 2
- Exotoxin S, disrupts host cell function by
ADP-ribosylating G-proteins
- LPS (fever, hypotension)

C. Evasion of host immune defenses:

Alginate (anchors bugs, antiphagocytic and anti-complement)

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11. *L. pneumophila* - a fastidious bacteria

L. pneumophila -a fastidious bacteria

- A. Gram-negative rod, motile**
- B. Aerobic**
- C. Fastidious, requires cysteine and iron**
- D. Intracellular pathogen of amoebae**
 - can infect alveolar macrophages**

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12. Encountering *L. pneumophila*

Encountering *L. pneumophila*

- A. Multiplies in water reservoirs**
 - chlorine-resistant**
 - can thrive in 0 to 63°C waters**
- B. Aerosols can contain *L. pneumophila***
 - cooling towers, misters**

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13. Two different diseases caused by *L. pneumophila*

Two different diseases caused by *L. pneumophila*

1. Legionaire's disease

- 2 to 10 day incubation period
- fever, pneumonia
- 15% mortality
- 5% attack rate
- usually immunocompromised host

2. Pontiac fever

- 1 to 2 day incubation period
- fever, chills, headache, malaise
- self-limiting infection
- 90% attack rate
- attacks everyone

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14. Additional features

Additional features...

- No horizontal spread
- Median age of patients is 55
- 2/3 of patients are smokers or having underlying disease
- Risk factors: renal dialysis, immunosuppression therapy
cancer, emphysema, diabetes, smoking, alcohol

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15. Immune response to *L. pneumophila*

Immune response to *L. pneumophila*

- **Mucociliary clearance in healthy lung**
- **Cell-mediated immunity in infected lung:**
 - influx of PMNs which restrict growth
 - complement deposition
 - macrophage activation restricts growth
 - cytolytic T-cells destroy infected cells

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