PSEUDOMONAS AERUGINOSA AND OTHER NON-FERMENTING BACILLI

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OBJECTIVES
• Describe the type of patients who acquire Pseudomonas aeruginosa infections
• List major toxins produced by Pseudomonas aeruginosa and describe their principle effect on human cells.
• Discuss the association of Burkholderia cepacia complex and pulmonary infection in cystic fibrosis patients
• Describe the gene defect and resultant pathology of cystic fibrosis disease
**Pseudomonas aeruginosa**
and Other Non-Fermenting Bacilli

**OBJECTIVES**

- List diseases associated with *Stenotrophomonas maltophilia, Burkholderia cepacia complex, Burkholderia pseudomallei, Acinetobacter baumannii*,
- Name Non-Fermenting bacteria that are listed as potential bioterrorist agents

Some kid in PE told a shocker:
Bacteria lived in his locker!
(What bio-class beaker's
As rich as old sneakers
And socks full of microbes from soccer?)

Poem by A. M. Warren on OEDILF
Glucose Non-Fermenting Gram-Negative Bacilli

- Gram-negative, nonsporeforming bacteria, may be rods, or coccobacilli
- Obligate aerobes
- Good growth usually seen in 24 h
- Glucose not fermented
- Natural Habitat: water, soil, plants

The Oxidase Test

- Identify bacteria that produce cytochrome c oxidase, an enzyme of the bacterial electron transport chain.
  - Cytochrome c oxidase oxidizes the reagent (tetramethyl-p-phenylenediamine) to
**Pseudomonas aeruginosa**

**Key Characteristics**

- Gram negative rods
- Beta-hemolytic colonies
- Oxidase +

**Pseudomonas aeruginosa**

- Aerobic Gram negative rod
- Motile with polar flagella
- Mucoid polysaccharide slime layer
- Pili on cell surface

**Epidemiology**

- Environmental organism
- Grows in unsterile water, medications, disinfectants
- Hospital environment
- Moist areas
  - Sinks
  - Toilets
  - Cut flowers
  - Floor mops
  - Equipment
**Pseudomonas aeruginosa**

Infection

- Factors Predisposing to serious infection
  - Burn patients
  - Cystic fibrosis patients
  - Patients with hematologic malignancies
  - Immunocompromised patients
  - Can be part of the microbial flora in hospitalized patients and ambulatory, immunocompromised hosts

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**Pseudomonas aeruginosa**

Infection

Skin Infection

- Burn wounds
- Folliculitis
- Hot tubs, whirlpools, swimming pools, water slides
- Nail infections

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**Pseudomonas aeruginosa**

Infection

Pulmonary Infection

- Asymptomatic colonization
- Cystic fibrosis, chronic lung disease
- Severe necrotizing bronchopneumonia
- Most common cause of ventilator associated pneumonia (VAP)
**Pseudomonas aeruginosa**

**Infection**

- Urinary tract infections
- Ear infections
  - "Swimmers ear"
  - Malignant external otitis
  - Chronic otitis media
- Eye Infections
  - Bacteremia
  - Ecthyma gangrenosum
  - Endocarditis
  - IVDA and involves the tricuspid valve
  - Osteomyelitis

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**Pseudomonas aeruginosa**

**Infection**

- Bacteremia with ecthyma gangrenosum
  - EG is a well-recognized but uncommon cutaneous infection most often associated with a *Pseudomonas aeruginosa* bacteremia.
  - EG usually occurs in patients who are critically ill and immunocompromised and is almost always a sign of pseudomonal sepsis.

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**Pseudomonas aeruginosa**

**Infection**

Ecthyma gangrenosum

- Characteristic lesions are hemorrhagic pustules or infarcted-appearing areas with surrounding erythema that evolve into necrotic ulcers surrounded by erythema.
- The transformation of an early lesion to a necrotic ulcer may occur in as little as 12 h
**Pseudomonas aeruginosa**

**Virulence Factors**

- **Structural**
  - Capsule, Pili, LPS and pyocyanin
- **Toxins and Enzymes**
  - Exotoxin A
  - Exoenzyme S
  - Elastase
  - Others

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**Pseudomonas aeruginosa**

**Virulence Factors**

- **Exotoxin A**
  - Correlates with virulence
  - Blocks protein synthesis much like diphtheria toxin
    - Most likely contributes to dermatonecrosis in wounds and tissue damage in lungs
- **Exoenzyme S**
  - ADP-ribosylating toxin
  - Epithelial cell damage facilitates bacterial spread, tissue invasion and necrosis

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**Pseudomonas aeruginosa**

**Virulence Factors**

- **Elastase**
  - Results in tissue destruction and hemorrhagic lesions (ecthyma gangrenosum)
  - Two enzymes: Las A and Las B act synergistically to degrade elastin
  - Degrades complement components and inhibits neutrophil chemotaxis and function
**Pseudomonas aeruginosa**

**Lab Identification**

- **Culture**
  - Grows on blood producing spready colonies with a metallic sheen
  - Non-lactose fermenter on MacConkey agar
- **Identification**
  - Glucose Non-Fermenter
  - Oxidase positive
  - Beta hemolytic
  - Grape-like odor
  - Produces Pyocyanin-blue water soluble pigment (next slide)
  - Grows at 42°C

*Original Photo: P. Schreckenberger*

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**Pseudomonas aeruginosa**

**Lab Identification**

*Left: P. aeruginosa with blue-green pigmentation*  
*Right: Mucoid form of P. aeruginosa on MacConkey Agar*

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**Pseudomonas aeruginosa**

**Treatment**

- Resistant to many of the common antibiotics used for Gram negative infections
- Often not predictable
- Resistance due to several different mechanisms
- Combination therapy
**Burkholderia species**

- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- *Burkholderia cepacia complex*

**Burkholderia pseudomallei**

- Originally named *Pseudomonas*
- Changed to *Burkholderia* in 1992
- *B. mallei* and *B. pseudomallei* belong to a single genomospecies

**Burkholderia pseudomallei**

**Epidemiology**

- Habitat: soil, water, vegetation of S.E. Asia, 20° north and south of equator.
- Primarily found in India, Thailand, Vietnam, northern Australia. Also endemic in China, Taiwan, Laos
- Disease: Melioidosis
- Category B biothreat agent
**Burkholderia pseudomallei infection**

Melioidosis

- **Acute Disease:** septicemia with metastatic lesions. 95% mortality if untreated
- **Subacute Disease:** most common. TB like pneumonia with cellulitis and lymphangitis
- **Chronic Disease:** localized chronic cellulitis. Treat with antibiotics before draining otherwise become bacteremic

**Burkholderia cepacia complex**

- Formerly a Pseudomonas
- 18 species
- Recovered from water sources, wet surfaces, detergent solutions
- 60% isolated from respiratory tract infections
- Major clinical problem in patients with cystic fibrosis (CF) and chronic granulomatous disease (CGD)
- Urinary tract infections
- Septicemia
- Other opportunistic infections

**Overview of Cystic Fibrosis**

- Most common autosomal recessive genetic disease in Caucasians
- Caused by a mutation in gene: cystic fibrosis transmembrane conductance regulator (CFTR)
- Regulates components of sweat, digestive juices, mucus
- Persons without CF have two working copies of CFTR gene, only one is needed to prevent CF.
- CF develops when neither allele can produce a functional CFTR protein and therefore has autosomal inheritance.
- Approx. 1:25 persons of European descent, and 1:30 Caucasian Americans, carry CFTR gene mutation.
Overview of Cystic Fibrosis

- Mutation in CFTR results in defects in innate immunity including:
  - decreased nitric oxide levels
  - failure to internalize bacteria in bronchial epithelial cells
  - increased inflammation in CF airway
  - abnormal electrolyte transport causing thick, dry, sticky mucus

- Abnormal mucus adversely affects mucociliary clearance providing an ideal niche for chronic lung infection.

Overview of Cystic Fibrosis

- Over 85% of premature deaths in CF are due to cardiopulmonary failure secondary to chronic lung infection.
- In the US, median life expectancy is 37 years.
- Lung transplant is often necessary as CF worsens.
- CF may be diagnosed by many different methods including newborn screening, sweat testing, and genetic testing.

Burkholderia cepacia complex

- Resistant to most antibiotics
- Glucose non-fermenter
- May be yellow pigmented
- Slow oxidase positive

Original Photo: Paul C. Schreckenberger
**Stenotrophomonas maltophilia**

- First called Pseudomonas then Xanthomonas and now Stenotrophomonas
- Opportunistic infection
  - Bacteremia
  - Pneumonia
  - Meningitis
  - Wound infections
  - Urinary tract

**Epidemiology**

- Habitat:
  - Worldwide distribution
  - Soil, water, animals, vegetation, crops
  - Not part of normal skin or gastrointestinal flora but can be recovered from almost any clinical site
  - Respiratory tract most common (>60%)

**Infection**

- >95% of all clinical infections are hospital acquired
- 2nd leading cause of Gram-negative non-fermentative bacillary infections
- Hallmark of *S. maltophilia* disease is life-threatening systemic infections in debilitated patients (usually malignancy)
**Stenotrophomonas maltophilia**

**Lab Identification**

- Good growth on blood agar and MacConkey
- Oxidase negative
- Some strains have yellow pigment

**Stenotrophomonas maltophilia**

**Treatment**

- Multi-drug resistant organism
- Intrinsically resistant to carbapenems
- Report: “Drug of choice is trimethoprim-sulfamethoxazole (SXT)”

**Acinetobacter baumanii**

**Key Characteristics**

- Gram negative coccobacilli
- Non-lactose fermenter
- Oxidase – Chalky negative
**Acinetobacter baumanii**

**Epidemiology**
- **Habitat**
  - Free living in water and soil
  - Isolated foods, hospital air, inanimate objects, numerous human sources
  - Common gram-negative organism carried on skin of hospital personnel
  - Found on hospital equipment

**Infection**
- Low virulence
- Implicated in community acquired and nosocomial infections
- Recovered from numerous human sources: blood, sputum, urine, feces, vagina
- Found to colonize 45% of inpatient tracheostomy
- Often multi-drug resistant

**Lab Identification**
- Gram negative coccobacilli on Gram stain
- May be initially reported as Gram positive
- Good growth on blood agar and MacConkey
- Oxidase negative
- Non-motile
A gram-negative coccobacillus was recovered from the blood of a patient in the ICU. It was an oxidase-negative, organism, that grew on MacConkey agar and was initially reported as Gram positive cocci. An epidemiologic investigation revealed that the patient in the next room had the same kind of infection. What is the likely agent of infection in this case.

A. Acinetobacter baumanii  
B. Citrobacter koseri  
C. E. coli  
D. Listeria monocytogenes  
E. Neisseria meningitidis

A gram-negative rod grows as a colorless colony on a MacConkey agar plate. Further laboratory testing shows the organism is oxidase positive, does not ferment glucose, produces a sweet grape-like odor and grows at 42°C. Which of the following clinical infections is most likely to be caused by this organism?

A. Ear infection after swimming in a fresh water lake  
B. Melioidosis  
C. Community acquired urinary tract infection  
D. Community acquired pneumoniae  
E. Gastroenteritis following ingestion of contaminated water