PSEUDOMONAS

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Review questions

1. What is the clinical importance of Pseudomonas?
2. What are the salient cultural & biochemical features of Pseudomonas?
3. Write down the pathogenesis of Ps. Aeroginouusa?
4. Can pseudomonas cause infection in healthy individuals?
5. What are the predisposing factors for Pseudomonas infections?
6. What are the virulence factors of pseudomonas?
7. What is the mechanism of action of Exotoxin A?
8. Name some pigment producing bacteria?
9. Enumerate the diseases caused by Ps. Aeroginouusa.
10. How pseudomonas differs from Enterobacteriaceae?
- *Pseudomonas* is often encountered in hospital and clinical work because it is a major cause of hospital acquired (nosocomal) infections.
- Its main targets are immunocompromised individuals, burn victims, and individuals on respirators or with indwelling catheters.
- Additionally, these pathogens colonize the lungs of cystic fibrosis patients, increasing the mortality rate of individuals with the disease.
- Infection can occur at many sites and can lead to urinary tract infections, sepsis, pneumonia, pharyngitis, and a lot of other problems.
- Rarely cause of infection in healthy individuals. Its non-invasive nature limits its pathogenic capabilities.
Pseudomonads are motile, Gram-negative rods that utilize glucose oxidatively.

These bacteria are clinically important because
- they are resistant to most antibiotics
- they are capable of surviving in conditions that few other organisms can tolerate.

They also produce a slime layer that is resistant to phagocytosis.
Taxonomy

- **Family** – Psedomonadaceae
- **Important members**
  - *Pseudomonas aeruginosa*,
  - *P. alcaligenes*,
  - *P. chlororaphis*,
  - *P. fluorescens*,
  - *P. luteola*.
  - *P. mendocina*,
  - *P. monteilii*,
  - *P. pseudalcaligenes*,
  - *P. putida, P. stutzeri*
General Characteristics

- Gram-negative
  - Obligate Aerobe
  - motile
- Widely distributed in soil and water, human gut (10%)
  - diverse metabolic capabilities
  - many can grow in distilled water to $>10^6$ per ml
  - growth on wide range of carbon sources
  - readily available for nosocomial infections
- Susceptible to drying, airborne spread less likely
*Pseudomonas aeruginosa*

- *Pseudomonas aeruginosa* is the epitome of an **opportunistic pathogen** of humans.
- The bacterium almost never infects uncompromised tissues, yet there is hardly any tissue that it cannot infect, if the tissue defenses are compromised in some manner.
Pseudomonas aeruginosa is the most frequently isolated non-fermenter in the laboratory. It has several features that distinguish it from other species of Pseudomonas:

- It can grow at 42 degrees celsius
- Produces a bluish pigment (pyocyanin) and a greenish pigment
- Characteristic fruity odor
Important cultural properties

- Oxidase +
- Beta-hemolytic
- Characteristic odor and color
- Motile
Pathogenesis

- Disease rare in healthy individuals
  - chronic external otitis

- Disease most common in those with
  - natural immunologic deficiency
  - immunosuppressive therapy
  - burns
  - chronic pulmonary disease (cystic fibrosis)
  - IV narcotic use
  - renal dialysis

- Most common sites of infection: urinary tract, burns
Pathogenesis...

- Septicemia, abscesses
- Corneal infections
- Meningitis
- Bronchopneumonia
- Subacute endocarditis
List of Disease produced

1. Endocarditis.
2. Respiratory infections.
5. Ear infections including external otitis.
6. Eye infections.
8. Urinary tract infections.
10. Skin and soft tissue infections, including wound infections, pyoderma and dermatitis.
1. **Endocarditis.** *Pseudomonas aeruginosa* infects heart valves of IV drug users and prosthetic heart valves. The organism establishes itself on the endocardium by direct invasion from the bloodstream.

2. **Respiratory infections.** Respiratory infections caused by *Pseudomonas aeruginosa* occur almost exclusively in individuals with a compromised lower respiratory tract or a compromised systemic defense mechanism. Primary pneumonia occurs in patients with chronic lung disease and congestive heart failure. Bacteremic pneumonia commonly occurs in neutropenic cancer patients undergoing chemotherapy. Lower respiratory tract colonization of cystic fibrosis patients by mucoid strains of *Pseudomonas aeruginosa* is common and difficult, if not impossible, to treat.
**Bacteremia.** *Pseudomonas aeruginosa* causes bacteremia primarily in immunocompromised patients. Predisposing conditions include hematologic malignancies, immunodeficiency relating to AIDS, neutropenia, diabetes mellitus, and severe burns. Most *Pseudomonas* bacteremia is acquired in hospitals and nursing homes. *Pseudomonas* accounts for about 25 percent of all hospital acquired Gram-negative bacteremias.

**Central Nervous System infections.** *Pseudomonas aeruginosa* causes meningitis and brain abscesses. The organism invades the CNS from a contiguous structure such as the inner ear or paranasal sinus, or is inoculated directly by means of head trauma, surgery or invasive diagnostic procedures, or spreads from a distant site of infection such as the urinary tract.
- **Ear infections including external otitis.** *Pseudomonas aeruginosa* is the predominant bacterial pathogen in some cases of external otitis including "swimmer's ear". The bacterium is infrequently found in the normal ear, but often inhabits the external auditory canal in association with injury, maceration, inflammation, or simply wet and humid conditions.

- **Eye infections.** *Pseudomonas aeruginosa* can cause devastating infections in the human eye. It is one of the most common causes of bacterial keratitis, and has been isolated as the etiologic agent of neonatal ophthalmia. *Pseudomonas* can colonize the ocular epithelium by means of a fimbrial attachment to sialic acid receptors. If the defenses of the environment are compromised in any way the bacterium can proliferate rapidly and, through the production of enzymes such as elastase, alkaline protease and exotoxin A, cause a rapidly destructive infection that can lead to loss of the entire eye.
• Bone and joint infections.

- *Pseudomonas* infections of bones and joints result from direct inoculation of the bacteria or the hematogenous spread of the bacteria from other primary sites of infection. Blood-borne infections are most often seen in IV drug users, and in conjunction with urinary tract or pelvic infections. *Pseudomonas aeruginosa* has a particular tropism for fibrocartilagenous joints of the axial skeleton. *Pseudomonas aeruginosa* causes chronic contiguous osteomyelitis, usually resulting from direct inoculation of bone, and is the most common pathogen implicated in osteochondritis after puncture wounds of the foot.
Urinary tract infections.

- Urinary tract infections (UTI) caused by *Pseudomonas aeruginosa* are usually hospital-acquired and related to urinary tract catheterization, instrumentation or surgery. *Pseudomonas aeruginosa* is the third leading cause of hospital-acquired UTIs, accounting for about 12 percent of all infections of this type. The bacterium appears to be among the most adherent of common urinary pathogens to the bladder uroepithelium. As in the case of *E. coli* urinary tract infection can occur via an ascending or descending route. In addition, *Pseudomonas* can invade the bloodstream from the urinary tract, and this is the source of nearly 40 percent of *Pseudomonas* bacteremias.
Gastrointestinal infections.

- *Pseudomonas aeruginosa* can produce disease in any part of the gastrointestinal tract from the oropharynx to the rectum. As in other forms of *Pseudomonas* disease, those involving the GI tract occur primarily in immunocompromised individuals. The organism has been implicated in perirectal infections, pediatric diarrhea, typical gastroenteritis, and necrotizing enterocolitis. The GI tract is also an important portal of entry in *Pseudomonas* septicemia.
Skin and soft tissue infections, including wound infections, pyoderma and dermatitis.

- *Pseudomonas aeruginosa* can cause a variety of skin infections, both localized and diffuse. The common predisposing factors are breakdown of the integument which may result from burns, trauma or dermatitis; high moisture conditions such as those found in the ear of swimmers and the toe webs of athletes and combat troops, in the perineal region and under diapers of infants, and on the skin of whirlpool and hot tub users; neutropenia; and AIDS. *Pseudomonas* has also been implicated in folliculitis and unmanageable forms of acne vulgaris.
Virulence factors

1. Adhesins
2. Invasins
3. Motility/chemotaxis
4. Toxins
5. Antiphagocytic surface properties
6. Defense against serum bactericidal reaction
7. Defense against immune responses
8. Genetic attributes
9. Ecologic criteria
- **Adhesins**
  - fimbriae (N-methyl-phenylalanine pili)
  - polysaccharide capsule (glycocalyx)
  - alginate slime (biofilm)

- **Invasins**
  - elastase
  - alkaline protease
  - hemolysins (phospholipase and lecithinase)
  - cytotoxin (leukocidin)
  - siderophores and siderophore uptake systems
  - pyocyanin diffusible pigment
- **Motility/chemotaxis**
  - flagella

- **Toxins**
  - Exoenzyme S
  - Exotoxin A
  - Lipopolysaccharide

- **Antiphagocytic surface properties**
  - capsules,
  - slime layers
  - LPS
- Defense against serum bactericidal reaction
  - slime layers, capsules
  - LPS
  - protease enzymes

- Defense against immune responses
  - capsules, slime layers
  - protease enzymes
- **Genetic attributes**
  - genetic exchange by transduction and conjugation
  - inherent (natural) drug resistance
  - R factors and drug resistance
  - plasmids

- **Ecologic criteria**
  - adaptability to minimal nutritional requirements
  - metabolic diversity
  - widespread occurrence in a variety of habitats
Alginate (polysaccharide)

- Viscous gel around bacteria
- Coating may protect from phagocytosis in lung infections
- Only produces septicemia in patients with neutropenia
- Turned off in vitro, rapidly turned back on in vivo
Exotoxin A

- A:B toxin (1:1)
- Most clinical isolates, those without = less virulent
- Binds to receptor, internalized
- Regulation by iron
- Similar in structure, function to diphtheria toxin
Other Virulence Factors

- 90% pigmented
  - common diagnostic feature
  - involved in iron acquisition
- Pyocyanin
  - antibacterial, aids colonization
  - damages endothelial tissue \textit{in vitro}
  - formation of superoxide, peroxide
- Pyochelin mediates conversion of superoxide to hydroxyl
- Fluorescein: fluoresces in tissue
Broadly resistant to antibiotics, plasmid-mediated

Resistance mediated by loss of appropriate porins for entry

Treatment often fails, mortality > 80%
Reported susceptibilities

- Ureidopenicillins,
- Aminoglycosides,
- Ceftazidime,
- Fluoroquinolones,
- Carbapenems

Multiresistance may occur
Treatment

- Because *P. aeruginosa* is commonly resistant to antibiotics, infections are usually treated with two antibiotics at once. Pseudomonas infections may be treated with combinations of **ceftazidime** (Ceftaz, Fortraz, Tazicef), **ciprofloxacin** (Cipro), **imipenem** (Primaxin), **gentamicin** (Garamycin), **tobramycin** (Nebcin), **ticarcillin-clavulanate** (Timentin), or **piperacillin-tazobactam** (Zosyn).

- Most antibiotics are administered intravenously or orally for two to six weeks. Treatment of an eye infection requires local application of antibiotic drops.
Prevention

- Most hospitals have programs for the prevention of nosocomial infections. Patients with cystic fibrosis may be given periodic doses of antibiotics to prevent episodes of pseudomonas pneumonia.
- Minor skin infections can be prevented by avoiding hot tubs with cloudy water;
  - avoiding public swimming pools at the end of the day;
  - removing wet swimsuits as soon as possible; bathing after sharing a hot tub or using a public pool;
  - cleaning hot tub filters every six weeks; and using appropriate amounts of chlorine in the water.
Pseudomonas mallei

- Glanders in horses, transmitted to man
- Rare in the West, usually found in Asia, Africa, Middle East
- Necrosis of nasal mucus membranes, lymphatics, lymph nodes, skin
- Acute or chronic pneumonia may also occur
Burkholderia pseudomallei

- 15 species in genus, *B. cepacia* and *B. pseudomallei* only human pathogens
- *B. pseudomallei* causes melioidosis
  - endemic to Southeast Asia, Northern Territory of Australia; significant number of cases were diagnosed in returning Vietnam veterans
  - infection by exposure to organism in soil and surface water
Benign pulmonary disease

- Rapidly fatal septicemia with disseminated abscesses
- Latency leads to recrudescence (up to 26 years)

Virulence factors
- metalloprotease, serine protease
- lipase, phospholipase C, hemolysin
- lethal toxin not yet identified