Pseudomonas

What is pseudomonas?[1]

Pseudomonas spp. are Gram-negative rod bacteria commonly found in soil, ground water, plants and animals. Pseudomonal infection causes a necrotising inflammation.

- Pseudomonads include a number of true *Pseudomonas* species as well as many species formerly classified in the genus.
- Pseudomonads are natural residents of soil and water. They rarely cause infections in healthy individuals.
- In immunocompromised patients, systemic infections can occur which may be severe and associated with a high mortality.

- The genus *Pseudomonas* once comprised over 100 species but over the period of a decade many of these have been reclassified into different genera. The main groups of pseudomonads of medical interest are:

    - The fluorescent or 'true' *Pseudomonas* - *P. aeruginosa*, *P. fluorescens* and *P. putida*.
    - *Burkholderia* spp. - within this genus, there are at least 30 species but the medically important species are *B. cepacia*, *B. pseudomallei* and *B. mallei*, which are associated with human and animal infection:

        - *B. cepacia* is an important pathogen of pulmonary infections in people with cystic fibrosis.
        - *B. pseudomallei* is the causal agent of melioidosis, a life-threatening septic infection prevalent in Southeast Asia and Northern Australia.
        - *B. mallei* causes glanders, a rare disease in horses and other species.
        - Both *B. pseudomallei* and *B. mallei* must be handled in category 3 containment facilities and their exchange between laboratories is restricted.
    - *Delftia acidovorans* - occasionally found in clinical specimens and the hospital environment.
    - *Brevundimonas* spp. - *B. diminuta* and *B. vesicularis* are rare in clinical specimens and of doubtful clinical significance.
    - *Stenotrophomonas maltophilia*:

        - May be clinically significant in severely immunocompromised patients and is increasingly isolated from sputum of patients with cystic fibrosis.
        - The overall incidence in 2017 for *S. maltophilia* bacteraemia was 0.8 cases/100,000 population in England, Wales and Northern Ireland.

- *Sphingomonas paucimobilis* - *S. paucimobilis* has been found in clinical material and recovered from hospital equipment.

The rest of this article is specific for infections caused by *P. aeruginosa*.

Pseudomonas aeruginosa

P. aeruginosa is an opportunistic pathogen that can cause a wide range of infections, especially in immunocompromised people and people with severe burns, diabetes mellitus or cystic fibrosis.

P. aeruginosa is relatively resistant to many antibiotics, but effective antibiotics include imipenem, meropenem, ceftazidime, ciprofloxacin, amikacin, gentamicin, tobramycin, and piperacillin combined with tazobactam.

Between 2015 and 2016, the resistance patterns for key antimicrobial agents remained broadly stable with small decreases in resistance for gentamicin (4% to 3%) and tobramycin (4% to 3%). Increases in resistance to imipenem (9% to 11%), amikacin (1% to 2%) and piperacillin\tazobactam (6% to 7%) were observed over the same time period.[2]

How common is pseudomonas? (Epidemiology)[3]

- *P. aeruginosa* is found almost anywhere but rarely affects healthy people. Most community-acquired infections are associated with prolonged contact with contaminated water.
- In April 2017, the government extended the surveillance of bacteraemias caused by Gram-negative organisms to include *P. aeruginosa*.
- In 2018, there were 4745 reported cases of *Pseudomonas* spp. bacteraemia in England, Wales and Northern Ireland.[4] Between 2009 and 2018, there was a 10.7% increase in cases but there was a 3.5% decrease from 2017 notifications.

- Studies suggest that *P. aeruginosa* may colonise up to one third of patients admitted to hospital. However, whether or not this causes clinical infection depends on the immune status of the host.[5] Pneumonia, urinary tract infections, surgical wound infections and bloodstream infections are the most common pathologies.
- In hospitals, *P. aeruginosa* particularly contaminates moist/wet reservoirs such as respiratory equipment and indwelling catheters.
- *P. aeruginosa* is also a frequent cause of chronic respiratory infection in patients with cystic fibrosis. As many as 80% of cystic fibrosis patients may be colonised in the lung with *P. aeruginosa* and, once established, it is very resistant to antibiotic treatment.

Symptoms of pseudomonas infection (presentation)[6]

Respiratory tract

- Pneumonia is seen in patients with immunosuppression and chronic lung disease.
- There is an increased risk in patients on mechanical ventilation, patients with neutropenia and in patients with HIV infection.
- Chronic infection of the lower respiratory tract with *P. aeruginosa* is common in patients with cystic fibrosis.

Bacteraemia

- There is an increased risk for people in hospitals and nursing homes and these tend to have a high case fatality rate.
- Skin shows characteristic skin lesions (ecthyma gangrenosum), which are haemorrhagic and necrotic with surrounding erythema, and most often found in the axilla, groin or perianal area.

Endocarditis

- May infect heart valves in intravenous drug abusers and also prosthetic heart valves.
- Thromboembolism may cause widespread infection, including in the central nervous system.

Central nervous system

- May cause meningitis and intracranial abscesses.
- Most infections result from direct spread from local structures (eg, the ear, mastoid or sinuses) but blood-borne spread may also occur.

Ear

- Common cause of chronic otitis media.
- May also cause otitis externa (including malignant otitis externa).

Eye

- In adults: common cause of bacterial keratitis, scleral abscess and endophthalmitis; risk factors include trauma and contact lenses.
- May cause ophthalmia neonatorum in neonates.
- Infection may also cause orbital cellulitis.

Bones and joints

- The spine, pelvis and sternoclavicular joints are the most common sites affected.
- Risk factors include penetrating trauma, peripheral arterial disease, intravenous drug abuse and diabetes.

Gastrointestinal

- The clinical severity of infection is very variable.
- Severe pseudomonal diarrhoea may occur in neonates.
- Enteritis may present with prostration, headache, fever and diarrhoea (Shanghai fever).
- *Pseudomonas* spp. typhlitis most often occurs in patients with neutropenia and presents with a sudden onset of fever, abdominal distension and increasing abdominal pain.

Urinary tract infections

- Urinary tract infections are usually hospital-acquired and related to catheterisation or surgery.
- Severe infections may lead to renal abscess and bacteraemia.

Skin

- Green nail syndrome: may develop in people whose hands are frequently immersed in water.
- Secondary infections can occur in patients with eczema and tinea pedis; presents with a blue-green exudate with a fruity odour. Is also an important cause of secondary infection of burns.
- Common cause of whirlpool or swimming pool folliculitis: pruritic follicular, maculopapular, vesicular or pustular lesions occur where the body has been immersed in water. May lead to subcutaneous nodules, deep abscesses, cellulitis and fasciitis.
- Suppurative thrombophlebitis may originate from an intravenous cannula in situ.

Diagnosing pseudomonas (investigations)

- Blood cultures.
- Local investigations, dependent on the site of infection - eg, CXR, sputum, stool, urine cultures.
- Investigation of underlying health problems - eg, FBC, diabetes control indicators.

Management of pseudomonas infection[7]

There are emerging patterns of resistance, including multi-drug resistant strains. Knowledge of local patterns of infection, susceptibility and resistance are important to guide prescribing decisions.

- Carbapenems (eg, meropenem), cephalosporins (eg, ceftazidime, cefepime), aminoglycosides (eg, gentamicin, tobramycin, and amikacin), and fluoroquinolones (eg, ciprofloxacin and levofloxacin) are generally used as first-line therapy until culture and sensitivity results are available.[1]

- Serious infections are usually treated with ticarcillin or piperacillin, often in combination with an aminoglycoside.
- Novel antibiotics and antibiotic combinations are being developed to overcome anticipated growth in antibiotic resistance - eg:
    - Ceftolozane-tazobactam.
    - Ceftazidime-avibactam.
    - Imipenem-cilastatin-relebactam.

Cystic fibrosis

Nebulised antipseudomonal antibiotic treatment has been shown to be effective and improve lung function in patients with cystic fibrosis. A Cochrane report concluded that tobramycin was supported by the most evidence, but further research was needed concerning quality of life, survival and nutritional outcomes.[8] There is some evidence that oral antibiotics may work just as well but high-powered trials are required.[9]

Pseudomonal meningitis

Treatment options for pseudomonal meningitis include intravenous ceftazidime, carbapenems (meropenem and imipenem), aminoglycosides (gentamicin, amikacin or tobramycin) and ciprofloxacin, often in combination with intrathecal (IT) agents such as aminoglycosides or colistin.[10]

Malignant otitis externa

Malignant otitis externa requires aggressive treatment with systemic combinations of antibiotics and surgery. Duration of treatment depends on the response to treatment, but reassessment should occur frequently - every 4-6 weeks.[11]

Eye infections

Eye infections: in cases of small superficial ulcers, topical therapy, consisting of an ophthalmic aminoglycoside or quinolone antibiotic is an alternative. Endophthalmitis requires aggressive antibiotic therapy (parenteral, topical and intraocular).

Urinary tract infections

Urinary tract infections: piperacillin/tazobactam combination or an aminoglycoside are the antibiotics of choice for severe infection. These drugs have a synergistic effect and can be given together.[12] Ciprofloxacin continues to be a preferred oral agent.

Burns

Burn sepsis: requires aggressive surgical debridement. Whirlpool baths should be avoided.[13]

Surgery

- Debridement of necrotic tissue.
- Removal of infected medical devices if possible.
- Malignant otitis requires debridement of granulation tissue and necrotic debris.
- Surgery may be required for bowel necrosis, perforation, obstruction or abscess drainage.
- Vitrectomy may be needed in cases of endophthalmitis.

Complications of pseudomonas[6]

- Thromboembolism from pseudomonal endocarditis may cause brain abscess, cerebritis, mycotic aneurysms.
- Local spread from ear infections can cause sinusitis, mastoiditis, osteomyelitis, cranial nerve palsy, venous thrombosis, meningitis and brain abscesses.
- Gastrointestinal infection can cause bowel perforation and peritonitis.
- Skin and soft tissue infections can cause gangrene.

Prognosis

- Prognosis depends on the site of infection and the underlying health of the individual patient.

- Acute fulminant infections (eg, bacteraemic pneumonia, septicaemia, burn sepsis and meningitis) are associated with significant mortality.

Prevention of pseudomonas

The following measures are important in all environments but especially in hospitals and nursing homes:

- Strict adherence to rules of general hygiene.
- Normal infection control measures should apply.
- Aseptic procedures - eg, Venflon® (peripheral (venous) cannula) and catheter insertion.
- Strict isolation is required for patients with severe burns.
- Proper cleaning, sterilisation and disinfection of reusable equipment.
- Prophylactic antibiotics are not recommended as they result in the emergence of resistant strains of bacteria.
- Vaccines against *P. aeruginosa* have been under development for several years but have yet to be marketed.[14] Targeted monoclonal antibody immunotherapies however, have progressed to clinical trials.[15]
- Studies using genomic sequencing show that some strains of *Pseudomonas* spp. rapidly colonise water supply systems in hospitals. Identification of these sources could enable appropriate preventative measures to be taken before clinical spread occurs.[5]

Further reading

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