

# Pseudomonas aeruginosa

## Summary

*Pseudomonas* are gram negative organisms with the ability to easily adapt to environmental challenges. *Pseudomonas aeruginosa* (*P. aeruginosa*) is the most relevant *Pseudomonas* species causing disease in humans.

*Pseudomonas aeruginosa* is considered an important opportunistic gram-negative bacterium, known to cause severe infections, particularly among immunocompromised hosts. *P. aeruginosa* is recognized as a concerning pathogen in acute care facilities, particularly in Intensive Care Units (ICUs) and long-term care facilities. Risk factors for *P. aeruginosa* infections include age, heart disease, diabetes mellitus, chronic pulmonary disease, antibiotic use and invasive procedures. The most common *P. aeruginosa*-associated infections include pneumonia, bacteremia, urinary tract infections, meningitis, skin and soft tissue infections.

*Pseudomonas* is intrinsically resistant to multiple antibiotics. Due to its innate resistance and keen capability to acquire additional resistance, therapeutic options are limited. Antibiotics from the Carbapenem group are considered an optimal resource for the treatment of serious infections. They are often considered the last option to treat an infection with *Pseudomonas*. The emergence and rapid spread of Carbapenem resistance is highly concerning and will be the focus of attention in this chapter.

## Agent

*Pseudomonas* are aerobic organisms, ubiquitous in soil, plants, water and animals. The predilection of this organism for water makes it an ideal pathogen in the setting of moist environments, such as in patients on mechanical ventilation or exposed to contaminated water.

*P. aeruginosa* virulence factors include the ability of forming biofilm and the ability to produce toxins that can destroy tissue. Given its affinity for moist environments and biofilm formation, *P. aeruginosa* is one of the most common pathogens associated with ventilator associated pneumonias and catheter associated urinary tract infections. The rates of *P. aeruginosa* infections are particularly high in ICUs and Nursing Homes.

The main concern with this organism is that *P. aeruginosa* has the intrinsic capability of resisting the action of most clinically available antibiotics. Mechanisms through which it resists antibiotics include, alluding the action of antibiotics by eliminating the channels known as porins, through which antibiotics enter the cell or, by altogether, actively expelling the antibiotic outside the cell utilizing an efflux pump.

*P. aeruginosa* also has encoded in its chromosome the capability of producing an enzyme that renders the organism resistant to the action of antibiotics from the beta-lactam group. The AmpC enzyme, hydrolyzes most penicillins and cephalosporins with the exception of cefepime.

Other than the AmpC enzyme, most other enzymes that hydrolyze antibiotics can be acquired by *P. aeruginosa* via DNA molecules known as plasmids, which are commonly transferred among bacteria. Many of the enzymes that render *P. aeruginosa* resistant to beta-lactams and monobactams (aztreonam), known as extended spectrum beta-lactamases (ESBLs) are acquired through plasmids. Plasmid exchange is highly frequent in nature.

Carbapenems, kill *P. aeruginosa* in a similar way that beta-lactams do but can penetrate through the cell much better than beta-lactams. They also tend to be more stable against many beta-lactamases than antibiotics from the beta-lactam group. Antibiotics in the carbapenem class include: imipenem, meropenem, ertapenem and doripenem. Of these, only imipenem,

meropenem and doripenem are active against *Pseudomonas aeruginosa*. Ertapenem has no activity against this organism.

Until recently, most of the carbapenem resistance observed in *P. aeruginosa* revolved around the loss of a specific channel [OprD] which made the organism impermeable to the drug. This mechanism confers resistance to imipenem and to a lesser to other carbapenems. In recent years the acquisition of novel extended spectrum beta-lactamases, particularly metallo-beta-lactamases have become a worldwide concern, as they effectively eliminate the use of carbapenems to treat *P. aeruginosa* infections, making infections close to untreatable.

## Transmission

Reservoir: *Pseudomonas* is not a common bacterium that inhabits the healthy human microbiome. Changes in the microbiome are typically necessary in order to develop long term colonization with this organism. The use of antimicrobial agents, gastrointestinal disease and diet may be predisposing factors. Individuals with chronic pulmonary diseases such as cystic fibrosis and bronchiectasis are also highly predisposed to colonization of their respiratory tract with *P. aeruginosa*.

*P. aeruginosa* can be found on inert surfaces in the healthcare setting, including stethoscopes, chairs, bedrails, door handles, elevators, respiratory therapy equipment, bronchoscopes, endoscopes, cleaning equipment such as mops and buckets and almost every piece of equipment used at bedside. It is also particularly commonly found in bathtubs, hot tubs, shower heads, water baths and sinks.

Less virulent community acquired infections caused by *P. aeruginosa* include hot tub associated folliculitis, otitis externa (swimmer's ear) and nail infections. Pneumonias associated to contaminated auto air conditioners and home humidifiers have also been reported. Long term colonization with this organism may occur but its true duration and prevalence is not known. Prevalence and duration of colonization appears to be lesser than for similar organisms from the *Enterobacteriaceae* or *Acinetobacter* groups.

Mode of Transmission:

- Exogenous
  - Through the hands of healthcare workers.
  - Through contaminated environmental surfaces.
- Endogenous
  - Transformation of an initially sensitive colonizing organisms that subsequently becomes resistant.

Period of communicability: Currently unknown.

## Clinical Disease

Incubation Period: There is no defined incubation illness period. Host specific factors and co-morbidities are the main predisposing factors for the development of infection.

Illness: The organism is known to cause the following diseases:

Bacteremia of unknown origin.

Infective Endocarditis.

Pneumonia

- Healthcare associated.
- Nosocomial.
- Ventilator associated.
- Community acquired.
- Urinary tract Infections.
- Osteomyelitis.
- Skin and Soft Tissue Infections.
  - Ecthyma gangrenosum.
  - Body piercing.
  - Hot tub folliculitis.
  - Paronychia.
- Ear Infections.
  - Simple otitis externa (swimmers ear).
  - Malignant otitis externa.
- Eye Infections.
  - Endophthalmitis.
  - Keratitis.

## Laboratory Diagnosis

Diagnosis is made based on clinical presentation and culturing of the organism.

## Treatment

*P. aeruginosa* that is not expressing multi-drug resistance may be treated with ceftazidime, cefepime, piperacillin-tazobactam, ticarcillin-clavulanic acid, ciprofloxacin or high dose levofloxacin. aminoglycosides such as gentamicin, tobramycin and amikacin, can be active against *Pseudomonas* but their toxicity, combined with lack of data demonstrating favorable outcomes, makes this antibiotic class less desirable as single therapy. The use of continuous or extended intravenous infusion rate of beta-lactams is preferred to interval dosing, as this maintains levels above the minimum inhibitory concentration at a constant rate.

Due to increased rates of resistance, carbapenems are often used to treat infections with *P. aeruginosa*. In the USA, carbapenems are only available for intravenous use. Once an organism is considered resistant to a carbapenem, it is considered resistant to all antibiotics in this category.

Treatment options are highly decreased if the organism is multi-drug resistant, carbapenem resistant organism. Rarely carbapenem-resistant *P. aeruginosa* (CRPA) will exhibit in vitro susceptibility to third and fourth generation cephalosporins such as ceftazidime and cefepime. These may only have utility for low inoculum infections, excluding life or limb threatening infections. Combination of ceftazidime/avibactam may sometimes be effective in the treatment of some strains of CRPA. At the time that this manuscript was written, the only other treatment considered as acceptable is colistin. Colistin toxicity is high and must be used with caution and only when needed.

## Surveillance

The prevalence of CRPA and carbapenemase-producing *P. aeruginosa* (CPPA) in the United States is not fully known but given its worldwide prevalence, it is assumed the prevalence is increasing at a rapid pace.

Routine screening for CRPA and CPPA is not currently recommended.

Screening for colonization may be considered for high risk populations and settings such as ICUs and nursing homes and/or, during outbreaks. Pros and cons must be considered by each organization. While rectal swabs are routinely used for surveillance purposes for other carbapenem resistant organisms, the utility of this method as a screening tool for CRPA and CPPA is debatable, as the organism primarily colonizes the respiratory tract.

Microbiologists and infection prevention professionals at each institution should determine the risk that CPPA carries at their institution and consider applicable options for surveillance and detection.

### *Laboratory criteria –*

*Pseudomonas* is easily grown in clinical laboratories. Most automated laboratory analyzers can accurately identify the organism. Clinical laboratories routinely use phenotypic patterns to advise clinicians of susceptibilities. Clinicians may infer resistance mechanisms based on susceptibility patterns, but this may be inaccurate as this organism may have multiple mechanisms contributing to resistance at once yet, not necessarily express it in a way that may be detectable based on phenotypes.

As previously mentioned, Beta-lactamases are abundant among *P. aeruginosa*. Beta-lactamases are classified into four major groups:

1. Extended Spectrum Beta-lactamases (ESBLs) that are inhibited by clavulanic acid.
2. Metallo-Beta-lactamases (MBL).
3. Cephalosporinases (AmpC).
4. Oxacillinases (OXA).

Much of the carbapenem resistance among *P. aeruginosa* is due to the production of metallo-beta-lactamases (MBLs). Currently, 10 subclasses of MBL enzymes are known. Of these, IMP and VIM are spread worldwide, including the US.

Most clinical laboratories do not have the capability of determining whether a carbapenem resistant organism is a carbapenemase producing organism or not. The number of laboratories acquiring technology that affords the capability of identifying these enzymes is increasing but at the present time, the use of advanced technologies that, not only can detect the presence of a carbapenemase but also identify enzyme class, is limited.

Detection of carbapenemase can be achieved by using the Modified Hodge Test (Attachment A). This test may be particularly useful for detection of KPCs and OXA48 but not NDMs. This is a basic technique available to many commercial and clinical laboratories. However, the results are subject to the interpretation of the user, typically matching levels of experience.

The presence or absence of Carbapenemase is suspected or confirmed as follows:

*Confirmed* – Identification of the enzyme by an experienced laboratory including CDC, CDC Regional Laboratories or State Laboratories.

*Probable* – A positive Modified Hodge Test in the hands of an experienced operator.

*Suspect* –Resistance to one carbapenem is used as predictor for resistance to all carbapenems. A *P. aeruginosa* is considered carbapenem resistant if the MIC is  $\geq 4$   $\mu\text{g/ml}$  for imipenem, meropenem or doripenem. *P. aeruginosa* should be always be assumed to be resistant to ertapenem.

#### Reporting:

Report all suspected or confirmed cases of Carbapenem resistant *P. aeruginosa* within 24 hours to the Epidemiology and Response Division (ERD) at 505-827-0006. Clinical isolates are to be forwarded to the State Public Health Laboratory (SLD) for further characterization. Information needed includes: patient's name, age, sex, race, ethnicity, home address, home phone number, occupation, and health care provider. Information should also be entered into NM-EDSS per established procedures.

#### Control Measures:

1. Case management: Individuals known to either have an infection with CRPA should receive appropriate antibiotic treatment. No decolonization strategies are established at the present time.
2. Contact management: Contact precautions should be instituted for patients known to have CRPA in acute care settings. Hand hygiene is at the core of prevention of transmission and must be emphasized. Device utilization should be minimized. Antimicrobial agents must be used exercising optimal clinical judgment and scientific evidence. Inappropriate antibiotics, incorrect antibiotics and/or incorrect dosing may lead to increased resistance.
3. Prevention: To prevent the spread of multi-drug resistance organisms (MDROs) in acute care settings, contact precautions should be instituted for patients known to have MDROs, including CRPA. In non-acute and/or long-term care settings, gowning and gloving should be done during secretion management, toileting and device manipulation. Unless the person represents a high risk for transmitting the organism, there is no need to restrict access to social and recreational activities. Education of staff about appropriate hand hygiene techniques, environmental cleaning and disinfection are crucial to prevent spread. Instituting solid antibiotic stewardship programs is indispensable to prevent further resistance development due to selective pressure.
4. Outbreak: Cohorting of staff and patients is recommended in the case of outbreaks. Surveillance cultures may or may not be helpful in the case of CRPA and will depend on specific scenarios. Chlorhexidine bathing has been found to be useful decreasing multidrug resistant healthcare associated infections and colonization rates, particularly in the ICU setting. This intervention may be particularly useful during an outbreak.
5. Precautions similar to those recommended for CRE by CDC should be observed. Please refer to CDCs toolkit at: <https://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf>.

## Management of *Pseudomonas aeruginosa* infections in Child Care Centers

Refer to recommendations above.

## References

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See *Pseudomonas* Fact Sheets ([English](#)) ([Spanish](#)).