

Pseudomonas aeruginosa

Pseudomonas aeruginosa is a common bacterium that can cause disease in animals, including humans. It is found in soil, water, skin flora, and most man-made environments throughout the world. It thrives not only in normal atmospheres, but also in hypoxic atmospheres, and has, thus, colonized many natural and artificial environments. It uses a wide range of organic material for food; in animals, the versatility enables the organism to infect damaged tissues or those with reduced immunity. The symptoms of such infections are generalized inflammation and sepsis. If such colonizations occur in critical body organs, such as the lungs, the urinary tract, and kidneys, the results can be fatal. Because it thrives on moist surfaces, this bacterium is also found on and in medical equipment, including catheters, causing cross-infections in hospitals and clinics. It is implicated in hot-tub rash. It is also able to decompose hydrocarbons and has been used to break down tarballs and oil from oil spills. On 29 April 2013, scientists in Rensselaer Polytechnic Institute, funded by NASA, reported that, during spaceflight inside the International Space Station, *P. aeruginosa* bacteria seem to adapt to the microgravity and the biofilms formed during spaceflight exhibited a column-and-canopy structure that has "not been observed on Earth".

Identification

It is a Gram-negative, aerobic, coccobacillus bacterium with unipolar motility. An opportunistic human pathogen, *P. aeruginosa* is also an opportunistic pathogen of plants. *P. aeruginosa* is the type species of the genus *Pseudomonas* (Migula).

Characteristics

Members of the genus display the following defining characteristics:

Rod-shaped

- Gram-negative
- One or more polar flagella, providing motility
- Aerobic
- Non-spore forming

- positive catalase test
- positive oxidase test.

Other characteristics that tend to be associated with *Pseudomonas* species (with some exceptions) include secretion of pyoverdine, a fluorescent yellow-green siderophore^[13] under iron-limiting conditions. Certain *Pseudomonas* species may also produce additional types of siderophore, such as pyocyanin by *Pseudomonas aeruginosa* and thioquinolobactin by *Pseudomonas fluorescens*. *Pseudomonas* species also typically give a positive result to the oxidase test, the absence of gas formation from glucose, glucose is oxidised in oxidation/fermentation test using Hugh and Leifson O/F test, beta hemolytic (on blood agar), indole negative, methyl red negative, Voges–Proskauer test negative, and citrate positive.

P. aeruginosa secretes a variety of pigments, including pyocyanin (blue-green), pyoverdine (yellow-green and fluorescent), and pyorubin (red-brown). King, Ward, and Raney developed *Pseudomonas* Agar P (King A medium) for enhancing pyocyanin and pyorubin production, and *Pseudomonas* Agar F (King B medium) for enhancing fluorescein production.

P. aeruginosa is often preliminarily identified by its pearlescent appearance and grape-like or tortilla-like odor *in vitro*. Definitive clinical identification of *P. aeruginosa* often includes identifying the production of both pyocyanin and fluorescein, as well as its ability to grow at 42°C.

P. aeruginosa is capable of growth in diesel and jet fuel, where it is known as a hydrocarbon-using microorganism (or "HUM bug"), causing microbial corrosion.^[3] It creates dark, gellish mats sometimes improperly called "algae" because of their appearance

Although classified as an aerobic organism, *P. aeruginosa* is considered by many as a facultative anaerobe, as it is well adapted to proliferate in conditions of partial or total oxygen depletion. This organism can achieve anaerobic growth with nitrate as a terminal electron acceptor, and, in its absence, it is also able to ferment arginine by substrate-level phosphorylation. Adaptation to microaerobic or anaerobic environments is essential for certain lifestyles of *P. aeruginosa*, for example, during lung infection in cystic fibrosis patients, where thick layers of lung mucus and alginate surrounding mucoid bacterial cells can limit the diffusion of oxygen.

Nomenclature

The word *Pseudomonas* means "false unit", from the Greek *pseudo* (Greek: $\psi\epsilon\upsilon\delta\omicron$, false) and *monas* (Latin: *monas*, from Greek: $\mu\omicron\upsilon\sigma$, a single unit). The stem word *mon* was used early in the history of microbiology to refer to germs, e.g., Kingdom Monera.

- The species name *aeruginosa* is a Latin word meaning verdigris ("copper rust"), as seen with the oxidized copper patina on the Statue of Liberty. This also describes the blue-green bacterial pigment seen in laboratory cultures of the species. This blue-green pigment is a combination of two metabolites of *P. aeruginosa*, pyocyanin (blue) and pyoverdine (green), which impart the blue-green characteristic color of cultures. Pyocyanin biosynthesis is regulated by quorum sensing, as in the biofilms associated with colonization of the lungs in cystic fibrosis patients. Another assertion is that the word may be derived from the Greek prefix *ae-* meaning "old or aged", and the suffix *ruginosa* means wrinkled or bumpy.
- The derivations of **pyocyanin** and **pyoverdine** are of the Greek, with *pyo-*, meaning "pus", *cyanin*, meaning "blue", and *verdine*, meaning "green". Pyoverdine in the absence of pyocyanin is a fluorescent-yellow color.

Genome

The genome of *P. aeruginosa* is relatively large (6-7 Mb) and encodes around 6,000 (predicted) open reading frames (ORFs), depending on the strain. There are 5,021 genes that are conserved across all five genomes analyzed, with at least 70% sequence identity. This set of genes is the *P. aeruginosa* core genome.

strain:	PA2192	C3719	PA01	PA14	PACS2
genome size (bp)	6,905,121	6,222,097	6,264,404	6,537,648	6,492,423
ORFs	6,191	5,578	5,571	5,905	5,676

The G+C-rich *Pseudomonas aeruginosa* chromosome consists of a conserved core and a variable accessory part. The core genomes of *P. aeruginosa* strains are largely collinear, exhibit a low rate of sequence polymorphism, and contain few loci of high sequence diversity, the most notable ones being the pyoverdine locus, the flagellar regulon, *pilA*, and the O-antigen biosynthesis locus. Variable segments are scattered throughout the genome, of which about one-third are immediately adjacent to tRNA or tmRNA genes. The three known hot spots of genomic diversity are caused by the integration of genomic islands of the pKLC102/PAGI-2 family into tRNA^{Lys} or tRNA^{Gly} genes. The individual islands differ in their repertoire of metabolic genes, but share a set of syntenic genes that confer their horizontal spread to other clones and species. Colonization of atypical disease habitats predisposes to deletions, genome rearrangements, and accumulation of loss-of-function mutations in the *P. aeruginosa* chromosome. The *P. aeruginosa* population is characterized by a few dominant clones widespread in disease and environmental habitats. The genome is made up of clone-typical segments in core and accessory genome and of blocks in the core genome with unrestricted gene flow in the population.

Cell-surface polysaccharides

Cell-surface polysaccharides play diverse roles in the bacterial "lifestyle". They serve as a barrier between the cell wall and the environment, mediate host-pathogen interactions, and form structural components of biofilms. These polysaccharides are synthesized from nucleotide-activated precursors, and, in most cases, all the enzymes necessary for biosynthesis, assembly, and transport of the completed polymer are encoded by genes organized in dedicated clusters within the genome of the organism. Lipopolysaccharide is one of the most important cell-surface polysaccharides, as it plays a key structural role in outer membrane integrity, as well as being an important mediator of host-pathogen interactions. The genetics for the biosynthesis of the so-called A-band (homopolymeric) and B-band (heteropolymeric) O antigens have been clearly defined, and much progress has been made toward understanding the biochemical pathways of their biosynthesis. The exopolysaccharide alginate is a linear copolymer of β -1,4-linked D-mannuronic acid and L-glucuronic acid residues, and is responsible for the mucoid phenotype of late-stage cystic fibrosis disease.

The *pel* and *psl* loci are two recently discovered gene clusters, which also encode exopolysaccharides found to be important for biofilm formation. A rhamnolipid is a biosurfactant whose production is tightly regulated at the transcriptional level, but the precise role it plays in disease is not well understood at present. Protein glycosylation, in particular of pilin and flagellin, is a recent focus of research by several groups, and it has been shown to be important for adhesion and invasion during bacterial infection.

Pathogenesis

An opportunistic, nosocomial pathogen

of immunocompromised individuals, *P. aeruginosa* typically infects the pulmonary tract, urinary tract, burns, wounds, and also causes other blood infections.

Infections	Details and common associations	High-risk groups
Pneumonia	Diffuse bronchopneumonia	Cystic fibrosis patients
Septic shock	Associated with a purple-black skin lesion ecthyma gangrenosum	Neutropenic patients
Urinary tract infection	Urinary tract catheterization	
Gastrointestinal infection	Necrotising enterocolitis (NEC)	Premature infants and neutropenic cancer patients
Skin and soft tissue infections	Hemorrhage and necrosis	Burns victims and patients with wound infections

It is the most common cause of infections of burn injuries and of the outer ear (otitis externa), and is the most frequent colonizer of medical devices (e.g., catheters). *Pseudomonas* can, in rare circumstances, cause community-acquired pneumonias, as well as ventilator-associated pneumonias, being one of the most common agents isolated in several studies.^[20] Pyocyanin is a virulence factor of the bacteria and has been known to cause death in *C. elegans* by oxidative stress. However, research indicates salicylic acid can inhibit pyocyanin production. One in ten hospital-acquired infections are from *Pseudomonas*. Cystic fibrosis patients are also predisposed to *P. aeruginosa* infection of the lungs. *P. aeruginosa* may also be a common cause of "hot-tub rash" (dermatitis), caused by lack of proper, periodic attention to water quality. The most common cause of burn infections is *P. aeruginosa*. *Pseudomonas* is also a common cause of postoperative infection in radial keratotomy surgery patients. The organism is also associated with the skin lesion ecthyma gangrenosum. *P. aeruginosa* is frequently associated with osteomyelitis involving puncture wounds of the foot, believed to result from direct inoculation with *P. aeruginosa* via the foam padding found in tennis shoes, with diabetic patients at a higher risk.

Toxins

P. aeruginosa uses the virulence factor exotoxin A to inactivate ADP-ribosylate eukaryotic elongation factor 2 in the host cell, much as the diphtheria toxin does. Without elongation factor 2, eukaryotic cells cannot synthesize proteins and necrotise. The release of intracellular contents induces an immunologic response in immunocompetent patients. In addition *P. aeruginosa* uses an exoenzyme, ExoU, which degrades the plasma membrane of eukaryotic cells, leading to lysis

Triggers

With low phosphate levels, *P. aeruginosa* has been found to activate from benign symbiont to express lethal toxins inside the intestinal tract and severely damage or kill the host, which can be mitigated by providing excess phosphate instead of antibiotics.

Plants and invertebrates

In higher plants, *P. aeruginosa* induces symptoms of soft rot, for example in *Arabidopsis thaliana* (Thale cress) and *Lactuca sativa* (lettuce). It is also pathogenic to invertebrate animals, including the nematode

Caenorhabditis elegans, the fruit fly *Drosophila* and the moth *Galleria mellonella*. The associations of virulence factors are the same for plant and animal infections.

Quorum sensing

Regulation of gene expression can occur through cell-cell communication or quorum sensing (QS) via the production of small molecules called autoinducers. QS is known to control expression of a number of virulence factors. Another form of gene regulation that allows the bacteria to rapidly adapt to surrounding changes is through environmental signaling. Recent studies have discovered anaerobiosis can significantly impact the major regulatory circuit of QS. This important link between QS and anaerobiosis has a significant impact on production of virulence factors of this organism. Garlic experimentally blocks quorum sensing in *P. aeruginosa*.

Biofilms and treatment resistance

Biofilms of *P. aeruginosa* can cause chronic opportunistic infections, which are a serious problem for medical care in industrialized societies, especially for immunocompromised patients and the elderly. They often cannot be treated effectively with traditional antibiotic therapy. Biofilms seem to protect these bacteria from adverse environmental factors. *P. aeruginosa* can cause nosocomial infections and is considered a model organism for the study of antibiotic-resistant bacteria. Researchers consider it important to learn more about the molecular mechanisms that cause the switch from planktonic growth to a biofilm phenotype and about the role of quorum sensing in treatment-resistant bacteria such as *P. aeruginosa*. This should contribute to better clinical management of chronically infected patients, and should lead to the development of new drugs.

Diagnosis

Depending on the nature of infection, an appropriate specimen is collected and sent to a bacteriology laboratory for identification. As with most bacteriological specimens, a Gram stain is performed, which may show Gram-negative rods and/or white blood cells. *P. aeruginosa* produces colonies with a characteristic "grape-like" or "fresh-tortilla" odor on bacteriological media. In mixed cultures, it can be isolated as clear colonies on MacConkey agar (as it does not ferment lactose) which

will test positive for oxidase. Confirmatory tests include production of the blue-green pigment pyocyanin on cetrimide agar and growth at 42°C. A TSI slant is often used to distinguish nonfermenting *Pseudomonas* species from enteric pathogens in faecal specimens.

Treatment

P. aeruginosa is frequently isolated from nonsterile sites (mouth swabs, sputum, etc.), and, under these circumstances, it often represents colonization and not infection. The isolation of *P. aeruginosa* from nonsterile specimens should, therefore, be interpreted cautiously, and the advice of a microbiologist or infectious diseases physician/pharmacist should be sought prior to starting treatment. Often no treatment is needed.

When *P. aeruginosa* is isolated from a sterile site (blood, bone, deep collections), it should be taken seriously, and almost always requires treatment

P. aeruginosa is naturally resistant to a large range of antibiotics and may demonstrate additional resistance after unsuccessful treatment, in particular, through modification of a porin. It should usually be possible to guide treatment according to laboratory sensitivities, rather than choosing an antibiotic empirically. If antibiotics are started empirically, then every effort should be made to obtain cultures, and the choice of antibiotic used should be reviewed when the culture results are available.

Phage therapy against *P. aeruginosa* remains one of the most effective treatments, which can be combined with antibiotics, has no contraindications and minimal adverse effects. Phages are produced as sterile liquid, suitable for intake, applications etc. Phage therapy against ear infections caused by *P. aeruginosa* was reported in the journal *Clinical Otolaryngology* in August 2009

Antibiotics that have activity against *P. aeruginosa* may include:

- aminoglycosides (gentamicin, amikacin, tobramycin, but *not* kanamycin)
- quinolones (ciprofloxacin, levofloxacin, but *not* moxifloxacin)
- cephalosporins (ceftazidime, cefepime, cefoperazone, ceftipime, ceftolozan, but *not* cefuroxime, cefotaxime)
- antipseudomonal penicillins: carboxypenicillins (carbenicillin and ticarcillin),

and ureidopenicillins (mezlocillin, azlocillin, and piperacillin). *P. aeruginosa* is intrinsically resistant to all other penicillins.

- carbapenems (meropenem, imipenem, doripenem, but *not* ertapenem)
- polymyxins (polymyxin B and colistin)^[34]
- monobactams (aztreonam)

These antibiotics must all be given by injection, with the exceptions of fluoroquinolones, aerosolized tobramycin and aerosolized aztreonam. For this reason, in some hospitals, fluoroquinolone use is severely restricted to avoid the development of resistant strains of *P. aeruginosa*. In the rare occasions where infection is superficial and limited (for example, ear infections or nail infections), topical gentamicin or colistin may be used.

Antibiotic resistance

One of the most worrisome characteristics of *P. aeruginosa* is its low antibiotic susceptibility, which is attributable to a concerted action of multidrug efflux pumps with chromosomally encoded antibiotic resistance genes (e.g., *mexAB*, *mexXY* etc.) and the low permeability of the bacterial cellular envelopes. In addition to this intrinsic resistance, *P. aeruginosa* easily develops acquired resistance either by mutation in chromosomally encoded genes or by the horizontal gene transfer of antibiotic resistance determinants. Development of multidrug resistance by *P. aeruginosa* isolates requires several different genetic events, including acquisition of different mutations and/or horizontal transfer of antibiotic resistance genes. Hypermutation favours the selection of mutation-driven antibiotic resistance in *P. aeruginosa* strains producing chronic infections, whereas the clustering of several different antibiotic resistance genes in integrons favors the concerted acquisition of antibiotic resistance determinants. Some recent studies have shown phenotypic resistance associated to biofilm formation or to the emergence of small-colony variants may be important in the response of *P. aeruginosa* populations to antibiotics treatment

Pathology

P. aeruginosa rarely causes disease in healthy humans. It is usually linked with patients whose immune system is compromised by diseases or trauma. It gains access to these patients' tissues through the burns, for the burn victims, or through an underlying disease, like cystic fibrosis. First, *P. aeruginosa* adheres to tissue surfaces using its flagellum, pili,

and exo-S; then, it replicates to create infectious critical mass; and lastly, it makes tissue damage using its virulence factors.). Since the powerful exotoxins and endotoxins released by *P. aeruginosa* during bacteremias continue to infect the host even after *P. aeruginosa* has been killed off by antibiotics, acute diseases caused by *P. aeruginosa* tend to be chronic and life-threatening. Furthermore, with the exception of the cystic fibrosis strain, most *P. aeruginosa* strains that attack compromised patients tend to be nonmucoid . And even though a small amount of patients infected by *P. aeruginosa* developed severe sepsis with lesions with black centers, most patients exhibited no obvious pathological effects of the colonization.

P. aeruginosa communicates with other cells through quorum-sensing. This form of communication allows the cells to regulate gene production which results in control of certain cell functions. One of the enzymes responsible for quorum sensing is tyrosine phosphatase (TpbA). This enzyme relays extracellular quorum sensing signals to polysaccharide production and biofilm formation outside the cells. *P. aeruginosa* attaches to surfaces by way of biofilm production. Quorum-sensing can be a drug target to cure infections caused by *P. aeruginosa*. Quorum-quenching is used to blocks the signaling mechanism of quorum-sensing and prevents biofilm formation in *P. aeruginosa*. Yi-Hu Dong and his colleagues were able to prevent biofilm formation in mice under laboratory conditions .*P. aeruginosa* secrets many virulent factors to colonize the cells of its host. For example, exotoxin A, the most toxic protein produced by *P. aeruginosa*, catalyzes the ADP-ribosylation to form ADP-ribosyl-EF-2, which inhibits the protein synthesis of the host's cells. Moreover, elastase, an extracellular zinc protease, attacks eukaryotic proteins such as collagen and elastin and destroys the structural proteins of the cell. It also breaks down human immunoglobulin and serum alpha proteins (pseudomonas aeruginosa is an environmentally ubiquitous opportunistic pathogen. Epidermal infections often result from *P. aeruginosa* infiltrating through a human host's first line of defenses, entering the body through the skin at the site of an open wound. *P. aeruginosa* is a common member of hospital bacterial communities where it can infect immune- compromised individuals including burn victims. *P. aeruginosa* is a source of bacteremia in burn victims. Following severe skin damage, the prevalence of *P. aeruginosa* in the environment increases the probability of the organism accessing the bloodstream through the burn victim's exposed deep epidermal tissue. Previous research of antibody-mediated host defenses indicates that on the fifth day after the initial burn, Fc receptor expression is reduced in

polymorphonuclear leukocytes (PMNs). Without the Fc receptor, PMN chemotaxis is greatly reduced and the PMNs become less effective at preventing infection.

P. aeruginosa can be transmitted to a host via fomites, vectors, and hospital workers who are potential carriers for multiply-antibiotic-resistant strains of the pathogen. Furthermore, any *P. aeruginosa* already present on a burn victim's skin before the injury can transform from an innocuous organism on the surface of the skin to a source of infection in the bloodstream and body tissues of the same individual.

The pili and flagella of *P. aeruginosa* play a vital role in the infection of burns and wounds. Controlled infection of burn wounds on animal and plant models with *P. aeruginosa* strains devoid of pili and flagella demonstrate a trend of decreased virulence. Without these morphological virulence factors, the bacteria exhibit a substantially decreased survival rate at the wound site and a decreased ability to disseminate within the host organism [36]. The spread of *P. aeruginosa* within host organisms is also dependent on the microorganism's elastase production and other protease mechanisms. Bacterial elastase and other bacterial proteases degrade the host's proteins, including the structural proteins within membranes, disrupting the host's physical barriers against the spread of infection. Elastase also assists *P. aeruginosa* in avoiding phagocytotic antibody-mediated cytotoxicity at the site of the wound by inhibiting monocyte chemotaxis.

PRINCIPLES OF TREATMENT

The following principles apply to the treatment of serious *P. aeruginosa* infections:

- Delayed therapy correlates with increased mortality.
- All infected catheters should be removed, and, whenever possible, abscesses or obstructions should be drained or removed.
- Combination therapy is indicated in certain high risk patients and in severe infections.

Combination versus monotherapy — One of the most controversial management questions involves the use of combination or monotherapy for serious infections due to *P. aeruginosa*.

Antimicrobial agents are needed to treat *Pseudomonas* infections. Two antipseudomonal drug combination therapy (eg, a beta-lactam antibiotic with an aminoglycoside) is usually recommended for the initial empiric treatment of a pseudomonal infection, especially for patients with neutropenia, bacteremia, sepsis, severe upper respiratory infections

(URIs), or abscess formation. The choice of antibiotic also depends on the site and extent of infection and on local resistance patterns.^[7] Reports of more resistant strains of *Pseudomonas* organisms to the currently used antimicrobials are causing much concern.

B. cepacia has grown resistant to aminoglycosides, antipseudomonal penicillins, and most beta-lactam agents. Some strains are variably susceptible to third-generation cephalosporins, ciprofloxacin, trimethoprim-sulfamethoxazole, ampicillin-sulbactam, chloramphenicol, or meropenem.

Because human cases of glanders are rare, limited information is available about antibiotic treatment of the organism in humans. Sulfadiazine has been effective in experimental treatments of animals and humans. *B. mallei* organisms are usually sensitive to tetracyclines, ciprofloxacin, streptomycin, novobiocin, gentamicin, imipenem, ceftazidime, and sulfonamides. Resistance to chloramphenicol has been reported. Treatment duration is often prolonged, from 1-2 months, often combined with surgical drainage.

Ceftazidime alone or in combination with either trimethoprim-sulfamethoxazole or amoxicillin clavulanate is the therapy of choice for *B. pseudomallei*. The organism is usually sensitive to imipenem, penicillin, doxycycline, azlocillin, ceftazidime, ticarcillin-clavulanic acid, and ceftriaxone. Initiate treatment early in the course of the disease. The organism is resistant to ciprofloxacin and aztreonam. Treatment is often prolonged, from 3-12 months, with the longest duration of therapy used for chronic extrapulmonary disease.

Pseudomonas vaccines are also currently used to reduce infection risks in patients with cystic fibrosis (CF) and are still under investigation. *Pseudomonas aeruginosa* infections include the following:

- **Bacteremia**
 - Empiric antibiotics are often started before the organism is identified.
 - Whether single-drug or combination therapy is most effective in patients who have bacteremia and neutropenia is debated. The author is unaware of any prospective randomized comparison between monotherapy and combination drug therapy for patients with pseudomonal bacteremia. Duration of treatment is at least 2 weeks.
- **Bone and skin infections**
 - A 4-week course of aminoglycoside antibiotics is often successful for managing vertebral osteomyelitis.

- Sternoarticular pyarthrosis has been managed effectively with aminoglycoside and antipseudomonal penicillin if administered for at least 6 weeks.
- Patients with osteomyelitis of the pubic symphysis require treatment for at least 4 weeks with an antipseudomonal penicillin and aminoglycoside combination. Surgical intervention is not usually indicated.
- Patients with osteochondritis require medical and surgical treatment. Parenteral administration of 1-2 antipseudomonal agents is recommended before surgical debridement. The recommended regimen continues postsurgical treatment for 1-2 additional weeks with oral (PO) ciprofloxacin.
- Chronic contiguous pseudomonal osteomyelitis requires 4-6 weeks of combination therapy, in addition to surgical debridement.
- Burn wound sepsis management requires early intervention with daily wound inspection and systemic antibiotic combination regimens. Monotherapy is not indicated.
- Management of pseudomonal cellulitis includes the use of PO antibiotic for 7-10 days; this often resolves a localized infection.
- Pseudomonal toe web infections require initial debridement with applications of silver nitrate or 5% acetic acid to the toe webs and the dorsal and planter areas. Following this initial treatment, apply a topical antibiotic, silver sulfadiazine cream, or Castellani paint until infection resolves. PO quinolone effectively reduces the duration of infection.
- Pseudomonal folliculitis is often self-limited; treatment may require only application of silver sulfadiazine cream or 5% acetic acid wet compresses for 20 minutes 2-4 times daily with topical antibiotics.
- **CNS infections**
 - Ceftazidime, cefepime, or meropenem are the antibiotics of choice because of their high CNS penetration. Initially, consider double coverage with an aminoglycoside for patients with adequate renal function. Aztreonam, ciprofloxacin, or levofloxacin are indicated for patients with renal failure and those allergic to beta-lactam. Imipenem-cilastatin should be avoided because of the risk of seizures. Intrathecal treatment should also be considered. Treatment duration should be at least 2 weeks.
 - Antibiotics can be used in the initial treatment of brain abscesses that are multiple, small (ie, < 2 cm), poorly distributed, or relatively difficult to access. Antibiotic therapy duration depends on the speed of abscess shrinkage, but therapy usually lasts 2-6 weeks.
- **Ear and eye infections**

- Otitis media in at-risk populations should be treated with antipseudomonal agents for at least 10 days.
- Chronic suppurative otitis media requires daily aural toilet and treatment with antibiotics (eg, ceftazidime, mezlocillin, ciprofloxacin), and often surgical treatment.
- Otitis externa can be treated with local care using an acetic acid compress and daily aural cleaning.
- Management of malignant externa otitis should be aggressive and involve both medical and surgical therapies. The conventional therapy (ie, an aminoglycoside and a beta-lactam agent with antipseudomonal activity) is needed for at least 4 weeks to treat localized infections and 6-8 weeks or longer to treat extensive disease. Monotherapy using ceftazidime intravenously (IV), cefepime IV, or ciprofloxacin PO for 6 weeks has been reported effective.
- If gram-negative rods are isolated from the Gram stain of an eye infection, immediately start a combined topical and subconjunctival (or subtenon) therapy of aminoglycoside antibiotics. Aminoglycoside solution (not ointment) must be applied to the affected eye every 30-60 minutes. Subconjunctival therapy is needed for the first 3 days of treatment. Total duration of therapy is at least 1 week. An alternative therapy uses a quinolone antibiotic solution. The addition of parental or PO antipseudomonal antibiotics also has been beneficial.
- Pseudomonal endophthalmitis requires immediate antibiotic therapy, using aminoglycoside and antipseudomonal penicillin administered via a parenteral and subconjunctival, topical, or intraocular route. Therapy duration depends on the clinical improvement.
- **GI and GU infections**
 - Treat GI manifestations of pseudomonal infection with antibiotic therapy for patients with severe localized or systemic infections.
 - The treatment modality for urinary tract infection (UTI) depends on the presence of sepsis, degree of chronicity, potential sites of persistent infection, and local antibiotic susceptibility. Ideally, indwelling urinary catheters should be removed. If the catheter cannot be removed, consider treating only symptomatic episodes or exacerbations because it is not feasible to totally eradicate the organism. Aminoglycosides and quinolones remain the agents of choice.
- **Cardiovascular (CV) and respiratory infections**
 - To treat endocarditis, administer an antipseudomonal beta-lactam with high-dose aminoglycoside for approximately 6 weeks.
 - According to the criteria used in France to select antibiotics to treat VAP, the following 2 risk factors must be considered: (1) administration of broad-spectrum antibiotics in the previous 15 days and (2) mechanical ventilation for fewer than 7 days or for 7 or more

days. The extended factors predict the involvement of multiresistant nosocomial *P aeruginosa*, suggesting administration of carbapenems to those who have undergone mechanical ventilation of 7 or more days and who have been exposed to antibiotics in the prior 15 days.

- The role of antibiotic prophylaxis or chronic suppression of respiratory pseudomonal infections in patients with CF is controversial. Among the promising treatment plans are intermittent aerosolization of antibiotics to patients with CF who have established pseudomonal lung infections.
- Choices for empiric antibiotic treatment in patients with a history of *Pseudomonas* infection requires review of previous culture sensitivity.
- More widely accepted is the treatment of children with pseudomonal infections by using fluoroquinolone, especially children with previous therapeutic failure or resistance to multiple other antibiotics.^[8] Treatment often continues until symptoms resolve (ie, 1-2 wk).
- Inhalation of mucolytic and hydrating agents, postural drainage, and chest physiotherapy often are therapies used together. Bronchial lavage also has been used to remove respiratory secretions.