

Pseudomonas aeruginosa: Burn Infection, Treatment and Antibacterial Resistance

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Abstract

Pseudomonas aeruginosa is an opportunistic pathogen causing severe, acute and chronic nosocomial infections in immunocompromised, catheterized or burn patients. Various types of virulent factors have been identified in *P. aeruginosa*, suggesting their contribution to the pathogenesis of the disease. The organism is generally resistant to numerous antimicrobial agents due to natural resistance in particular impermeability or mutations and acquisition of resistant determinants. Plasmid and integron have a crucial role in acquisition of mobile elements. Most treatment failures are related to inappropriate initial antibiotic therapy with insufficient coverage of multidrug resistant (MDR) pathogens, the rationale for using combinations of antibiotics to cover MDR gram-negatives. However, clinical data supporting this strategy are limited. In fact, systematic combination therapy may have contributed to the overuse of antibiotics and to the emergence of MDR microorganisms. Nevertheless, combination therapy is the best strategy to treat severe infections due to suspected MDR *Pseudomonas*. Optimally, therapeutic strategies should be sufficiently broad to cover relevant pathogens while minimizing the risk for emergence of antimicrobial resistance. Polymyxin E (colistin) and carbapenems are the most effective antibiotics against MDR isolates.

Keywords: *Pseudomonas aeruginosa*; Multidrug-resistance; plasmid; Integron

Introduction

Pseudomonas aeruginosa is a gram-negative rod measuring 0.5 to 0.8 μm by 1.5 to 3.0 μm . Almost all strains are motile by means of a single polar flagellum. It is a free-living bacterium, commonly found in soil and water. This bacterium, a member of the gamma proteobacteria, is a gram-negative, aerobic rod belonging to the bacterial family pseudomonadaceae.¹ Based on conserved macromolecules (e.g. 16S ribosomal RNA), the family includes only members of the genus *Pseudomonas* which are cleaved into eight groups. *P. aeruginosa* is a typical species of its group which contains 12 other members.² Almost all the clinical cases of *P. aeruginosa* infection can be associated with the compromise of

host defense such as burn patients. While many cases of *P. aeruginosa* infection can be attributed to general immunosuppression (e.g. AIDS patients),^{3,4} in neutropenic patients undergoing chemotherapy,⁵ such scenarios predispose the host to a variety of bacterial and fungal infections, and therefore do not yield information which is specific to the pathogenesis of *P. aeruginosa*. In this respect, three of the more informative human diseases caused by *P. aeruginosa* are: 1) bacteremia in severe burn victims; 2) chronic lung infection in cystic fibrosis patients; and 3) acute ulcerative keratitis in users of extended-wear soft contact lenses. Observations and experimental evaluation of various bacterial virulence factors have shed a great deal of light on how *P. aeruginosa* is able to cause disease in a wide variety of organs, secondary to disruption of the normal physiologic function. Such insights provide an understanding at the molecular and cellular level of how and why *P. aeruginosa* has become such an important pathogen in human infection.

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***P. aeruginosa* Bacteremia in Severe Burn Victims**

Bacterial infection following severe thermal injury can be most simplistically attributed to extensive breaches in the skin barrier. The fact that *P. aeruginosa* occurs so commonly in the environment makes it extremely likely that an individual suffering severe burns will be challenged with this microorganism before the burns can heal. Burn hospitals often harbor multidrug-resistant *P. aeruginosa* that can serve as the source of infection. *P. aeruginosa* has been found to contaminate the floors, bed rails, and sinks of hospitals, and has also been cultured from the hands of nurses.⁶ Besides transmission through fomites and vectors, bacterial flora can be carried into a hospital by the patient and can be an important source of infection for the same individual after injury.⁷ Regarding multidrug resistance, Hsueh et al.⁸ reported single multidrug-resistant strain of *P. aeruginosa* over a period of several years, and concluded that the strain was carried by some patients asymptotically through several rounds of antibiotic treatment which were administered to treat *Pseudomonas* and non-*Pseudomonas* infections. This scenario can be worse during the spread of *P. aeruginosa* from one patient to another; the persistence of this strain takes place in patients throughout several courses of antibiotic treatment. It has been proved that during admission of patients in burn centers, a limited number of common strains cross-contaminate burn victims mostly when their lesions scrubbed in the bathroom.⁹

***P. aeruginosa* Virulence Factors in Burn Infection**

Numerous *P. aeruginosa* virulence factors contribute to the pathogenesis of burn wound infection. Rahme et al. highlighted the occurrence of virulence factors of *P. aeruginosa* contributing to pathogenesis in burn wound infection of rodents.¹⁰ A significant role has also been established for *P. aeruginosa* pili and flagella. Experiments comparing infection of burn wounds by pilus and flagellum deficient *P. aeruginosa* strains clearly demonstrate that the bacteria deficient in either of these structures have reduced virulence, both in their ability to persist at the wound site, and in their ability to disseminate throughout the host organism.¹¹ Dissemination of *P. aeruginosa* throughout the host is also partially dependent upon produc-

tion of bacterial elastase and other proteases.¹² Elastase has been shown to degrade collagen and non-collagen host proteins, and to disrupt the integrity of the host basement membrane.¹³ Proteases can have adverse effects on several aspects of the innate and acquired host immune response. For example, elastase inhibits monocyte chemotaxis,¹⁴ which could adversely affect early clearance of *P. aeruginosa* from wound sites by phagocytosis, as well as subsequent presentation of bacterial antigens to the host immune system.¹⁵ The *lasR* gene encodes a protein critical for initiation of the quorum sensing response involved in virulence factor production and biofilm formation, indicating that other factors controlled by *lasR* are critical determinants of *P. aeruginosa* pathogenesis in burn wound infection.¹⁶ Other *P. aeruginosa* virulence factors reported to be involved in pathogenesis of burn wound infection include phospholipase C,¹⁷ the ferripyochelin-binding protein,¹⁸ lipopolysaccharide (LPS),¹⁹ and exoproducts secreted by type III secretion apparatus.²⁰ While the loss of the skin's barrier function is certainly an important factor in burn wound infection, its compromise fails to explain the relatively narrow range of bacterial pathogens which are typically cultured from infected burn wounds.²¹ It is, therefore, likely that additional host defense mechanisms specific to some pathogens are more compromised in severe burns. A reduction in infection following local application of polyclonal human antibody to burn sites has been reported,²² suggesting that in the untreated burn wound, immunoglobulin exists at subprotective levels. The possibility of a local deficiency of antibody-mediated immunity in burn wounds is further supported by an earlier report²³ stating that Fc receptor expression by polymorphonuclear leukocytes (PMNs) decreases by the fifth day post-injury in burn victims. Complement has also been shown to be depleted in burn wounds,²⁴ probably due to local consumption of complement components. Local deficiencies in protective antibody complement proteins, and PMN Fc receptors may explain the defects in random migration and chemotaxis of PMNs observed at burn wound sites. Taken together, these data suggest that the ability to colonize a burn wound depends upon the concerted impairment of several host immune mechanisms, and that the importance of *P. aeruginosa* in such infections is due to its ability to take advantage of the host immune compromise and secrete a variety of important virulence factors. *P. aeruginosa* produces two extracellular protein toxins, exoenzyme S and exotoxin A. Exoenzyme S has

the characteristic subunit structure of the A-component of a bacterial toxin, and it has ADP-ribosylating activities.²⁵ Exoenzyme S is produced by the bacteria growing in the burned tissue and may be detected in the blood before the bacteria are present. It has led to the suggestion that exoenzyme S may act to impair the function of phagocytic cells in the bloodstream and internal organs as a preparation for invasion by *P. aeruginosa*.²⁶ Exotoxin A has exactly the same mechanism of action as the diphtheria toxin; it causes the ADP ribosylation of eucaryotic elongation factor 2, resulting in inhibition of protein synthesis in the affected cell.²⁷ Although it is partially-identical to diphtheria toxin, it is antigenically distinct. It utilizes a different receptor on host cells than diphtheria toxin does; otherwise, it enters the cells in the same manner and has the exact enzymatic mechanism. The production of exotoxin A is regulated by exogenous iron, but the details of the regulatory process are distinctly different in *C. diphtheriae* and *P. aeruginosa*.²⁸ Exotoxin A appears to mediate both local and systemic disease processes caused by *P. aeruginosa*. It has necrotizing activity at the site of bacterial colonization and is therefore thought to contribute to the colonization process.^{29,30} Table 1 is a summary of the virulence determinants of *P. aeruginosa*.

Candidate Vaccines for High Risk People

Although antibiotic therapy has considerably improved the management of infectious diseases in general, many *P. aeruginosa* infections are not fully treated or eradicated by the application of anti-pseudomonal drugs and can, thus, become chronic infections. For instance, burn patients that survive the initial burn trauma can become colonized with antibiotic-resistant, hospital-derived *P. aeruginosa* strains that are not easily eradicated with antibiotic therapy.^{31,32} In cystic fibrosis patients, when the strains are eventually selected out by antibiotic therapy to become multiply-resistant, an increase in the rate of decline in lung function is seen when compared to patients infected with antibiotic susceptible strains.³³⁻³⁵ Several *P. aeruginosa* antigens are used for vaccine development including lipopolysaccharide alone, polysaccharides alginate, extracellular proteins, exotoxin A, and killed whole cell.³⁶⁻³⁹ However, none of them are clinically available to use for people who are at risk such as firefighters or infected patients (Immunocompromised and cystic fibrosis patients). Nevertheless, at the present time some

candidate vaccines are under first to third stage of experimental clinical trials.⁴⁰

Table 1: Summary of the virulence determinants of pathogenic *Pseudomonas aeruginosa*

Adhesins
pili (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
pili
Toxins
Exoenzyme S
Exotoxin A
Lipopolysaccharide
Antiphagocytic surface properties
capsules, slime layers
LPS (Lipopolysaccharide)
Biofilm construction
Defense against serum bactericidal reaction
slime layers, capsules, biofilm
LPS
protease enzymes
Genetic attributes
genetic exchange by transduction and conjugation
inherent (natural) drug resistance
R factors and drug resistance plasmids
Ecological criteria
adaptability to minimal nutritional requirements
metabolic diversity
widespread occurrence in a variety of habitats

Treatment of Infections

Topical antimicrobial therapy

It has been proved that an effective topical antimicrobial agent substantially reduces the microbial load on the open burn wound surface and reduces the risk of infection.^{41,42} Selection of topical antimicrobial therapy should be based on the agent's ability to inhibit the microorganisms recovered from burn wound surveillance cultures and monitoring of the nosocomial infections acquired in the burn unit. Prescription is also based on the individual preparation of the topical agent (e.g., ointment or cream versus solution or dressing) and its pharmacokinetic properties. Burn

units may rotate the use of various topical antimicrobial preparations on a regular basis to decrease the potential for development of antibiotic resistance.^{43,45} Topical antibiotic agents should first be applied directly to the patient's dressings before application to the burn wound to prevent contamination of the agent's container by burn wound flora. The inhibitory action of silver is due to its strong interaction with thiol groups present in the respiratory enzymes in the bacterial cell.^{46,47} Silver has also been shown to interact with structural proteins and preferentially bind with DNA nucleic acid bases to inhibit replication.^{48,46} For this reason, silver has recently been shown to be highly toxic to keratinocytes and fibroblasts and may delay burn wound healing if applied indiscriminately to debrided healing tissue areas.⁴⁸⁻⁵⁰ Moist exposure therapy, using a moisture-retentive, has been shown to act as an effective antibacterial agent while promoting rapid autolysis debridement and optimal moist wound healing in partial-thickness injury.^{51,52} Moisture-retentive ointment also resulted in earlier recovery of keratinocytes with improved wound healing and decreased scar formation.⁵³ Silver nitrate is most effective before the burn wound becomes colonized. The burn wound needs to be cleansed of emollients and other debris before a multilayered dressing is applied to the burn wound and subsequently saturated with silver nitrate solution. Effective use of this preparation, therefore, requires continuous application with secondary occlusive dressings, making examination of the wound difficult. The silver ion in AgNO₃ also quickly binds to elemental chlorine ions so that repeated or large-surface application of this solution may lead to electrolyte imbalance (e.g., hyponatremia and hypochloremia).^{40,54} Silver nitrate antibacterial activity is limited to the burn wound surface.^{55,56} This agent demonstrates the bacteriostatic activity against gram-negative aerobic bacteria such as *P. aeruginosa* and *E. coli*, but it is not active against other genera, including *Klebsiella*, *Providencia*, and *Enterobacter*.^{40,57} Silver nitrate also has limited antifungal activity so that nystatin should be used concomitantly.^{58,59}

Silver Sulfadiazine

This agent is a combination of sodium sulfadiazine and silver nitrate. The silver ion binds to the microorganism's nucleic acid, releasing the sulfadiazine, which then interferes with the metabolism of the

microbe.⁴⁶ It is easy to use and painless when applied and can be used with or without a dressing. Limited systemic toxicity with repeated daily or twice-daily application has occurred aside from the development of leukopenia.^{60,61} Silver sulfadiazine has excellent broad-spectrum antibacterial coverage against *P. aeruginosa* and other gram-negative enteric bacteria, although some resistance has recently been reported.^{41,62} In addition, this agent has some activity against *Candida albicans*, but enhanced antifungal activity can be achieved by using nystatin in combination with silver sulfadiazine.⁵⁸ Although silver sulfadiazine dissociates more slowly than silver nitrate, there is still poor penetration into the wound.^{54,55} Silver sulfadiazine is only absorbed within the surface epidermal layer, which limits its effectiveness in some patients with severe injuries. In Europe, a combination of cerium nitrate and silver sulfadiazine has been used to combat this problem.^{63,64} It has been shown to reduce the inflammatory response to burn injury, decrease bacterial colonization, and provide a firm eschar for easier wound management.⁶⁴

Mafenide Acetate

Topical mafenide acetate cream allows open burn wound therapy and regular examination of the burn wound surface because it is used without dressings. Mafenide acetate is applied a minimum of twice daily and has been shown to penetrate the burn eschar.⁵⁴ The 5% solution must be applied to saturate gauze dressings, and these need to be changed every 8 hours for maximal effect. Mafenide acetate solution appears to be as effective as the cream preparation when used in this way.^{41,65} Mafenide acetate (Sulfamylon) cream has a broad spectrum of activity against gram-negative bacteria, particularly *P. aeruginosa*, but it has little activity against gram-positive aerobic bacteria such as *Staphylococcus aureus*.⁴¹ This agent also inhibits anaerobes such as *Clostridium spp.* Because protracted use of mafenide acetate favors the overgrowth of *C. albicans* and other fungi, this agent should be used in combination with nystatin to prevent this complication due to its limited antifungal activity.^{58,59} This compound is converted to p-sulfamylvanzoic acid by monoamide oxidase, a carbonic anhydrase inhibitor, causing metabolic acidosis in the burn patient.^{41,42} In burn patients with inhalation injury and a concomitant respiratory acidosis, the use of mafenide acetate over a large burn surface area or

the repeated application of this compound can be fatal. Mafenide acetate also decreases the breaking strength of healed wounds and delays healing.⁶⁶

Acticoat AB Dressing

This product is a specialized dressing, consisting of two sheets of high-density polyethylene mesh coated with nanocrystalline silver (e.g., ionic silver with a rayon-polyester core).⁶⁷⁻⁶⁹ The more controlled and prolonged release of nanocrystalline silver to the burn wound area allows less-frequent dressing changes, reducing the risk of tissue damage, nosocomial infection, patient discomfort, and the overall cost of topical therapy.^{67,70} Acticoat AB provides the most comprehensive broad-spectrum bactericidal coverage against important burn wound pathogens of any topical antimicrobial preparation currently marketed.^{67,70} These dressings have a potent antibacterial activity against most aerobic gram negatives, including *P. aeruginosa* and antibiotic resistant members of the family *Enterobacteriaceae* as well as aerobic gram-positive bacteria, including MRSA and vancomycin resistant *Enterococci*.^{67,69,70} If the burn wound surface has minimal exudates, these specialized dressings can remain in place for several days and retain antibacterial activity.⁷⁰

Resistance to Antimicrobial Agents

Resistance to topical antimicrobial agents

Although resistance to silver sulfadiazine in *P. aeruginosa* was reported, its resistance mechanism has not been determined.⁶² It is suggested that resistance of *Pseudomonas* to silver based topical antimicrobials in part is based on the mutation of outer membrane proteins that transport ions including silver across bacterial membrane.^{71,72} Gentamicin-resistant strains of *P. aeruginosa* which were isolated from burned patients have been reported.⁷³ These strains showed cross-resistance to silver sulfadiazine but their resistance was unstable and did not persist on subculture media. According to a report in USA, an epidemic sepsis of *Enterobacter cloacae* in burned patients occurred and resulted into 13 deaths.⁷⁴ The MIC values of silver sulfadiazine for these strains were 3200 µg/ml whilst the strains isolated from non-burned patients were all sensitive to silver sulfadiazine. Similarly, Rosenkranz et al. isolated two silver

sulfadiazine resistant strains of *Enterobacter cloacae* in a burn unit where silver sulfadiazine was in use. These strains showed high resistance to silver sulfadiazine (MIC= 400 µg/ml) and were cross-resistant to silver benzoate but not to silver nitrate.⁷⁵ Recently we also demonstrated that *P. aeruginosa* isolated from burned patients were resistant to silver sulfadiazine while most of them were sensitive to silver nitrate solution.⁷⁶

Resistance to Antibiotics

Resistance due to mutations

Various penicillins, cephalosporins, carbapenems, monobactams, aminoglycosides, fluoroquinolones, and polymyxins have been used to treat patients infected with *P. aeruginosa* and are active against most isolates. All, however, are prone to being compromised by mutational resistance. Mutations to topoisomerases II and IV confer fluoroquinolone resistance more readily in *P. aeruginosa* than in *Enterobacteriaceae*, because *P. aeruginosa* has a poorer inherent susceptibility.⁷⁷ Derepression of the chromosomal AmpC β-lactamase reduces susceptibility to penicillins and cephalosporins although the level of resistance depends on the degree of derepression, which is more variable than that in *Enterobacter* mutants.⁷⁸ The up-regulation of *MexAB-OprM* compromises the fluoroquinolones, penicillins, cephalosporins, and, to some extent, meropenem (although not imipenem), and it also enhances resistance to many other drugs that lack useful antipseudomonal activity.⁷⁸⁻⁷⁹ Up-regulation of other efflux systems, for example *MexCD-OprJ* and *MexEF-OprN* confers resistance to fluoroquinolones and some β-lactams; up-regulation of *MexXY-OprM* also affects aminoglycosides.⁸⁰ There is better evidence that increased impermeability is a mechanism of aminoglycoside resistance, for example in the “small-colony variants” which are sometimes selected during gentamycin therapy and in isolates with reduced susceptibility to all aminoglycosides, carbapenems and fluoroquinolones.⁸¹⁻⁸⁴

Multidrug Resistance due to Mutations

No single mutation compromises every antipseudomonal drug. Nevertheless, up-regulated efflux can simultaneously compromise fluoroquinolones and most β-lactams, leaving only the aminoglycosides (which lack reliable efficacy as antipseudomonal monother-

apy) and imipenem (to which mutational resistance evolves at high frequency). A combination of upregulated efflux, loss of OprD and impermeability to aminoglycosides compromises every drug class except the polymyxins. Each of the necessary mutations arises in 1 cell per 107 to 109 cells, and, although simultaneous emergence is mathematically and biologically improbable, sequential emergence is all too likely because infections resistant to the first antibiotic administered are likely to be treated with a second antibiotic, and so on. Mutations that up-regulate efflux may act additively with those effecting permeability, β -lactamase expression, or topoisomerase susceptibility so as to exacerbate resistance.⁸⁵ Accumulation of sequential mutations may be facilitated by hypermutators, which either lack the ability to perform DNA proofreading or mismatch repair, or which use DNA polymerases with a reduced copying fidelity. Because resistance is most likely to emerge in hypermutators, antibiotics may select for hypermutators, thereby increasing the probability that further resistance will emerge.⁸⁶

Acquisition of Genes and Multidrug Resistance

Many acquired β -lactamases and aminoglycoside-modifying enzymes have been noted in *P. aeruginosa*.⁸⁷⁻⁸⁹ Resistance to oxyimino-aminothiazolyl cephalosporins, monobactams, and penicillins but not to carbapenems has been reported as a result of expression of potent aminoglycoside-modifying enzymes.⁹⁰ Metallo- β -lactamases enzyme rapidly hydrolyzes penicillins, cephalosporins, and carbapenems but not aztreonam.⁹¹ Resistance to penicillins and cephalosporins usually accompanies production. A variety of enzymes have been identified from Japan, Taiwan, France, Greece, South Korea, Italy and Canada.⁹¹⁻⁹³ The genes for resistance are often carried as cassettes within integrons, which are natural recombination systems that assemble series of acquired genes behind a single promoter. This organization facilitates gene recombination. Critically, the β -lactamase genes are often adjacent to aminoglycoside 6-N acetyltransferase [*aac(6)-Ib*] determinants.^{91,94,95}

Prevalence of Multidrug Resistance

P. aeruginosa isolated from patients in burn center were resistant to most classes of antibiotics. According

to a survey conducted in Ghotbeddin Burn hospital (Shiraz, Iran) almost all *P. aeruginosa* isolated from burn patients were resistant to all tested anti-Pseudomonal antibiotics except carbapenems (meropenem and imipenem).⁹⁶ Moreover, several reports from Iran confirmed multidrug resistance of burn's isolates.⁹⁷⁻⁹⁹ It seems likely that most of this multidrug resistance reflects the accumulation of multiple mutations, although this surmise remains to be confirmed by molecular studies, and although reports from other parts of the world document extreme multidrug resistance associated with acquired resistance genes. In a hospital in Thessaloniki, Greece, a serotype with cross-resistance to aztreonam, aminoglycosides, and ciprofloxacin persisted for 3 years, with 1211 isolates of this strain recovered.¹⁰⁰ In South Korea, resistant isolates of *P. aeruginosa*, with the hydrolyzing enzyme being found in organisms at 9 out of 29 hospitals were surveyed. Moreover, a detailed study at one Korean Hospital revealed dissemination in multiple *P. aeruginosa* lineages.

Prevention and Management of Multi-Drug Resistance

The selection of resistant mutants, a risk associated with any antipseudomonal therapy, varies with the type and dosage of antibiotic used and the infection site. It revealed a 2-fold greater risk of selection for resistance when imipenem, rather than ciprofloxacin, ceftazidime, or piperacillin, was used.^{101,102} It is often assumed that combination therapy prevents the selection of mutational resistance, but evidence for this is scanty. In addition, single efflux mutations may affect both the β -lactams and the fluoroquinolones, thereby undermining the use of combinations of these drugs. The original emergence of multi-drug resistance in association with plasmids and integrons is less predictable than mutational resistance because it depends on the random escape of genes to mobile DNA. However, once such resistance emerges, either the host strain can spread among patients or the resistance can disseminate among strains. When strains have multiple mutational or acquired resistance, the choice of therapy is often frighteningly limited, especially because most clinicians would prefer to use a synergistic combination for serious Pseudomonal infections. No new fluoroquinolone offers better antiPseudomonal activity than ciprofloxacin, and none retains activity against ciprofloxacin-resistant isolates.

Where resistance is mutational, tobramycin and meropenem are the drugs most likely to retain activity, because they are the aminoglycoside and the β -lactam with the best inherent activity against *P. aeruginosa*. Isolates with efflux-mediated resistance to meropenem, penicillins, and cephalosporins might, however, retain susceptibility to imipenem. Although meropenem is usually a more active carbapenem, this possibility should always be considered. In instances in which all chances of β -lactam, aminoglycoside, and quinolone use are lost, the polymyxins remain the drugs of last resort. Despite their significant toxicity, they have been used with some success. Levin et al.¹⁰³ reported that the use of intravenous polymyxin E (colistin) was successful in 35 (58%) out of 60 patients treated for multidrug-resistant *Pseudomonas* and acinetobacter infections although it was associated with a failure rate of 75% when used for the treatment of pneumonias. Perhaps most disturbing is the dearth of new drug options. Clinafloxacin was slightly more active than ciprofloxacin, but its development has been suspended, and no other antiPseudomonal antibiotic is in advanced development. For the long term, multi-drug efflux inhibitors are promising for use with fluoroquinolones or β -lactams¹⁰⁴, and metallo- β -lactamase inhibitors¹⁰⁵ are the focus of laboratory investigation. Unless new drugs are developed, it is hard to escape the conclusion that multi-drug-resistant *Pseudomonas* strains will be an increasing reality and that the use of polymyxins will increase, despite their toxicity.

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Conclusion

P. aeruginosa infections identify those of a pathogen with many potentially virulent factors that allow it to colonize and infect essentially any mammalian tissue. The organism possesses a multitude of factors that promote adherence to host cells and mucins, damage host tissue, elicit inflammation and disrupt defense mechanisms. Due to impairment of the skin barrier in burn patients and frequent scrubbing, debridement and manipulation of the burn site, cross-contamination of MRD strains of *Pseudomonas* and colonizing of MDR strains is more likely. In spite of the ubiquitous nature of this microorganism and the frequency with which it is encountered, most human hosts counteract the infectious process effectively via the innate immune system. A more detailed molecular and cellular understanding of the bacterial and host factors is crucial to an overall comprehension of the pathogenic process of *Pseudomonas*, and will be of increasing importance to the development of preventative strategies to be sought for this major human pathogen. Selection of multi-drug resistant *Pseudomonas* in burn centers can be facilitated through transmission from person to person as well as extensive applications of antipseudomonal antibiotics. To overcome inappropriate treatment of burn patients infected with *P. aeruginosa*, periodical antibacterial susceptibility surveys for the bacteria isolated from burn patient are warranted.

Conflict of interest: None declared.

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