AN OVERVIEW ON ANTIBIOTIC RESISTANCE OF *PSEUDOMONAS AERUGINOSA*

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Abstract

P. aeruginosa, being a leading cause of nosocomial infections, encouraged several studies to discuss its sharing part in hospital-acquired infection, clinical impact of multi-drug resistance and mechanisms of such resistance. The present essay highlights the data of drug resistance in *Pseudomonas aeruginosa* with a special emphasis on types, genetics and different mechanisms of resistance to understand the emergence, spread, and persistence of antibiotic resistance, and summarizes the optional treatment feasible for these resistant bacteria.

Treatment options for multidrug-resistant *P. aeruginosa* infections are quite limited in most cases. However, immunotherapy is a promising new modality being explored. Prevention of emergence of resistance through combination therapy and pharmacokinetic strategies are studied. There is presently no reason to doubt that strategies of optimal prescribing, including control of antibiotic use, should be a leading priority in the effort to improve therapeutic outcomes in pseudomonal infections.

Finally, it is needless to underline the importance of strict compliance to infection control measures to escape the horizontal transmission of multiresistant *Pseudomonas* clones.

(Key words: *Pseudomonas aeruginosa*, nosocomial infections, multi-drug resistance, mechanisms of resistance).

List of Abbreviations

ABC	ATP-binding cassette
ADP	Adenosine diphosphate
AIDS	Acquired immunodeficiency syndrome
ALG	Alginate
AP	Alkaline protease
ATP	Adenosine triphosphate
BALT	Bronchus-associated lymphoid tissue
CF	Cystic fibrosis
CM	Cytoplasmic membrane
CNS	Central nervous system
DFO-Ga	Desferrioxamine-gallium
EDTA	Ethylene diaminetetraacetic acid
EF2	Elongation factor 2
EPIC	European Prevalence of Infection in Intensive Care
ESBL	Extended spectrum β-lactamase
ETA	Exotoin A
GPs	General Practitioner
HCWs	Health care workers
HM	Human milk

H_2O_2	Hydrogen peroxide
H_2S	Hydrogen sulphide
ICU	Intensive care unit
IFN	Interferon gamma
IV	Intravenous
LPS	Lipopolysaccharide
MAR	Multiple antibiotic resistance
MBLs	Metallo-β-lactamases
Mbp	Molar base pair
MDR	Multidrug resistance
MDRPA	Multidrug-resistant *Pseudomonas aeruginosa*
MFS	Major facilitator superfamily
MIC	Minimal inhibitory concentration
MYSTIC	Meropenem Yearly Susceptibility Test Information Collection
n[a]	Number of strains tested
NA[b]	Not available
NAD	Nicotinamide adenine dinucleotide
NNISS	National Nosocomial Infection Surveillance System
OM	Outer membrane
PA-IIL	Fucose>fructose/mannose-binding lectin
PBPs	Penicillin-binding proteins

PCR	Polymerase chain reaction
PE	Elastase
PG	Peptidoglycan
PLC	Phospholipase C
QS	Quorum-sensing
RJ	Royal jelly
RNA	Ribonucleic acid
RND	Resistance nodulation division
TNF	Tumor necrosis factor
VPS	Ventriculoperitoneal shunt

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Pseudomonas aeruginosa is a gram- negative aerobic rod belonging to the bacterial family *Pseudomonadaceae*. These bacteria are common inhabitants of soil, water and decaying matter. They are able to colonize many clinical environments including disinfectant solutions, dialysis fluid and equipment. They tend to persist in hospitals where an exchange can occur between patient and environmental habitats. *Pseudomonas* causes a variety of diseases which include, urinary tract infection, respiratory tract infection, dermatitis, bone and joint infections. These infections are often severe, life threatening and usually difficult to treat because of the limited susceptibility to antimicrobial agents and the high frequency of emergence of antibiotic resistance during therapy **(Reuter et al., 2002).**

Kobayashi and Erimini, 2006 concluded that, *P. aeruginosa* is responsible for about 10% of all hospital-acquired infections and showing higher rate of resistance**.** In their study of antimicrobial susceptibility in Egypt on isolates from patients in surgical zones and intensive-care units in the largest two hospitals in Cairo during the year 2003.The highest resistance rate was shown by *Pseudomonas aeruginosa* (14.9%).

The problem of antibiotic resistance in *P.aeruginosa* is increasing. The heightened level of drug resistance is a result of the de novo emergence of resistance in a specific organism after exposure to antimicrobial and patient to patient spread of resistant organism. Also *P. aeruginosa* has properties that make it particularly problematic to hospitals, including inherent resistance to many drug classes, the ability to acquire resistance through mutation and a high virulence potential (**Livermore, 2002 and Giamarellou and Kanellakopoulou, 2008**). Accumulation of resistance after exposure to various antibiotics and cross-resistance

between agents may result in multidrug-resistant *Pseudomonas aeruginosa* (MDRPA) *(***National Nosocomial Infection Surveillance System, 2004*).***

Morbidity and Mortality information in patients infected with MDRPA is limited but available data shows a significantly higher burden of MDRPA infections compared with more susceptible *P.aeruginosa* infections. In various studies, MDRPA infections were associated with much higher hospitalization cost compared with the mean cost of patients with susceptible *P.aeruginosa* infections. A separate study reported an overall mortality rate of 67% in patients with MDRPA. The reason for increased mortality and health care costs in patients with MDRPA infections has been linked to inappropriate therapy or delay in starting therapy ***(*Harbarth et al., 2003 and Kang et al., 2003).**

The clinician worldwide will be fighting in the years to overcome emergence of MDRPA. So this spread can be best controlled by observing proper isolation procedures, aseptic techniques, careful cleaning and monitoring of different instruments. Also several combinations of drugs are used to treat sever infections and several types of vaccines are being tested, but none is currently available for general use till now **(D′Agata, 2004).**

The present essay was conducted to review the epidemiology of *P. aeruginosa* and considerable focusing was directed on drug resistance of *P. aeruginosa* including types, genetic background and mechanisms of resistance. Moreover, different management options were discussed as well as the various infection control measures taken to combat *Pseudomonas aeruginosa* infections and emergence of resistance.

The *Pseudomonads* are well known to plant microbiologists because they are one of the few groups of bacteria that are true pathogens of plants. But *P.aeruginosa* and two other species (now reclassified as *Burkholderia*) are pathogens of humans **(Todar, 2008).**

General Description

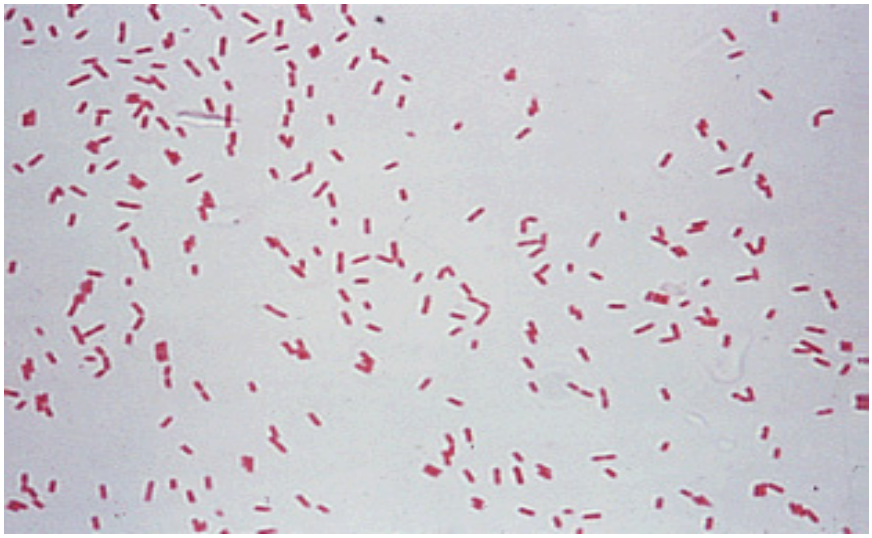

Figure (1): Gram stain of *Pseudomonas aeruginosa* (Todar, 2008).

P. aeruginosa are aerobic, non spore forming, non capsulated, gram-negative rods **(Holt et al., 1994).** They are motile due to the presence of one or more polar flagella, oxidase positive, catalase positive, indole and H_2S are not produced, these tests may be used to characterize *P.aeruginosa*, particularly when pyocyanin production is absent or doubtful, they grow on MacConkey´s agar, appearing as lactose- non fermenters **(Jawetz et al., 2004).** *P. aeruginosa* displays multiple phenotypes when a biofilm develops **(Sauer et al., 2002).**

P. aeruginosa grows readily on ordinary bacteriological media and is often readily identified by colonial appearances on nutrient agar.

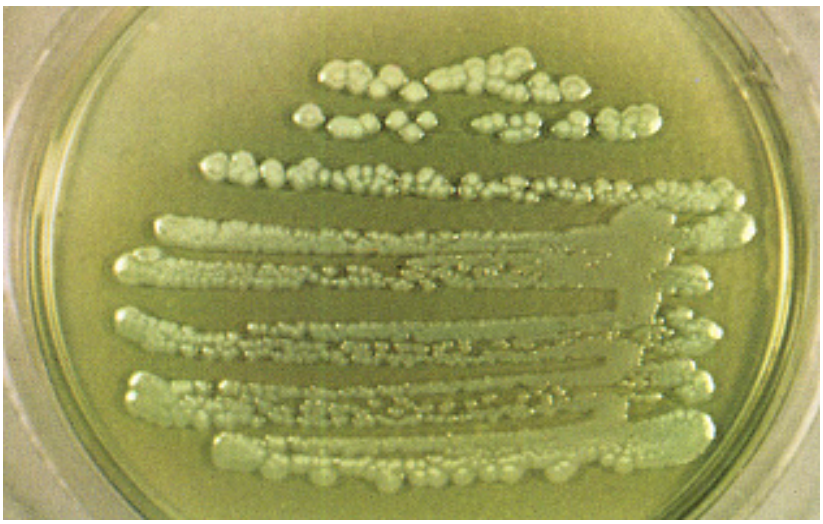

Figure (2)*: Pseudomonas aeruginosa* colonies on agar (Todar, 2008).

The smooth and mucoid colonies are presumed to play a role in colonization and virulence **(Jawetz et al., 2004).** Mucoid strains of *P.aeruginosa* produce profuse amount of an extracellular polysaccharide on agar culture which is chemically similar to alginic acid providing a matrix for the organisms to live in biofilm, protecting it from external environment **(Pier et al., 1983).**

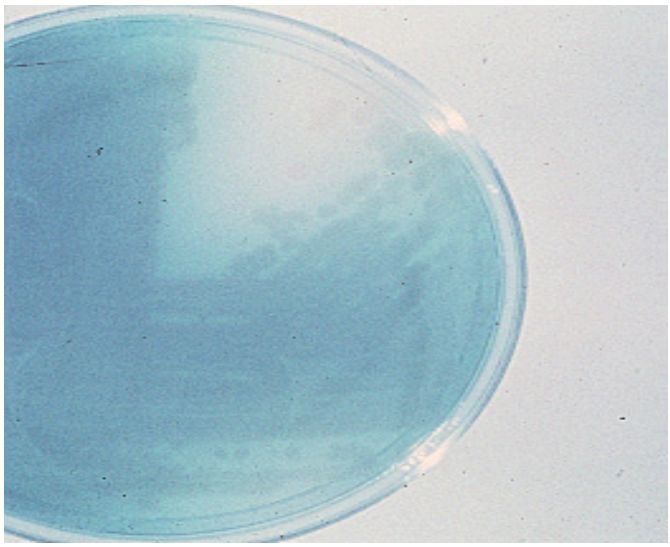

Figure (3): The soluble blue pigment pyocyanin is produced by many, but not all, strains of *Pseudomonas aeruginosa* (Todar, 2008).