**Pseudomonas in the chest**

*Pseudomonas aeruginosa* is one of the most important opportunistic organisms which involves the chest. It causes a wide spectrum of disease varying both in severity and in the site of involvement of the respiratory tract, and study of this spectrum provides insight into the relationship between host and invader.

Colonization of the upper respiratory tract is very rare in healthy individuals, but becomes common in association with severe illness in hospital. This is not merely due to exposure to the organism since *Pseudomonas* isolation rates are low among hospital workers and psychiatric in-patients (< 3%), rise in the moderately ill (22%) and are high (63%) in moribund patients (Johanson, Pierce & Sanford, 1969). Pre-existing chronic bronchitis, coma, hypotension and endotracheal intubation all predispose to colonization (Johanson et al., 1972) which becomes almost universal in patients needing prolonged artificial ventilation. Previous antibiotic treatment is probably not an important predisposing factor but rather a reflection of the severity of the patients illness. This colonization indicates a deficient clearance of *Pseudomonas* from the upper respiratory tract and correlates well with *in vitro* tests of adherence of the organism to epithelial cells (Johanson et al., 1980). Animal studies have shown adherence to be increased by viral infections and endotracheal intubation (Ramphal et al., 1980), and these studies indicate how a first line of host defence is breached by local injury, so allowing the *Pseudomonas* to flourish at a critical site for subsequent aspiration into the lower respiratory tract. Inhaled polymyxin given prophylactically reduces the incidence of colonization by *Pseudomonas* but not of Gram-negative pneumonia or death (Feeley et al., 1975).

Chronic colonization of lower respiratory secretions with *Pseudomonas* in chronic bronchitis or bronchiectasis is surprisingly rare despite inevitable contact with the organism and frequent broad-spectrum antibiotics. This suggests that excess mucous or defective mucociliary clearance does not allow colonization. In cystic fibrosis however, after adolescence, *Pseudomonas* colonization is almost universal (Fick, 1981). Once colonized the sputum continues to provide a heavy growth of *Pseudomonas* indefinitely and replacement by another organism is almost unknown. The mucoid variant *Pseudomonas* is usually isolated and this may revert to the rough form on repeated subculture. Patients tolerate this heavy colonization very well most of the time without illness or decline in lung function. Intermittently, however, malaise, weight loss or symptoms of acute bronchitis indicate that the passenger has become a pathogen. When this happens it is difficult to know why. There is seldom evidence of a second invader, and the resident *Pseudomonas* appears unchanged. Treatment with appropriate antibiotics usually cures the acute illness but does not eradicate the *Pseudomonas* although the number of organisms may be reduced for some time. Similarly regular inhaled antibiotics have recently been shown to reduce the number of episodes of illness without eradicating the organism (Hodson, Penketh & Batten, 1981). The relationship between host and opportunist is therefore very finely balanced and it may be that small changes in bacterial numbers are sufficient to tip the scales. Nevertheless *Pseudomonas* pneumonia is surprisingly rare although penetration of the organism to the alveolus must occur quite commonly. This is presumably because alveolar defences—macrophage clearance and systemic immunity are normal in cystic fibrosis.

*Pseudomonas* pneumonia is quite different, the host is severely ill and immunologically compromised. The contributory factors identified include neoplasia—especially haematological, cytotoxic drugs, steroids, chronic lung disease and a complicated postoperative course (Pennington, Reynolds & Carbone, 1973; Rose, Heckman & Unger, 1973; Iannini, Claffey & Quintiliani, 1974).
In these patients the sequence of events is probably as follows: upper respiratory tract colonization occurs early as described above, and is followed by aspiration of organisms to the lower respiratory tract. Aspiration of pharyngeal content during sleep is frequent in healthy adults and becomes very common when consciousness is depressed (Huxley et al., 1978). Impaired mucociliary clearance allows the organism to persist and penetrate to the alveolus. Multiplication and tissue invasion then occur because alveolar macrophage clearance and immune function are depressed. Pseudomonas is thus able to reach its full potential as an opportunistic pathogen. Mortality in initial reports was over 70% although with better treatment this may be reduced (McKendrick & Geddes, 1981). Treatment with an aminoglycoside and certain β-lactam antibiotics can be successful but the underlying state of the patient is probably the most important factor. Newer antibiotics such as ceftazidime are at present being evaluated.

Pseudomonas infections of the respiratory tract provide a rare opportunity to study pulmonary host defences. The range of disease from simple colonization to fatal pneumonia demonstrates the importance of both local clearance mechanisms and systemic defences, and furthermore emphasizes that the host is by far the most important variable in the confrontation. Future advances in treatment are likely to act on the host rather than the organism.

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References


The clinical relevance of pharmacokinetics
For much of human history therapeutics has been an empirical discipline. Notwithstanding the simple and rational appeal of empiricism many errors have resulted and this naive approach is demonstrably inadequate. For example, extracts of fox glove leaf were at one time given as an emetic; in the light of present day knowledge this practice didn't require it. Pharmacokinetics is just one of the many disciplines that is contributing to setting therapeutics on a rational footing.

The quantitative description of drug absorption, distribution, metabolism and elimination, that is pharmacokinetics, is the framework for making generalizations about drug disposition. For the drug industry pharmacokinetic studies have led to improvement in drug formulation resulting in better bioavailability and improved dosing regimes. To the clinician the overriding question, if this new discipline is to have any direct relevance, is whether it contributes to improved therapeutic efficacy and a reduced incidence of adverse effects.