Opportunistic Lung Infections

H. P. LAMBERT, MD, FRCP
Professor of Microbial Diseases, University of London, and Physician, St George’s Hospital Medical School, London

The variations in the pathogenicity of micro-organisms and of host resistance are so great that in one sense almost every lung infection may be regarded as opportunistic. Many of the common causes of pneumonia such as the pneumococcus are normal commensals of the upper respiratory tract and why they become pathogenic in the individual patient remains obscure. At the other extreme, patients with serious immune suppression become infected by organisms that normally have little relationship to the human host. In practice, opportunistic lung infections can be considered in two convenient, although overlapping, categories. First there are infections with common commensal and environmental bacteria in patients who have ordinary illnesses needing admission to hospital. Second are much less common infections occurring in patients with severe neutropenia and with cellular immune defects associated with transplantation or with treatment of malignant diseases (Table 1).

The Gram-negative pneumonias, about which there is an extensive literature, are rarely encountered in infections acquired outside hospital and are mainly associated with chronic disease, or alcoholism. For example, in a recent series of pneumonias, reported from Atlanta, Georgia (Sullivan et al., 1972), about 20 per cent were labelled as Gram-negative, but of the 292 patients in this series the majority were suffering from associated heart disease, alcoholism, chronic lung disease or diabetes. During the same period 400 patients with other uncomplicated pneumonias were treated as outpatients and the figure of 20 per cent is thus an overestimate of the incidence of these infections in hospital practice.

However, for true nosocomial pneumonia acquired in hospital, Gram-negative pneumonias are the largest group and pneumococcal pneumonia is again common, especially following organ transplants. In these series, most of the patients had associated conditions that would predispose them to infection. The organisms commonly involved in these infections were Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli and Proteus. Staphylococcal infections were also quite common in immune suppressed patients although they have been less of a problem in hospital practice in recent years.

Gram-negative lung infections acquired in hospital arise in a particular epidemiological pattern. This begins with widespread colonisation of the upper respiratory tract by the relevant organisms. The extent of this colonisation is affected by treatment in special areas such as intensive care units, the type of illness, the length of time in hospital and, particularly, the amount of antibiotics already given. All studies show the remorseless, often silent, build-up of preceding colonisation and the dangers of intensive care units where the three factors which particularly predispose to hospital infection come together most often, i.e. potentially dangerous organisms, illnesses associated with suppressed natural resistance, and procedures such as tracheal intubation or tracheostomy which render patients more liable to infection.

To summarise, opportunistic lung infections in uncomplicated diseases in patients in hospital may be caused by Gram-negative organisms including Klebsiella, pseudomonas and by staphylococci, while commoner causes of pneumonia such as the pneumococcus and Haemophilus influenzae are also important.

One special factor in opportunistic infection is the problem of aspiration pneumonia. Because of the large anaerobic population in the upper respiratory tract it is difficult or impossible to assess by testing sputum alone whether an anaerobic organism is important in lung infection. Bartlett et al. (1974) have shown that in about 80 per cent of these infections more than one organism is involved, usually as a mixture of anaerobes alone, or a mixture of aerobes and anaerobes together. Common aerobic Gram-negative organisms are more often found in aspiration pneumonia that develops in hospital than outside. This has obvious implications for the choice of

---

Table 1. Causes of pneumonia in patients with immune suppression.

| Bacteria | Str. pneumoniae | Staph. aureus | Gram-negative bacteria | M. tuberculosis | Atypical mycobacteria | Nocardia |
|----------|----------------|--------------|------------------------|----------------|-----------------------|---------|
| Viruses  | Cytomegalovirus  | Herpes simplex | Varicella-zoster | Adenovirus | Candida albicans | Cryptococcus |
| Fungi    | Candida albicans | Cryptococcus | Aspergillus | Pneumocystis carinii | Toxoplasma gondii |

This article is based on a paper given at a Teach-in at the Royal College of Physicians in April 1978.
antibacterial chemotherapy, prolonged treatment with high doses of penicillin being invaluable.

Following clinical examination and chest radiographs, diagnostic methods of value include cultures of blood and sputum, together with cultures from nose and throat swabs and faeces. Initial blood samples should be tested for viral and mycoplasmal antibodies and cold agglutinin titres and stored for comparison with subsequent samples. Other specimens of sputum or gastric washings should be examined by smear and culture for tubercle bacilli. Thereafter, treatment should begin with first choice 'empirical' chemotherapy. Ordinary sputum tests as they are commonly done in hospital are unreliable. The commonest reason why a Gram-negative organism is isolated from sputum is because the sputum has been collected after antibiotic treatment has led to colonisation of the upper respiratory tract. This happens within the space of a few hours. When these organisms have grown there is often no sign of respiratory infection of any significance but it remains essential to obtain as good a specimen of actual sputum as possible before starting antimicrobial treatment. Specimens obtained by transtracheal puncture would usually be more informative and this method should be more widely used, as it is in America.

In the second category of respiratory infections in patients with more severe immune suppression and neutropenia, infection with ordinary organisms, pneumococci, staphylococci and the Gram-negative organisms are again common, but here the infections may come on with much more alarming speed and present greater difficulties in diagnosis; for example, in a recent review of Gram-negative pneumonias (Valdivieso et al., 1977) a third of the patients had a normal chest X-ray at the onset of the illness and over half the species involved were pseudomonas or Klebsiella.

In addition to the usual bacteria, a much larger list of possible organisms must be considered, including bacteria, viruses, fungi and protoza. Special consideration will be given to some of these. Pneumocystis carinii has attracted a lot of interest in recent years. Although first described as a cause of infection in malnourished babies in nurseries, more recent reports have concerned patients with immunosuppression. About half of the reported infections occur in patients with leukaemia, mainly of the acute lymphoblastic type, and the rest are associated with the various kinds of immune deficiency present in transplant recipients. The main physical signs are dyspnoea and fever; about half the patients have a non-productive cough but only a third have abnormal chest signs. Nearly all patients have bilateral diffuse abnormalities on chest X-ray. Recent epidemiological studies in The Netherlands (Meuwissen et al., 1977) have found that evidence of infection with P. carinii develops in nearly all individuals with or without recognisable illness, the peak incidence being between one and fourteen years. If confirmed, these observations suggest that we are dealing with a common background of silent infection brought into clinical activity by immunosuppression. Another important recent finding is that treatment with 12 to 15 tablets of co-trimoxazole daily gives a recovery rate of about 70 per cent from P. carinii infections, which is about the same as with pentamidine but with much less toxicity (Hughes, 1976). Fever disappears within about three days of starting treatment and the chest X-ray returns to normal in about five to fifteen days. About half of those who fail to respond to co-trimoxazole can be successfully treated with pentamidine.

The important problem with the large number of other organisms that may cause pneumonia in immunosuppressed patients is that individual organisms do not cause specific identifiable clinical syndromes. Thus, about half the patients clinically diagnosed as having Pneumocystis carinii pneumonia turn out, in fact, to have pneumonia from some other cause. The cumulative toxicity of treating all the possible micro-organisms involved would be greater than the cost of making a positive diagnosis. Because most of these infections cannot be diagnosed from simple sputum tests and blood cultures, invasive procedures are needed in patients in whom they will carry considerable risks because of immune suppression and haemorrhagic tendencies. The invasive procedures that have been performed include:

- transthoracic needle aspiration,
- transthoracic lung biopsy,
- fibreoptic brush biopsy,
- fibreoptic transbronchial lung biopsy,
- open lung biopsy.

In various series the results, in terms of yield, and the complications of these procedures have varied widely. In very good hands, open lung biopsy seems about the safest and has about the highest yield. Needle aspiration with a 22 gauge spinal needle also seems to be a relatively safe procedure, provided the patient is not too breathless, has not got emphysema, will not need artificial ventilation, and does not have a major bleeding disorder.

The choice of procedures obviously depends on what expertise and skills are available locally and, to some extent, on the direction of clinical suspicions, as one procedure may be more favourable than another as a diagnostic method for one organism.

Thus, the diagnosis and rational treatment of patients with opportunistic respiratory infections can be considered as a staged procedure in which very often it will be unnecessary to go beyond ordinary conventional diagnostic manoeuvres, followed by a first choice of empirical chemotherapy, e.g. combinations of a penicillinase-resistant penicillin and a suitable aminoglycoside. However, in patients who do not respond to these initial manoeuvres, and especially in those who have severe forms of immune suppression, it may be necessary to go far beyond these initial steps. Transtracheal aspiration should be considered next and the more invasive diagnostic manoeuvres will normally have their main role in special centres.

Finally, two warnings. First, although the isolation of Gram-negative aerobic bacilli like Klebsiella or pseudomonas from the sputum is often used as the trigger for complicated regimes of chemotherapy, the great majority of these isolations are simply the result of taking sputum after chemotherapy has been started. Such isolates mainly represent the change in respiratory tract flora induced by antibiotic treatment and commonly do
not indicate any lower respiratory tract infection whatsoever. Always obtain a satisfactory specimen before starting chemotherapy. Secondly, by no means all the pulmonary disorders that occur in patients with immune suppression or in a hospital setting are infective, and other pulmonary conditions that may easily be confused with infection must be considered. These include pulmonary infarction, neoplasia, pulmonary oedema and other coincidental pulmonary disease.

References
Bartlett, J. G., Gorbach, S. L. and Finegold, S. M. (1974) American Journal of Medicine, 56, 202.
Hughes, W. T. (1976) New England Journal of Medicine, 295, 726.
Meuwissen, J., Tauber, I., Leeuwenberg, A., Backers, P. and Sieben, M. (1977) Journal of Infectious Diseases, 136, 43.
Sullivan, R. J., Dowdle, W. R., Marine, W. M. and Hierholzer, J. C. (1972) Archives of Internal Medicine, 129, 955.
Valdivieso, M., Gil-Extremera, B., Zomoza, J., Rodriguez, V. and Bodey, G. P. (1977) Medicine (Baltimore), 56, 241.

Book Review

Topics in Therapeutics 4. Edited by D. W. Vere. Pitman Medical, Tunbridge Wells, 1978. Price £7.

The series of College conferences, and their associated publications, have done much to re-establish the reputation of the Royal College of Physicians of London as a scientific body. The popularity of these conferences is attested by the hot competition for places at them. This volume contains the papers presented at the fourth conference devoted to clinical pharmacology and therapeutics. It covers a very wide range of topics of current interest from cimetidine in peptic ulcer to the use of analgesics in terminal care.

A potential weakness of this approach is that no subject is dealt with in great depth or breadth. Thus, the section on gastrointestinal disease consists of three short chapters, one on cimetidine, one on cromoglicate, and one on methonidazole. The second section on antibiotics has one on semi-synthetic penicillins and the other on the use of aminoglycoside antibiotics. There is a slight danger that this approach may give a somewhat unbalanced impression. For example, it is difficult to consider semi-synthetic penicillins without some discussion of drugs such as the cephalosporins that compete for their therapeutic place in the sun. The book is not intended, however, to be a textbook but more a review of current practice and in this it succeeds very well. I had picked it up intending to do the usual reviewer's filleting job and ended up by reading most of it. On reflection, I believe that my initial impression that too wide a sweep of subjects was covered is correct. Publications such as this are in the best sense ephemeral. One ought to read them today, dip into them for the next year or two and then throw them away after three years. They are part of one's current awareness.

Recommended reading for those who prescribe drugs, particularly in hospital.

C. T. DOLLERY

J. Roy. Coll. Physcns Vol. 13 No. 1 January 1979.