Chemotherapy of Pneumonias

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Ideally, the antibiotics chosen for the treatment of an infection should depend on the micro-organisms identified and their sensitivities. It is difficult to apply this principle to the treatment of respiratory tract infections because of the relative difficulty of obtaining satisfactory specimens of sputum and the uncertainty as to the relevance of the findings since some of the organisms detected may be present in the respiratory tract as normal commensals. Table 1 lists the commoner microorganisms involved in pneumonia. Prospective surveys of patients with pneumonia can provide some information on the incidence of the various causative agents, including viruses, but may be misleading because the studies have been made only on patients referred to hospital on account of particularly severe illness, failure of home treatment, or for social reasons. Such surveys may not therefore reflect the true incidence of the different types of pneumonia within the community, which perhaps explains why there was only a 10 per cent incidence of pneumococcal pneumonia in a recent survey in Bristol.

Distinction between Bacterial and Non-bacterial Pneumonia

From such surveys it is possible to obtain information about the clinical and pathological features of different types of pneumonia.

Sputum. In bacterial pneumonias initial sputum produced is usually purulent and may be blood-stained. In virus and mycoplasma pneumonias there is often a dry cough initially but when sputum production starts it is usual for the early specimens to be mucoid. These details of history may be a valuable aid because the sputum may become purulent within the first 24 hours and by the time specimens are examined it may appear mucopurulent, concealing these clues to possible causative organisms.

Headache. This may be a feature of all infections, and in bacterial pneumonia it is often present at the outset, particularly where there is associated influenza. Headache may be a very prominent and prolonged symptom in mycoplasma pneumonia and the patient may be suspected of having meningitis.

Pleuritic Chest Pain. This is a common feature in bacterial pneumonias but is rare with mycoplasma pneumonia.

Physical Signs. Much has been written about the discrepancy between radiological and physical signs in viral and mycoplasma pneumonias but it seems more likely that the physical signs are determined by the site and extent of consolidation rather than the causative organism. When a pattern of nodular shadowing on chest X-ray is present with mycoplasma pneumonia it is usually associated with few physical signs in the chest, but the pattern of shadowing on X-ray with this organism is much more often lobar or segmental and accompanied by appropriate physical signs.

White Blood Count. This may be of some assistance because it tends to be raised in bacterial pneumonias. Exceptions will occur, especially in the elderly and in patients who are very severely ill. In the Bristol survey, the mean white blood count was $15.5 \times 10^9$ litre in bacterial pneumonias and $8.8 \times 10^9$ litre in viral and mycoplasma pneumonias. As only one patient in the non-bacterial group had a white blood count above $15 \times 10^9$ litre it appears that a white count above this level makes a non-bacterial pneumonia most unlikely.

Cold Agglutinins. These were unreliable in distinguishing mycoplasma infections from other types of pneumonia. About 40 per cent of patients with mycoplasma infections had cold agglutinins in significant titres (i.e. greater than 1/32) but 18 per cent of patients with other types of pneumonia also had significant titres of cold agglutinins. Using a higher titre of cold agglutinins as the significant level did not increase the discrimination.

Chest X-ray. There are usually very few specific features that, on chest X-ray, will reliably indicate the cause of a particular pneumonia. Abscess formation is characteristic of staphylococcal pneumonia and cavitation of a

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lobe may occur in Klebsiella pneumonia. Sometimes pseudomonas pneumonia may also cause areas of cavititation. Apart from these, no radiological features are characteristic of particular organisms. It has been suggested that mycoplasma pneumonia causes a perihilar infiltration but the pattern is more often of lobar or segmental distribution and may involve more than one lobe. On occasions it may result in a diffuse nodular consolidation throughout the lung fields but this again is not diagnostic.

Features of Non-bacterial Pneumonia. The following may indicate possible non-bacterial pneumonia—

1. The initial sputum is mucoid.
2. Absence of pleurisy in spite of apparent lobar consolidation.
3. White blood count less than 15 x 10⁹/litre.
4. Known occurrence of an epidemic of Mycoplasma pneumoniae infections or a contact history suggesting the possibility of psittacosis or Q fever.

In patients with pneumonia an attempt should be made to isolate the offending organism from the sputum, and blood cultures and blood samples should be taken for viral antibody studies, but it is usually necessary to begin treatment before the results of these tests are available. The following classification is helpful in choosing initial antibiotic therapy.

The Previously Healthy and Untreated Patient

The pneumococcus is the most likely cause of pneumonia, and treatment with penicillin would be appropriate although ampicillin would also be effective. If there are atypical features such as those previously listed, or there is an epidemic of Mycoplasma pneumoniae infection, initial treatment with oxytetracycline would be effective against this organism and also against over 90 per cent of strains of pneumococci. Tetracyclines should be avoided in the young, in whom they will cause permanent staining of the teeth and bones, and in the elderly and all patients in whom poor renal function is known or suspected. With pneumonia following influenza the most likely causative organism is still Streptococcus pneumoniae but it is in these patients that staphylococcal pneumonia is prone to occur. In the obviously ill or deteriorating patient after influenza it would be wise to give a penicillinase-resistant antibiotic to cover for staphylococci. The incidence of penicillin-resistant staphylococci is now similar in both hospital and domestic populations; between 60 and 70 per cent are resistant. Treatment should begin with benzyl penicillin or ampicillin in combination with flucloxacillin.

Patients with Underlying Lung Diseases

In this group of patients Haemophilus influenzae and pneumococci are likely pathogens and ampicillin is probably the drug of choice, especially for patients with known chronic bronchitis or emphysema who develop pneumonia. Co-trimoxazole is a suitable alternative for patients who are allergic to penicillin.

In Life-threatening Illness

For patients with very severe pneumonias it is necessary to cover Gram-negative organisms and staphylococci. Gentamicin will be effective against staphylococci, Klebsiella pneumoniae and H. influenzae but penicillin would be needed in addition to cover for streptococci. It may be advisable to add flucloxacillin to cover for penicillinase-resistant staphylococci.

Failed Treatment

Patients in hospital practice tend to include groups who are not improving in spite of treatment, others who are deteriorating, and yet more in whom complications develop. There are no clear rules as to the course of action to be taken in these circumstances because there are usually a number of reasons why the patient has not improved. Commonly, antibiotic treatment has not been taken regularly or the antibiotic chosen may not have been appropriate; for example, ampicillin will have been ineffective in treating infections with Mycoplasma pneumoniae and most of the cephalosporins are relatively ineffective in H. influenzae infection. Pneumonia secondary to bronchial obstruction, as with a bronchial carcinoma, is likely to be slow to resolve. Persistent illness may indicate that a lung abscess or empyema has developed. In these circumstances the diagnosis of pneumonia should always be questioned. Several conditions are frequently confused with pneumonia, including left ventricular failure, which may on X-ray look like bronchopneumonia, pulmonary infarcts, and the infiltrates of bronchopulmonary aspergillosis.

Table 2 summarises the antibiotics appropriate for the specific infections, and is intended as a guide.

| Table 2. Antibiotics appropriate for specific infections. |
|----------------------------------------------------------|
| Pneumococcus | Penicillin or ampicillin |
| Staphylococcus | Flucloxacillin, gentamicin, cephalosporins |
| Klebsiella | Gentamicin |
| H. influenzae | Amoxicillin or co-trimoxazole |
| Mycoplasma | Oxycycline |
| Q fever | Erythromycin |

Antibiotic Resistance

Between 60 per cent and 70 per cent of staphylococci are not resistant to penicillin and the incidence of resistance is the same in both hospital and home populations. About 1.5 per cent of Haemophilus influenzae are resistant to ampicillin but the exact figure varies from region to region. About 3 per cent of strains of this organism are resistant to tetracycline but, again, there is regional variation in resistance. Some 7 per cent of pneumococci are resistant to tetracyclines and penicillin-resistant pneumococci have recently been reported from South Africa. It seems likely that the incidence of resistant strains of organisms will steadily increase so that due account must be taken of these changing patterns.

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