# COMMUNITY-ACQUIRED PNEUMONIA

## What is new in aetiology and treatment

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Community-acquired pneumonia (CAP) remains a considerable problem in terms of morbidity, mortality and use of hospital resources despite the remarkable advances in antibiotic therapy. It is estimated that in the U.K. 1 per 1000 in the general population is admitted with pneumonia annually (1) and pneumonia accounts for about 10 times as many deaths (in U.K.) as all other infections combined (1). The mortality in published series has ranged from 6.7 - 18% in the British series (1) and 6-24% in the U.S.A. (1). These percentages change according to the organism causing the pneumonia and the age of the patient. The past 20 years have been marked by striking changes in the pattern of pneumonias, as manifested by new diseases, new modes of transmission and new manifestations of old diseases.

In Malta pneumonia is also a common cause of hospital admission and we are at the moment carrying out a study to determine the frequency and the clinical pattern of the disease locally. Hospital cases are however only part of the total incidence of CAP as many cases are treated at home and never reach hospital. In fact the incidence of CAP is unknown but estimates vary between 1-10 per 1000 of the population. (2,3)

In the evaluation of a patient with pneumonia, the usual histo- pathological classification is of little value to the clinician. Indeed, having made the diagnosis, the major consideration is to interpret the clinical setting in which the pneumonia occurs in order to infer from this the most likely aetiological diagnosis. To do this one has to have some idea of common aetiological agents in the community as well as determine the condition of the host and the environment in which the pneumonia develops.

Table 1 (1-7) summarises the aetiological frequencies of CAP in various studies reported over a 15 year period. There is a high incidence of unidentified causative micro organisms, probably due to antibiotics given prior to hospital admission, masking the infective organisms when sputum culture is attempted. In fact when other tests like counter immuno-electrophoresis (CIE) were carried out, (5), only in 2 to 4% of cases was the causative organism undetected. Strep. pneumonia was still the most common cause in almost all the series even though there was an increasing incidence of viral and mycoplasmal pneumonias. Mycoplasma, which lacks a cell wall, occurs usually in epidemics which occur at intervals of 4-5 years. Legionella pneumophilia is also increasing in frequency. It is therefore important to monitor the pattern of aetiologies of pneumonias at regular intervals, as the frequency of various agents changes over the years. In a study from Yale (8), the changing pattern of causes of pneumonia between 1969 to 1972 and 1979 to 1982 were compared. Table 2 showed that there was a decrease in bacterial causes from 63% to 48% as well as an increase in fungal and viral causes. These changes in incidence reflect changes in the pattern of medical practice over the years where there is an increase in patients with some degree of immunosuppression either because of the nature of the disease or as part of the therapy (9).

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**TABLE 1** AETIOLOGIES OF COMMUNITY-ACQUIRED PNEUMONIA 1971-1987

| Author | No of Patients | % Unknown | % Viral or Mycoplasma | % S Pneum. | % S Aureus | % H Influ. | % Gram Neg | % Legionella | % OTHER |
|---|---|---|---|---|---|---|---|---|---|
| FEKETY 1971 | 100 | 29 | 5 | 62 | 1 | - | 2 | - | 1 |
| SULLIVAN 1972 | 292 | 36 | 7 | 35 | 6 | 5 | 11 | - | - |
| WHITE 1981 | 210 | 52 | 29 | 11 | 4 | 2 | 1.5 | 1.5 | 4 |
| MACFARLANE 1982 | 127 | 2.4 | 11 | 76 | 2.4 | 3 | 0.8 | 15 | 5.5 |
| McNABB 1984 | 80 | 36 | 6.25 | 56 | 3.75 | 6.25 | 1.25 | 1.25 | 3.25 |
| MARRIE 1987 | 301 | 34 | 20.3 | 8.6 | 4.6 | 6.3 | 2 | 3.9 | 20 |
| BTC STUDY 1987 | 453 | 33 | 25 | 34 | 1 | 6 | 1 | 2 | 7 |

**TABLE 2** INFECTIOUS PNEUMONIAS IN HOSPITALISED PATIENTS: THE CHANGING SPECTRUM AT THE YALE NEW HAVEN MEDICAL CENTRE

| Pathogenic Agents Isolated | July 1969 to Jan.1972 (%) | July 1979 to Jan. 1982 (%) |
|---|---|---|
| Total bacterial causes | 63.8% | 48.6% |
| Total fungal | 7.2% | 13.2% |
| Total viral | 17.5% | 32.9% |
| Total Patients Reviewed | 935 | 1,175 |

(FICK R.B. et, THE AMERICA JOURNAL OF MEDICINE, 1983, 74,2)

**TABLE 3** CATEGORIES OF PATIENTS WITH PNEUMONIA

| | | |
|---|---|---|
| TYPE I | - | PNEUMONIA IN A PREVIOUSLY HEALTHY PATIENT |
| TYPE II | - | PNEUMONIA IN PREVIOUSLY UNHEALTHY LUNGS |
| TYPE III | - | POST-INFLUENZAL PNEUMONIA |
| TYPE IV | - | PNEUMONIA IN A COMPROMISED PATIENT |
| TYPE V | - | HOSPITAL ACQUIRED PNEUMONIA |

Table 3 shows the categories of patients in which different types of pneumonias occur in various groups of patients. This is helpful as it can give a good indication as to the likely aetiological causes of the pneumonia. The main causative agents of severe pneumonia in previously healthy patients, are likely to be either pneumococcal, mycoplasmal or viral. Table 4 Though the real prevalence of pneumococcal pneumonia in hospital practice is difficult to determine, becauseof pre-admission antibiotic therapy, it should still be considered as the most common cause of CAP in a previously healthy subject. It is worrying to note that thereare emerging reports of pneumococci which are penicillin resistant (10) especially in South Africa and New Guinea where penicillin prophylaxis used to be given because of pneumococcal epidemics (11).

In the last 15 years Legionella and a member of the Chlamydia genus known as TWAR have also emerged as potential pathogens in this type of patient (12). A dramatic outbreak of pneumonia (182 cases with 29 deaths) in a Philadelphia Legionnaires convention in July 1976 led to the identification of a unique, fastidious, Gram-ve, aerobic, intracellular bacillus the following January. Retrospective studies identified this organism in cases of pneumonia occurring 25 years earlier. The commonest species (24 in all) is Legionella pneumophila and this has 12 subgroups. The incidence of Legionnaires' disease in various series of CAP ranges from 1-27%. In Malta there were some imported cases of Legionnaires' disease some of whom died. One case was in a man who had not gone abroad but the local source was not identified. Maltese sources are becoming more likely with the increasing use of air-conditioners. Legionella produces a lobar pneumonia or bronchopneumonia and can show CXR progression whilst the patient is on treatment.

An important feature is the lack of purulent sputum in the presence of a consolidation. Extrapulmonary involvement ranging from diarrhoea to changes in mental status may be seen in 25-75% of patients. All environmental sources of the organism are related to water and include cooling towers, condensers, humidifiers, air-conditioners, nebulizers filled with tap water, aerosols created by showers or water faucets. The primary method of environmental control has been to increase water temperature and chlorination. The early administration of erythromycin (4g/ day IV for at least 3 weeks) _+ Rifampicin is most important as the overall case fatality is 5-25% in previously healthy patients and up to 80% in immunocompromised patients (12).

A newly described Chlamydia organism called TWAR was shown to be the cause of 6% of pneumonias in 301 patients admitted to a Nova Scotia Hospital between 1981 and 1984 (7). It was the third most common cause in this study by Marrie, causing a mild pneumonia in teenagers; In patients with a pre-existing chronic lung condition, it can produce a severe illness. Its name is derived from the laboratory designation of the first two isolates TW183 and AR39. It is distinct from C. trachomatis and C. psittaci and the drug of choice for its treatment is erythromycin. The diagnosis is made through micro- immunofluorescence using TWAR as antigen.

Patients with previously unhealthy lungs are susceptible to a different spectrum of organisms causing their pneumonias (Table 5). Pneumococcus together with Haemophilus influenzae is still the commonest organism causing pneumonia in chronic bronchitics and in patients with non-cystic fibrosis bronchiectasis, while

**TABLE 4** LIKELY AETIOLOGICAL AGENTS OF PNEUMONIA IN PREVIOUSLY HEALTHY PATIENTS

| | | | | |
|---|---|---|---|---|
| VIRUSES | - | INFLUENZA | - | ADENO-VIRUS |
| BACTERIA | - | PNEUMOCOCCUS<br>LEGIONELLA | | |

MYCOPLASMA
CHLAMYDIA, PSITTACI, TWAR
COXIELLA BURNETI
MYCO. TUBERCULOSIS: RARE BUT LETHAL, HIGHLY TREATABLE

**TABLE 5** LIKELY AETIOLOGICAL AGENTS OF PNEUMONIA IN PATIENTS WITH PREVIOUSLY UNHEALTHY LUNGS

| | | |
|---|---|---|
| COPD PATIENTS AND NON-CYSTIC FIBROSIS BRONCHIECTASIS | - | PNEUMOCOCCUS<br>HAEMOPHILUS<br>BRANHAMELLA CATARRHALIS<br>MYCOPLASMA<br>VIRUSES |
| CYSTIC FIBROSIS PATIENTS | - | PSEUDOMONAS a.<br>STAPHYLOCOCCUS au. |

**TABLE 6** COMMUNITY ACQUIRED PNEUMONIA IN IMMUNOSUPPRESSED PATIENTS

| | | |
|---|---|---|
| - | PNEUMOCYSTIS C. | |
| - | VIRAL ESPECIALLY CMV | |
| - | FUNGI | - CRYPTOCOCCUS<br>- CANDIDA<br>- NOCARDIA<br>- ZYGOMYCETES |
| - | BACTERIA | - GRAM-VE BACILLI<br>- STAPH. AUREUS<br>- MYCOBACTERIA |

Pseudomonas and Staph. aureus are the commonest micro-organisms in cystic fibrosis patients.

Branhamella catarrhalis used to be thought of as just a commensal but is being increasingly recognised as a cause of lower respiratory tract infection in this group of patients. This is a Gram-negative, aerobic diplococcus. The majority (50-70%) of strains produce B-lactamases and are thus resistant to penicillins but sensitive to erythromycin, tetracycline or ciprofloxacin (13). In post-influenzal pneumonias, one must never forget its association with Staph. aureus, but again pneumococcus is the commonest cause of pneumonia in these patients.

The number of immunosuppressed patients in the community today has increased because of drugs such as steroids, organ transplants, and diseases with disturbed immunity - the best known being the acquired immunodeficiency syndrome (AIDS). Such pneumonias require urgent attention as they carry a worse prognosis.

The actiological agents in these patients constitute a different spectrum of micro-organisms, fungi, viruses and protozoa as causes of pneumonia. Gram-ve bacilli, staph. aureus and mycobacteria especially the atypical ones constitute the majority of the bacteria causing such infections. (Table 6).

The immediate institution of treatment with the most appropriate antibiotics is vital if the prognosis is to be improved. In a 90- centre study with 450 patients (1) with CAP, there were no deaths in patients who received antibiotics before hospitalisation. It was also found that certain features predicted a worse prognosis in patients with pneumonia. (Table 7). Not all these features will be present in the same patient but the presence of any of them should alert the physician to hospitalise the patient urgently.

Finally the following therapeutic regimes are suggested for the various types of CAP. In patients who were previously healthy Erthromycin is a good choice as all the common microorganisms involved including the potentially lethal Legionella are sensitive to it. When resistance is encountered amoxicillin or tetracycline are good alternatives. (Table 8).

In patients with previously unhealthy lungs a different group of antibiotics (Table 10P) are suggested as most of the organisms responsible are resistant to erythromycin. A new and important antibiotic group in this context are the 4-amino Quinolones which are derivatives of nalidixic acid. They are rapidly bactericidal acting on DNA gyrase (an enzyme which manipulates bacterial DNA so as to be able to be 'packed' in the small bacterium); they have excellent WBC and tissue compartment penetration and have good bio-availability when given orally. There are no naturally occurring quinolases and so resistance is very unlikely to occur quickly if at all. Ciprofloxacin is the best quinolone as regards the respiratory system (14) and has a very wide spectrum when compared to other antibiotics. Sputum levels of ciprofloxacin are in the order of 70% of serum levels and even higher in lung parenchyma greatly exceeding the M.i.C. of important respiratory pathogens. Overall efficacy in chest infections is over 90%. Its empirical use in CAP

**TABLE 7** CLINICAL FEATURES ASSOCIATED WITH INCREASED MORTALITY

1. AGE > 60 years
2. RESPIRATORY RATE > 30/min.
3. DIASTOLIC B.P. < 60 mm.Hg.
4. CYANOSIS
5. MENTAL CONFUSION
6. LOW PaO2 < 8 KPa.
7. VERY LOW OR VERY HIGH WBC COUNT

**TABLE 8** ANTIBIOTIC REGIME FOR COMMUNITY ACQUIRED PNEUMONIA IN A HEALTHY HOST

- PNEUMOCOCCUS
- LEGIONELLA — ALL SENSITIVE TO ERYTHROMYCIN
- MYCOPLASMA
- CHLAMYDIA
- OTHER SUGGESTED ANTIBIOTICS IF MICRO-ORGANISM IS RESISTANT
  - TETRACYCLINE
  - AMOXICILLIN

(especially in patients with previously healthy lungs) is inadvisable in view of the ready availability of suitable alternatives, as well as the relatively poor susceptibility of pneumococcus. Flucloxacillin or amoxycillin + clavulinic acid are usually given in post-influenzal pneumonia due to the possibility of Staph. pneumonia. Ciprofloxacin can also be used.

In Pneumonias in immunosuppressed patients treatment must start treatment empirically without delay and changed if necessary according to sensitivity results. Admission to hospital in such cases is mandatory. Table 10 shows recommendations of antibiotics regimes in immunosuppressed patients. These recommendations were modified from one by Masur (15).

## IN CONCLUSION,

- Act fast in treating suspected pneumonia
- Though Strep.pneumonia is still the commonest cause, think of newer agents and consider host and environment in which pneumonia developed.
- Though Erythromycin is still the first line drug, newer agents may be indicated.
- Refer to hospital immunocompromised patients with clinical features of pneumonia.

**TABLE 9** ANTIBIOTIC REGIME FOR COMMUNITY ACQUIRED PNEUMONIA IN PATIENTS WITH PREVIOUSLY UNHEALTHY LUNGS

- AMOXICILLIN
- CLAVULANATE - POTENTIATED AMOXCILLIN
- CIPROFLOXACIN
- CO-TRIMAXAZOLE
- CEPHALOSPORIN + AMINOGLYCOSIDE IN THE HOSPITAL ENVIRONMENT

**TABLE 10** RATIONAL ANTIMICROBIAL THERAPEUTIC REGIMENS FOR IMMUNOSUPPRESSED PATIENTS WITH EXTENSIVE PNEUMONIAS

| REGIMEN | SUSPECTED PATHOGENS LIKELY TO BE ADEQUATELY TREATED |
|---|---|
| CO-TRIMOXAZOLE (high dose) OR TRIMETHOPRIM + DAPSONE OR PENTAMIDINE IV OR NEBULIZED | PNEUMOCYSTIS C. |
| ERYTHROMYCIN | LEGIONELLA, MYCOPLASMA |
| DHPG (ganciclovir) | CMV |
| QUADRUPLE THERAPY | MYCOBACTERIA |
| AMPHOTERICIN | FUNGAL INFECTION |
| CEPHALOSPORIN | AEROBIC GRAM + ve COCCI |
| AMINOGLYCOSIDE | AEROBIC GRAM - ve COCCI |

MODIFIED FROM MASUR et al, JAMA. MARCH 22/29. VOL. 253 NO.12.

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