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RESPIRATORY TRACT DISEASE

Influenza and its Complications—II

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An article in last week's Current Practice discussed the general features of influenzal infections, and the complications that occur in the chest. This week further complications and treatment are described.

Non-respiratory Complications

Although it might be expected that influenza is likely to be followed frequently by complications involving the nose and ear, such as sinusitis and otitis media, in practice this does not seem to be the case. There are in fact no actual figures for the rate of occurrence of these complications either in those who were previously healthy or in those who had suffered from ear trouble in the past. It is necessary, therefore, to be on the look-out for bacterial complications such as antral infection or otitis media during the week following the initial fever of influenza. A rare but unfortunate sequel of influenza is loss of the sense of smell (anosmia).

Neurological complications, though fortunately uncommon, are many and varied. A rise in the number of reported cases of "encephalitis" in England and Wales in 1957 occurred during the quarter occupied by the Asian epidemic. Case reports during this epidemic indicate an illness with severe headache, drowsiness progressing to coma, signs of meningism and of upper-motor-neurone lesions, and abnormal electroencephalograms. The cerebrospinal fluid is either normal or shows a slight increase in lymphocytes. A fatal outcome may ensue, but the pathological changes in the brain and cord are variable and include a haemorrhagic "encephalopathy" or a demyelinating condition. Sometimes influenza is followed by the Guillain-Barré syndrome of polyneuritis with high protein content of the cerebrospinal fluid, but this occurs sporadically at any time of the year. There is little direct evidence that any of these neurological illnesses during or after influenza are specifically caused by the influenza virus.

Psychotic symptoms of an organic dementia are also encountered infrequently. An acute confusional state with restlessness and disorientation was described in 1957 in children and young adults with Asian influenza. Delirium of the familiar febrile variety is much more likely, but chiefly occurs where there are serious chest complications. Recovery from such acute mental states is usually complete.

Cardiac complications may occur in those without previous disease, but are then confined to patients with severe influenzal pneumonia. Pericarditis is more likely than myocarditis, but both have been described. Auricular fibrillation is the commonest abnormality: usually it occurs during the most toxic phase of illness, and it often ceases with recovery. It is more likely in elderly than in young subjects and may indicate the presence of ischaemic heart disease. The adverse effects of influenza upon those with valvular, hypertensive, or ischaemic heart disease has already been mentioned. Acute pulmonary oedema or right heart failure may occur; they probably represent the effects of an actual viral lesion of the alveoli and bronchioles. The occurrence of influenza in a pregnant woman with mitral stenosis represents a potentially hazardous situation which requires careful supervision. The same applies to any patient with valvular or other type of heart disease in whom a relatively slight degree of embarrassment of the pulmonary circulation may precipitate failure.

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Diagnosis

The differential diagnosis of the uncomplicated case of influenza from other short-term pyrexial illnesses is relatively unrewarding, and difficult from a laboratory standpoint. It is not easy to decide in the early stages whether the fever is due to a respiratory tract infection or to some unrelated condition such as a urinary tract infection, infectious hepatitis, or even meningitis. The lack of prominence of the respiratory signs in influenza in the early stages is unfortunate; but the appearance of the patient with his heavy-eyed languor, the reddening of the conjunctivae, coated tongue, and pharynx which is never quite normal are helpful pointers. The first case in a family or an outbreak probably cannot be diagnosed with certainty, but thereafter the problem is simpler. There is only one rapid method of deciding whether influenza virus is present in the throat, sputum, or nasal secretions. This is by fluorescent-microscopy—a method still in the phase of research and development. Virus can be recovered by inoculation of material from throat swabs into tissue cultures or fertile hens' eggs, but there must be no delay in the transport of the swab to the laboratory. In any case the minimum time required to ascertain the presence of virus is three days, and most laboratories require longer. Failure to recover virus does not mean that influenza virus is not concerned in the illness.

The confirmation of a diagnosis of influenza requires the examination of paired serum samples collected in the acute stage and seven to ten days later; results may be positive even when no virus has been recovered. Sera can be tested not only for antibodies to the influenza viruses but against a battery of respiratory virus antigens such as parainfluenza virus, adenoviruses, and so on. It is important to realize that febrile cases of acute respiratory disease resembling influenza may be due to a number of the enteroviruses, including Coxsackie A and B viruses and particularly Coxsackie A21. Most of these, but not the Coxsackie A21, can be recovered better from stool specimens than from throat swabs. Adenoviruses also are recovered as well from stools as from the throat, so that full investigation of the obscure febrile case must include the collection and dispatch of faeces to the laboratory. Unfortunately it is still true that the patient is usually well by the time that the laboratory results are available to the practitioner so that it is easy to be discouraged by the essential difficulties of the subject. Unless

family doctors do investigate their patients, however, there is no likelihood that the pattern of all the various respiratory virus infections of the community will ever be understood.

The second diagnostic problem is the differential diagnosis of complicated influenza, which begins by assessment of the degree of involvement of the lungs. The presence or absence of chest pain, dyspnoea, cyanosis, rales in the chest, and dullness to percussion, and the appearance of the chest *x*-ray films, enable the type of complication to be assessed. In hospital this is aided by bacteriological examination of the sputum. Testing of the pathogenic organisms for sensitivity to antibiotics enables the therapy to be placed on a firm basis. The decision whether to move a patient into hospital or not must be made often on grounds of illness or of social conditions rather than on physical signs. The degree of dyspnoea and tachycardia are also more reliable pieces of evidence than the height of the fever. It is important to lose no time in the accurate diagnosis of influenzal pneumonia. Pneumococcal infections, which usually cause good signs of consolidation, will respond better to treatment than staphylococcal infections, in which often there are few chest signs, but grave toxaemia may occur. The availability of nursing care and of oxygen and the ease of administering antibiotics by injection all argue in favour of hospital care, particularly in the elderly.

As to differential diagnosis, it is obvious that acute bronchitis or bronchiolitis associated with influenza in the adult will not be much different from the same lower respiratory disease due to common cold viruses (rhinoviruses). In infants the respiratory syncytial virus and in young children either this or the parainfluenza viruses are endemic causes of winter infections of the lower respiratory tract, and these outnumber infections due to the influenza virus. An important cause of apparent acute broncho-bronchiolitis, but one in which the chest *x*-ray shows a mottled or hazy opacity, is the *Mycoplasma pneumoniae* (pleuropneumonia-like-organism), once thought to be a virus. A prolonged incubation interval of three to four weeks occurs between cases in this infection, which may, however, involve members of a family *in seriatim*. Many cases never pass beyond the stage of bronchitis, and a proportion of these and of the cases of atypical pneumonia develop cold red-cell agglutinins in the serum.

Treatment

Uncomplicated influenza should be treated symptomatically only. Although numerous chemical substances are known which inhibit the multiplication of the virus in the laboratory in eggs, tissue cultures, or even mice, none has a degree of activity which is adequate for therapy once the infection has begun. The patient should be put to bed if there is fever, and the relief of headache, cough, and sleeplessness requires attention. The golden rule is the simpler the remedy the better. Paracetamol or a compound aspirin tablet are helpful for relief of headache, but patients should not be encouraged to remain at work or ambulant by their use. Codeine in a linctus, or one of the newer cough suppressant drugs such as pholcodine, can be used for dry, irritating, and useless cough, but should not be used if there is sputum. A simple barbiturate hypnotic, glutethimide, or chloral hydrate are useful for insomnia.

The vexed question of antibiotics for the prevention of bacterial complications should be resolved by attention to the patient. If he or she has chronic disease of the chest or heart or a history of recurrent otitis media then antibiotics are indicated. The choice will probably be in favour of an oral antibiotic, and tetracycline 0.25 g. six-hourly is probably the best form of prophylaxis. There is no justification for its use or for that of any other antibiotic in uncomplicated influenza in previously well persons.

When chest complications are present the best antibiotic is benzylpenicillin 0.5 mega unit six-hourly until the result of sputum examination is available. If the bacterial flora of the sputum is of mixed Gram-positive and Gram-negative organisms then streptomycin 0.5 g. intramuscularly six-hourly should be used in addition to penicillin. If only Gram-negative organisms are found such as *H. influenzae*, tetracycline, erythromycin, or ampicillin should be used in doses of 0.5 g. orally six-hourly. If there is clinical suspicion of a staphylococcal pneumonia, or if staphylococci are the dominant organisms in the sputum, a mixture of benzylpenicillin and either methicillin or cloxacillin should be used intramuscularly. This is to cover the possibility of resistance to penicillin on the part of the staphylococci. The required dose is 1 mega unit of penicillin and 1 g. methicillin every four hours. Oral treatment is not recommended because of the likelihood of impaired absorption in gravely ill persons. Cloxacillin, which has no advantage over methicillin if given intramuscularly, can be substituted for methicillin after the patient has begun to recover and is then used orally (0.5 g.) every four hours. It need not be used if the staphylococcus was initially found to be sensitive to penicillin. Adjustment of all these recommendations may be necessary either when the antibiotic sensitivity of pathogenic organisms is known or there is a lack of clinical response. The use of other antibiotics such as fucidin and vancomycin active against penicillin-resistant staphylococci is discussed by the author.[2] The recent series[3] in the *British Medical Journal* on antibiotics should also be consulted. A state of shock accompanying severe pneumonia calls for supportive measures, including intramuscular drugs such as aramine for raising the blood-pressure, and hydrocortisone by slow intravenous drip. Oxygen is necessary if there is cyanosis or great restlessness.

In all cases antibiotic therapy is required for at least three days after a return of the temperature to normal, and in patients with extensive consolidation or previous chest disease the duration of therapy may need to be for three or more weeks. Convalescence is always slow in the elderly or chronically ill.

REFERENCES

[1] Report of the M.R.C. Working Party on Acute Respiratory Virus Infections, *Brit. med. J.*, 1965, 2, 319.

[2] Stuart-Harris, C. H., *Influenza and Other Virus Diseases of Respiratory Tract*, 2nd ed., 1965. London.

[3] *To-day's Drugs*, 1964. B.M.A., London.