Respiratory Infections—New Agents and New Concepts

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The new facts on respiratory infections that have caught my interest are not easily woven into a coherent whole, so I present a respiratory rag-bag for 1980.

Viruses as Causes of Otitis Media, Sinusitis and Febrile Convulsions

Viruses that usually cause mild and mainly upper respiratory tract illnesses may invade the lower respiratory tract, causing relapses of bronchitis in bronchitic subjects and episodes of wheeziness in children who are prone to 'wheezy bronchitis'.

As the nasal mucosa is continuous with the epithelial lining of the paranasal sinuses and internal ear, it is quite plausible that viruses should spread into these cavities. In children it is common to see minor changes in the eardrum, including a slight redness, occurring as part of a general respiratory virus infection and disappearing without specific treatment. Specific studies[1-3] have shown that children with otitis media may be infected with both viruses and pneumococci and that rhinoviruses may be found in a minority of patients with acute maxillary sinusitis, though bacteria are more common and may also be present. The virus may well be only a contributory cause, so it seems that, if clinical sinusitis appears to be more than part of a generalised respiratory virus catarrh, it is likely to be mainly bacterial.

In the early years of life febrile convulsions may often occur. We studied the patients passing through our hospital in one year[4] and found that most of them were infected with a virus. The viruses were adenoviruses, parainfluenza and enteroviruses, as there was no influenza epidemic that year. The virus disseminated from the respiratory tract, to be detected in blood, CSF or urine in one-third of patients, and this frequency must be an under-estimate. The reason for dissemination may lie in the high proportion of children with low IgA levels, indicating that they are likely to have a mild and probably temporary defect in immunity, particularly of the mucosal surfaces.

The Psyche and Virus-induced Colds

There is a great deal of dubious folk-lore about the cause of colds; for instance it is often said that they are induced by chilling, a supposition not supported by experiment. That individuals got bad colds when they were 'run down' or worried appeared to fall into the same category. However, when individuals with certain personality traits were experimentally inoculated with ill-characterised viruses, the frequency of colds, as detected by simple clinical recording, increased, but the increase may have been due to the manner of reporting the illnesses[5].

Totman and Reed at the Common Cold Unit have recently looked at the role of experimental and natural stress in modifying colds produced by the intranasal inoculation of a well defined rhinovirus[6, 7]. In the first study they manipulated the situation to produce 'cognitive dissonance'. In other words, they asked some volunteers if they would take an antiviral drug (actually a placebo), which would be followed by gastric intubation 'to test their enzymes'. It was expected that those who agreed to take the drug would have less symptoms because they had, to some extent, committed themselves to the success of the treatment. In fact, both those who agreed and those who did not had significantly more symptoms than others who were given the same virus and not asked to make any choice. Thus the expected cognitive dissonance effect was not seen, but the stress of the situation appeared to make the symptoms worse, more virus being detected in the nasal secretions of the stressed subjects. Unfortunately, they were also found to have lower serum antibody titres than the controls. When allowance was made for this the difference was no longer statistically significant. This experiment received prior approval from the ethical committee and the volunteers did not show any resentment when told later that they had been temporarily deceived.

Totman and Reed have subsequently done another study in which the volunteers' life situation was assessed on arrival at the Unit. Again they were inoculated with a well characterised rhinovirus, and again the results of the study suggested that stress makes colds worse (Table 1). The subjects whose life situation had recently shown a distinct change to which, presumably, they had had to adapt, had worse colds than those who had experienced no such change. Those with an introspective personality had worse colds than those who were extrovert. The virological results rather surprisingly indicated that psychologically predisposed individuals shed more virus, even allowing for serum antibody variations.
Table 1. Inoculation of volunteers with rhinovirus in relation to psychological tests.

| Schedule of recent experience | Total predicted symptoms and virus shedding | Additional variance accounted for: |
|-------------------------------|---------------------------------------------|-----------------------------------|
|                               |                                             | Symptom score | Virus shedding |
| Totman loss index             | 0.1                                         | 0.1              | 2.2              |
| Totman change index           | 4.65 (<0.05)*                              | 12.0            | 26.0 (<0.01)     |
| Extra-introversion            | 17.1 (<0.005)                              | 8.7 (<0.025)    | 0.3              |
| Neuroticism                   |                                              |                  |                  | *probability value — other results were not significant.

All this indicates that the psychological state can modify the response to a virus, as indicated by the symptoms and signs of an upper respiratory infection, and perhaps can alter the amount of virus shed. Efforts are being made to decide by endocrinological assays whether any particular physical indicator of stress can be associated with this change in response, but this work has not yet been analysed. I think, however, that it may well be of quite wide significance both because it seems to be an example of what in clinical work we often believe is occurring, namely that the patient’s feelings and attitude are altering his response to disease, and also because it is an experimental system in which it is ethical and practicable to investigate further this subject which, although it is so important, is one on which it is very hard to collect unambiguous and well controlled data.

The Legionella

The famous outbreak of Legionnaires’ disease in Philadelphia has been followed by the identification of the same or similar organisms in many places. Typical cases show a severe pneumonia, with impaired consciousness, abnormalities of liver and kidney function and no response to penicillin and other commonly used antibiotics.

The disease is a reminder that the last word has not been said on bacteria as the cause of disease. ‘Viral pneumonia’ used to be the common label for any case of pneumonia in a previously healthy subject in whom no obvious bacterial pathogen was found, especially if there was no leukocytosis, and particularly if the lung infiltration was not clearly segmental or lobar and response to antibiotics was poor. Then it was shown that some pneumonias were due to Mycoplasma pneumoniae infection, an organism that can be propagated in animals and tissue cultures, and certain specially enriched media, but may be very difficult to recognise in stained sections[8]. The story of the discovery of the Legionella is rather similar, except that there may still be serious difficulties in recovering the organism and that diagnosis is best made by serology.

The organism was grown from clinical material by inoculation of guinea-pigs and the yolk sac of embryonated eggs, but it also grows on suitable special media, particularly a charcoal yeast medium.

There are two features of Legionnaires’ disease which are of special interest. The first is the epidemiology. Although a number of cases have now been studied, both as outbreaks and sporadic occurrences, case-to-case transmission seems to be extremely rare. Infection seems to originate always from the environment and to be associated with particular places and times. Attention focuses on ventilation systems, ponds and other sources of aerosols, and recently organisms have been detected in water[9], both in natural collections and in such places as showers. It is postulated that these organisms are aerosolised and inhaled[10], yet there are strange features in this hypothesis. Why should organisms that can be persuaded to grow only in specialised media and in certain laboratory animals proliferate in the impoverished conditions of standing water? Maybe the outbreaks are intermittent because conditions are only suitable from time to time; maybe amoebae have to be present. However, some recent work with guinea-pigs suggests that the respiratory tract is infected relatively easily and there is a large range of dosage over which mild infections occur[11]. High doses are needed to give a lethal infection.

The second feature is that there appears to be a wide range of organisms in the Legionella group and a wide range of clinical responses[12] (Table 2). It turns out that

Table 2. Some members of the Legionella group and the cases in which they were apparently found[12].

| Legionella pneumophila          | Tatlock                          | Fort Bragg or pretibial fever | Pittsburgh pneumonia |
|--------------------------------|---------------------------------|-------------------------------|----------------------|
| Wiga (Allo)                    | diver’s pneumonia               |                               |                      |
| Heba                           | ptyriasis rosea                 |                               |                      |
| Allo                           | lymphatic leukaemia and pneumonia | after falling into a swamp    |                      |
| Allo                           | in natural water only           |                               |                      |

Fort Bragg fever, which affected American servicemen during the Second World War, and which was characterised by fever and a pretibial rash, may have been a Legionella infection; an organism isolated at the time[13] was thought to have come from a guinea-pig but may have come from the patient and is certainly a congener of other Legionellas[14]. It was first thought to be a Rickettsia-like organism because of the way it grew. Another outbreak due to Legionella took place at Pontiac in a health department, and the cases were febrile but the disease was quite mild. Severe cases usually occur in patients with some serious underlying disease.

The message is that milder diseases may be due to many members of the family of the Legionellas[15] and may be seen from time to time in clinical practice. To solve the riddle of this so-called new disease we need both clinicians with a high index of suspicion, and hard work in the bacteriology laboratory.

This article is based on a paper read at the Conference on Infection in Britain Today held at the Royal College of Physicians in November 1980.
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Book Review
Advanced Medicine 16. Edited by A. J. Bellingham. Pitman Medical, Tunbridge Wells, 1980. 384 pages. Price £16.

For those who have attended the annual Advanced Medicine Conference at the Royal College of Physicians, this book gives an opportunity for further consideration of the papers that have been heard as well as allowing one to catch up on papers missed. The conference gives those of us from the provinces an ideal excuse to visit London, often with our families. The apparently less interesting papers have to compete for attention with wives, the zoological gardens and, last year, the Viking exhibition. For those unable to attend the conference, the book gives the essence of the papers, if not always the flavour, as much of the value of the conference is in the discussion after each paper, either in the hall or over coffee. This collection of papers cannot, and does not pretend to be, a textbook, and cannot easily be used to dispel a point of ignorance or prepare for examinations. Nor is it a book for quick reference in the library. It needs to be borrowed, or preferably bought, so that sections of interest, or, even better, the whole book, can be read at leisure.

As there are 36 papers by as many authors, there are bound to be great differences in style of presentation, and in the readership for which the papers are intended. The heuristic approach to a familiar subject, such as that of Sherwood Jones to the management of asthma, or of Fenley to the management of hypoxia in chronic bronchitis and emphysema, is obviously intended for those at the sharp end of medicine and is very welcome for that. The more discursive topics, such as Mossberg's paper on the immotile cilia syndrome and the whole section on radiation oncology, while not necessarily directly relevant to the general physician, were nevertheless cleverly done and of great interest.

In contrast, Coles' contribution on recurrent bronchial infection and bronchiectasis, Russell's paper on biochemical aspects of platelet function, and the defects of platelet function by Hardisty, were arcane and impenetrable, at least to this physician.

By far the best complete section was that on diabetes mellitus, with no weak links. Turner's paper on haemoglobin, Al and Sönksen's account of home blood glucose monitoring were clear, concise, informative and easily digested, and of inestimable value to any physician who may at some time have the care of diabetics. Pyke and Callan on the aetiology of diabetes, insulin-dependent and insulin-independent respectively, made a somewhat complex concept both understandable and stimulating.

The section on drug metabolism was on the whole more comprehensible than one would normally expect of items written by pharmacologists. The highlight was certainly Orme's 'New Look' at drug interactions. He took a small number of combinations and looked at them in detail, allowing the general concepts of investigation to be clearly explained.

The section on immunology was balanced, with two theoretical papers, 'Modern concepts in auto-immunity' and 'Complement in disease', which were explicit and understandable. There were four papers on specific immunological disease, namely Sjögren's syndrome, systemic sclerosis, vasculitis, and immunological mechanisms in neurological disease. There were also three thoughtful papers on therapy, one on immune modifying drugs and two on plasma exchange.

One or two misprints made this Guardian reader feel at home. On first opening the book one is confronted with a long list of contributors even before the list of contents. The print used in the titles of the papers is rather small, making it difficult at first glance to determine the contents.

This is a book that is a must for the peripheral consultant in general medicine and one to be bought, not borrowed.

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