Q FEVER

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Q fever is a new disease, being first described in 1937. Owing to its newness and comparative rarity in this country it will be appropriate to open with a formal account of what is known of its epidemiology and clinical features. Although it is new, our knowledge of it has been rapidly gained and description of this process is an interesting example of how a disease is made. This will be the second section. Lastly the practical value of the disease to physicians in this country will be discussed.

Epidemiology and Clinical Features

The causative organism is the *Rickettsia burneti*, which is allied to the rickettsiae which cause the various forms of typhus and Rocky Mountain spotted fever. Biologically it is more related to the larger viruses than the smaller bacteria. It is an obligatory intracellular parasite and is cultured in laboratories in fertile hens' eggs. It is widely distributed in infected animals and humans and can be recovered from the blood, bone marrow, brain, lung, spleen, liver, placenta and other viscera. It can sometimes be seen in stained preparations. Infection may cause high fever, toxæmia and death. On the other hand it may be continuous and symptomless. Histologically the local reaction is seen to be an infiltration of macrophages. Pus, abscesses or granulomata are not formed.

Cattle, sheep and goats in certain parts of the world are infected. Probably wild animals are as well. Ticks that feed on these animals are also infected and may cause spread from animal to animal. Rickettsiae may be disseminated either by the flesh of dead animals, shed flesh such as placentae, by their milk, faeces and urine, or by the excreta of ticks. Since the organisms remain alive for a long time in ordinary climatic conditions, dust and litter from animal pens may be infective.

Infection does not normally spread from man to man and is always acquired through some sort of contact with animals. Isolation is therefore unnecessary. This may occur in abattoirs, meat

packing or hide dressing factories. The infection is then by inhalation or inoculation of blood dried in dust. It may occur in districts where dairy herds are infected, and results from drinking milk. It may occur by inhalation of dust from litter that has been used by infected cattle. It is also easily contracted as a laboratory infection by inhalation of culture egg splutterings when platinum loops are flame sterilized.

The first outbreaks in Australia were in abattoir workers, and American meat packers are also affected. The great outbreaks during the war in Italy and the Balkans were probably caused by infected litter. Drinking unpasteurized milk probably causes something under half of the endemic cases in California and England.

Clinical Features

A typical case may be described as follows. The incubation period is 16 to 18 days, with a minimum of 13 and maximum of 32. The fever starts suddenly and it is often possible to time its beginning to the hour. At first the symptoms may be mild so that the patient is not driven to bed for several days. The temperature then rises high, 104° F. being quite common. It sometimes falls to normal more than once a day, and these swings are accompanied by rigors and drenching sweats. It eventually falls by lysis. In view of the high temperature the pulse rate is initially remarkably slow. When the attack is fully developed, prostration is even more severe than might be expected from the height of the fever. Nocturnal delirium is quite common. Muscle and backaches are early symptoms, but these are soon overshadowed by headache, which is continuous behind the eyes or at the back of the head. Patients are wary of changing position and try to stifle coughing lest this aggravate the headache. They may prefer to be in a shaded room, but meningeal rigidity is absent.

Within a week a tickling unproductive cough begins. In the original Australian cases no chest

signs were noticed, but they are now known to be constant, though perhaps not prominent, in any moderately severe case. These signs consist in a small patch of persistent tissue paper crepitations and high-pitched bronchial breath sounds, usually at the base. They have to be carefully sought for. The radiological signs in the lungs, on the other hand, are quite obvious when present. The lesions are single or multiple and occur in the periphery of the lung. They are spherical and have a 'ground glass' appearance. Sometimes segmental or lobar consolidation is seen. These signs often persist for weeks after the fever.

Convalescence is usually remarkably rapid even after several weeks of severe illness, though the elderly may suffer for weeks or months from lassitude and pains in the legs and back. The death rate is difficult to estimate. Numbers are relatively small and a diagnosis is more likely to be made in those who are severely ill. A mortality of up to 4 per cent. has been recorded, but it is not ordinarily considered as a disease in which death is a likely hazard, except again in the elderly and those who are otherwise ill.

Variants of this picture are chiefly seen in degrees of severity. Subclinical infections occur, as might be expected, and have been found to account for a quarter of the cases in a given outbreak. Mild cases may last a day or so, moderate ones a week or two, and a few up to a month. Severe cases may lapse into a typhoid state or coma, and bed sores and phlebitis may develop in cases of this sort. The evidence of lung infection is not always limited to a hacking cough and minor physical signs. Purulent sputum and blood-staining have been observed. Pleural pain may be severe. Consolidation may be obvious and an effusion may form. In such cases the pneumonia dominates the clinical picture. Transient orchitis has been described in three cases and pains and swelling in the joints in a few others. A maculopapular rash has been seen in a score, but it is doubtful whether this was caused by the infection. Other cases with diplopia and signs of encephalitis have been seen.

Certain striking absences in the symptomatology should be noted. Gastro-intestinal symptoms are rare, apart from the anorexia and nausea of fever. There is no constant skin rash such as characterizes many other rickettsial infections. There is no coryza as is common in acute respiratory disease due to viruses. Enlargements of the spleen and glands are also notably absent. The blood picture remains essentially normal, though variations in the white cells, especially a lymphocytosis, do not exclude the diagnosis. The E.S.R. is high during the fever and usually drops rapidly to normal. The

cold agglutinin and *Streptococcus M.G.* agglutinin test are negative.

Rickettsiae are not sensitive to sulphonamides, penicillin or streptomycin. They are very sensitive to both chloramphenicol and aureomycin. The *Rickettsia burneti* is no exception, as can be shown in embryonated hens' egg infections and in laboratory animals. It is not very easy to prove their effect in human infection since the fever is often short-lived and its cessation in any given case may have been natural. Enough cases have, however, been treated by now to show that practically none continue febrile after treatment, though a few have shown a tendency to relapse. More cases have been treated by aureomycin yet there is no evidence to show that chloramphenicol is less efficient.

Development of Knowledge

The first step in recognizing the disease was clinical observation. It was obvious that Australian cattle workers were suffering from some febrile epidemic and a planned investigation was started to find out what it was. The result was the discovery in 1937 of the infecting organism. The characteristics that marked this out as a special epidemic were not the clinical features, for these were like any short-term fever. They were, first, their prevalence in an occupational group and, second, the explosiveness of the outbreak with many persons becoming ill at once and no case-to-case spread. The characteristics of the epidemic are quite obvious and were described again among the Mediterranean Forces, though in this case it was not immediately recognized as being Q fever.

At about the same time as Q fever was first described, some Americans were investigating a rickettsia that was found in a tick. They called it *R. diaporica* at first, though it was soon shown to be *R. burneti*. All this occurred at a period when the laboratory technique of dealing with rickettsiae was just being worked out. We know of the great strides bacteriology made at the end of the last century when methods of culture, staining and various serological tests were perfected. The same was just being done for the rickettsiae and some viruses, and it was then first possible to grow the organisms in embryonated hens' eggs, infect animals, make prophylactic vaccines and test infection by complement fixation. The methods were, in fact, at hand for studying Q fever, though it was still believed that it was confined to Australia.

The first sign that it was not so was the outbreaks among troops in Italy and Greece in 1943. The Germans were in occupation first and called it Balkan Grippe—recognizing it, in fact, as a special epidemic, but not presuming any cause

The British and Americans got it next. Most of us were quite happy to call it atypical virus pneumonia. We were familiar with this at home and there had been much discussion about it since the sulphonamides had cured the bacterial pneumonias and left the other kind uncured and revealed. But there were those who pointed out that there was no upper respiratory infection as was common with atypical (virus) pneumonia. The Americans accordingly investigated it, for they had pathologists who had worked with R. burneti and who were familiar with their indigenous rickettsial disease, Rocky Mountain spotted fever. They proved that this Mediterranean fever had been Q the whole time.

This failure of so many physicians (myself included) to recognize what is under their noses is a human attribute that must be taken into account. One naturally diagnoses diseases that one has seen at home or, like malaria, that are recognized to be common abroad. One would not have expected anyone to have thought of the rarity Q fever, but I think many of us were singularly slow to suspect the various forms of typhus which were almost certainly overlooked in North Africa. We were also unjustifiably complacent in our diagnosis of atypical pneumonia for, besides the upper respiratory symptoms, this is characterized by case to case spread, which Q fever is certainly not. The same failing was shown by the Americans and Canadians in their slowness to recognize diphtheritic polyneuritis which was very common among allied troops. The reason was simple—they had abolished it so effectively in their native land that not only had they no experience of it but they had forgotten it existed. All this impressed me so much that I determined to diagnose it in England and was enabled by a very rare chance to find the first active outbreak which was identified in this country.

Q fever could no longer be ignored and, with the development of laboratory methods, the post-war stage was set for its exploitation. Reports came in of groups of cases scattered widely over Europe and the New World. It turned out from complement fixation tests to be heavily endemic in Southern California owing to the unique arrangements of the dairying industry in Los Angeles, and in the rest of the state by infection from sheep. It was natural that an intensive clinical survey should be made in this area to see how many fevers were unrecognized Q, and many were found masquerading under other diagnoses. No fewer than 50,000 persons are known to have been infected in Los Angeles alone (1950). Serological surveys were also made in England and a few foci were found, of which the most important is in Kent. It is characteristic of Q that although its

distribution is world wide, its incidence is patchy. At the moment the most important investigations are concerned with finding out how these local outbreaks occur.

It also happened, and this has been rare in medicine, that the specific cures, chloramphenicol and aureomycin, were produced at the same time as the disease became generally known.

There is another trend that must be noted. When a new disease is described it is recognized by its most common and florid features. Later it is often found that it exists in other forms. It soon became apparent that *formes frustes* were common, for many people showed positive complement fixation tests without any symptoms at all. More important clinically is the suspicion that chronic Q fever exists. Cases with relapse of fever have been seen and in others the temperature has continued to rise at night for many weeks. Others have had recurrent bouts for several months. A few have remained ill for several years, and on one or two occasions endocarditis with multiple emboli has been seen. This suspicion is not yet proved, for although all the cases reported were shown to have had Q fever, the nature of the first febrile attack was uncertain in some and in others it could not be proved that the continuing fever was due to the persistence of the infection.

Value of the Disease

It may seem odd to discuss the value of a disease since diseases are thought to exist whether we value them or not. Illnesses certainly exist independently of what we think, but diseases are man's ideas about them. The diseases that doctors find useful to recognize change from time to time and medicine has even been practised without diseases at all. In present-day medicine we feel bound to recognize a disease with such clear-cut symptoms as Q, with such a characteristic epidemiology and, above all, with a specific aetiology.

We may, however, as practical physicians, decide whether we will diagnose it or not. Our views will depend on where we practise. It is obviously important, for example, to physicians in California. Here we will only consider Britain. A diagnosis may often be made on however insecure grounds because a disease is common. This certainly does not apply to Britain generally, though it does to Kent, where the incidence of positive complement fixation tests is as high, or higher, than in California. It may be made, however rare or unimportant the disease, because the clinical features are so obvious that they cannot be overlooked. This does not apply to Q for although the symptoms are remarkably constant they do not differ sufficiently from any other short-term fever. It is true that a diagnosis can be

certainly made by complement fixation tests, but in the vast majority of cases the fever will have gone before this is done. The case is different when one is confronted by an outbreak instead of a sporadic case. The occurrence of many cases of any fever acquires an importance even when the illness is slight. As has been pointed out, the explosive epidemic of Q fever is more diagnostic than the individual case history and this is an occasion when Q might well be borne in mind. Another reason for making a diagnosis is that it indicates appropriate treatment. Now chloramphenicol and aureomycin are specific for Q, and are, of course, effective against many other micro-organisms. So much so that it is common practice to give them in any undiagnosed fever that does not react to sulphonamides and penicillin. If this be so, the sporadic case of Q may well be cured without the necessity of even thinking of the diagnosis. Lastly, one may make a diagnosis to clear the air of what the patient has not got. It is here that

chronic Q fever might be important. Continued and especially recurrent bouts of fever and chronic illness are most distressing and puzzling things. Any physician who sees them would gladly accept a new diagnosis to supplement his already exhausted stock-in-trade. It is easy enough by complement fixation to exclude the disease, but at the moment it can only be regarded as a very remote possibility.

Note

Complement fixation tests can be done by any virus reference laboratory. They are, in fact, usually done on sera sent there from a febrile patient.

Full bibliography and review of the subject can be found in:

HUEBNER, R. J., JELLISON, W. L., and BECK, M. D. (1949), *Ann. intern. Med.*, **30**, 495.

BRONCHIECTASIS IN CHILDHOOD

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Definition and Aetiology

The association of a chronic productive cough with dilated and inflamed bronchi was observed by Laennec in 1819. The first case he used to illustrate his description of this disease was a boy aged 3½ years who had copious expectoration of foetid sputum since whooping cough three months earlier and the second was a woman of 72 years who for upwards of 50 years had suffered from an habitual cough producing opaque yellow sputum, frequent haemoptyses and oppressed breathing.

Though Laennec's description was under the heading of 'Dilatation of the Bronchi,' he referred to a clinical condition which could be diagnosed during life. Until the advent of bronchography the term bronchiectasis was used for this recognizable clinical syndrome, but since then the dilemma has arisen as to whether it is justifiable to use it to signify mere dilatation of the bronchi without the clinical accompaniments. Clearly a

chronic productive cough and abnormal signs in the chest without bronchial dilatation cannot constitute bronchiectasis, but if the term is used to cover the slight temporary bronchial dilatations so often observed during bronchography then another name will have to be coined to distinguish the chronic disease syndrome from the single physical sign.

In practice, clinicians retain the connotation of bronchiectasis in the original sense of a chronic, frequently debilitating disease in which there is, besides dilatation of bronchi, a constant or recurrent productive cough, abnormal physical signs in the chest and a liability to complications such as haemoptysis, pneumonia, pyaemic abscess or suppurative cachexia which may shorten the duration of life. The symptoms and signs of this disease result from accumulation and stagnation of secretions in dilated bronchi and, though they may resolve when secretions are no longer retained, there is always a tendency towards recurrence so