THE CHALLENGE OF THE RICKETTSIAL DISEASES

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Introduction

IT is probable that from the earliest times the Typhus group of fevers has proved to man a continuing challenge. It is with the story of its elucidation, however, that we are concerned, and in this context exanthematic typhus is responsible for some of the darkest pages of medical history.

The disease is now known to be due to a rickettsia transmitted from person to person by the common body louse. The reservoir is thus seen to be man himself, the disease being transmitted by means of infected lice. Given suitable conditions in a badly nourished population typhus can spread with tragic rapidity. Louse-borne typhus is therefore a disease of man and the only one of the Typhus group to assume epidemic proportions, the other rickettsial infections remaining consistently sporadic.

The early appreciation of fevers

It was Galen (B.C. 130-201) who defined pyrexia as praeternatural heat, "calor praeter naturam," but in the 4th Century B.C. Hippocrates (B.C. 460-360) had already described the use of touch to recognise degrees of fever, by which simple means he was able to differentiate clearly between continued, quotidian, (intermittent), tertian and quartan fevers (the latter forms were undoubtedly malaria). Yet nearly 2,000 years were to elapse before Sanctorius (A.D. 1561-1656) Professor of Medicine in Padua from 1611-1625 was the first actually to attempt to measure body heat, using for this purpose his "instrumentum temperamentorum," an open air-thermometer which was affected not only by changes in temperature but also by atmospheric pressure.

Although with the researches of Boyle, Hooke, Fahrenheit and Celsius, the next 200 years registered great improvements in the thermometer itself, it was not used for regular clinical observations of pyrexia until the early 18th century, and then only in Europe, where a hermetically-sealed thermometer filled with either alcohol or mercury was placed in the mouth, rectum, axilla, groin or even in the stream of urine. Pyrexia was, of course, still regarded as a disease rather than as a symptom. Then the German physician, Ludwig Traube (1818-1876), introduced to the practice of medicine the clinical temperature chart, thus opening the way to the recognition of behaviour patterns in various forms of fever.

Consequently by the middle of the 19th century the significance of body temperature became more generally appreciated and its measurement was soon adopted in British Hospitals. Two medical men who made useful contributions in this direction were Edmund Alexander Parkes (1819-1876), the Goulstonian Lecturer on Pyrexia to the College of Physicians in 1855, and William Aitken (1825-1892) who facilitated the more general use of the clinical thermometer, his instrument being some ten inches

in length. We are told that his colleague, Lauder Brunton (1844-1916) used to go into the wards of St. Bartholomew's Hospital with a pair of these thermometers in a case resembling that carried by a second with his pistols on his way to a duel.

The slender clinical thermometer which we use to-day was not invented until 1866 by Clifford Albutt (1836-1925) of Leeds, which was followed two years later by the publication of the first book devoted exclusively to clinical thermometry. Carl Wunderlich (1815-1877), Professor of Medicine in Leipzig presented his epoch-making study of the importance of body heat in disease, which was to revolutionise the clinical diagnosis of pyrexia. It was said of him that "he found fever a disease and left it a symptom" (McGuigan, 1937).

The History of Classical Typhus Fever

Typhus fever is one of the most documented epidemic diseases, one which since early times has always been associated with famine and war. Many references to pestilence in the Bible probably referred to epidemic typhus and as Murchison says "a complete account of this disease would cover the history of Europe for many centuries."

The long-debated cause of the Plague of Athens in 430 B.C. which followed the invasion of the Peloponnesian Army and subsequent condition of famine, is almost certainly established as typhus (MacArthur, 1954). In his clear account Thucydides, though not himself a medical man, described the signs and symptoms in detail; where they deviate it merely underlines both the common error of confusion with enteric fever and the possibility that the two diseases co-existed. In addition, he observes that those in attendance on the sick and many physicians were early victims, from which he concluded with almost inspired perspicuity, that the disease was passed from one person to another by contact, thus promoting the first conception of contagion.

Not until 1546 was this idea of contagion further developed. The Veronese epidemiologist, Hieronymus Frascatorius (1483-1553) in his book *De Contagione* gives us the first accurate account of the clinical features of typhus, distinguishing it from some other exanthemata. He was of the opinion that "this fever is contagious, not rapidly, not per fomites, but only by contact with the patient." He also goes on to say that "the seeds of disease multiply rapidly and propagate their like."

Today it seems hardly credible that the close association between typhus, vermin and overcrowding was not generally appreciated. It is even more surprising that it was not until early in the present century that body lice were finally incriminated as vectors of the disease. From early times, however, famine, war and abnormal weather seem to have been understood as factors favouring outbreaks of fevers, generally.

In England there were serious years of famine and scarcity in 1087, 1196, 1258 and 1315, and following each of them epidemic fever was rife. It is probable that most of these outbreaks were typhus fever (Creighton, 1944). Likewise, there is evidence of typhus fever occurring as early as 1414 in the London gaols of Ludgate and Newgate.

In Spain in 1489 outbreaks of spotted fever affected more than 17,000 soldiers of Ferdinand's Army which besieged the Moors in Granada. In the mid-16th century the disease in Italy was so prevalent that it spread rapidly throughout France. In 1552

epidemic typhus soon deciminated the Army of Charles V as it laid siege to the City of Metz. It re-appeared in 1566 in the Army of Maximilian II of Bavaria whence it again spread all over Europe; the cycle of famine, war and typhus will be seen to recur all through European history. The disease tends to reveal itself especially in winter when people huddle together over fires and fail to bathe and change their clothing regularly. From early times it was observed that children were likely to survive the illness while older persons frequently succumbed to it.

In England the incidence of typhus can be accurately traced since the days of Queen Elizabeth I, largely because of a series of judicial trials known as the "Black Assizes," held at Cambridge in the year 1522, at Oxford in the year 1577 and at Exeter in 1586. At this time the gaols which were often overcrowded, were managed on a contract system, one of the common reasons for such overcrowding being imprisonment for debt. Small wonder that the prisoners lived under unsavoury, disagreeable conditions, and that the judiciary, court officials, county gentry and men of the jury were thus at risk and readily became infected with typhus by contagion.

The story of each of these "Black Assizes" is similar, but the Oxford Assizes held on July 5th, 1577 is probably the best known of all. Twelve to fourteen days after the Assizes hundreds of persons were ill with putrid fever and every Oxford College, Hall or House had its victims. The trial concerned one named Rowland Jencks, a bookbinder and a Roman Catholic, who was accused for his heretical views against the Protestant faith. It is reported that when the prisoner was brought up from the cells he was observed to be wearing filthy clothes and was in a thoroughly unclean condition. His trial lasted two days, at the end of which he was found guilty and sentenced to have his ears cut off. In the weeks that followed a total of 510 persons died of typhus, at least 100 of them members of the university. Jencks eventually escaped across the channel and survived there for another 33 years.

Almost an identical story can be told of the Exeter Assizes of 1586, when the accused were 38 Portuguese seamen brought out of "a deep pit and stinking dungeon." They had been at sea for months without change of clothing. Once again, after about fourteen days a proportion of the judges, jury, lawyers and officials succumbed and the contagion smouldered on in Devon for more than six months afterwards.

Thomas Sydenham (1624-1689) probably the greatest clinician of the period, moved from Oxford to London in 1656. By no means a prolific writer he has nevertheless recorded careful observations on the diseases of his time and the severe epidemics of the year 1661, some of which were plague and others typhus. Sydenham seems to have understood clearly the protean character of many epidemic diseases. About that time Samuel Pepys also wrote in his diary "the season very sickly everywhere with strange and fatal fevers."

Epidemics raged with unremitting violence in 1665—the year of the Great Plague of London but since both this disease and typhus show haemorrhagic tendencies it is probable that both forms of pestilence occurred simultaneously. When in the following year, 1666, the Great Fire of London broke out it "Burnt out the seeds of plague" and typhus took its place. It was at this time that another famous doctor, Thomas Willis (1621-1675) settled in London. He also has given us a good objective account of the prevalence of these epidemic infections.

The Winter of 1683-84 was characterised by drought followed by a great frost, enabling a carnival to be held on the frozen River Thames. In 1686 severe malignant fever broke out. Described by Sydenham as a "new fever," there is no doubt that typhus had broken out again with renewed violence. Thereafter the same sequence of events recurred every 5 or 10 years with abnormal weather, bad seasons, scarcity, high food prices and famine, each being followed by outbreaks of typhus, with high mortality. For example, in the years 1709-10 the harvest was so poor that the price of wheat rose from 27s 3d. a bushel to 81s. 9d. a bushel, so that corn exports had to be prohibited. The Jacobite Rising in 1715 was the occasion for yet another outbreak of typhus. In the next few years, although Britain was prosperous, there were typhus epidemics in London and the North of England, especially among the poorer classes.

From 1721-29 there were outbreaks of a milder fever, known as slow fever or Febricula. Contemporary evidence suggests that these were relapsing fever, which we know is also spread by the body louse and can co-exist with typhus. In 1735 typhus was brought in by the Fleet to Plymouth and spread widely in the South-West. A protracted cold frosty winter occurred again in the years 1739-40 with inevitable shortages of food and fuel and once again it was possible to hold a "frost fair" on the frozen River Thames.

No one was surprised, therefore, when outbreaks of typhus, in the following year, played sad havoc with the population of England and Ireland. In the Winter of 1741-42 London suffered the highest mortality of all, with 7,500 typhus deaths recorded in the "Bills of Mortality" of the Capital. That City was densely overcrowded with people close-packed in dark badly-ventilated houses which huddled in its maze of narrow alleys, courts and streets. Another factor was the imposition of the window tax, to avoid which many windows in dwellings and buildings such as gaols had been bricked up. It is little wonder that the London house in which Jonathan Swift then lodged had a "thousand stinks in it "and that typhus and its prevalence was explained in terms of effluvia and bad air in the larger towns.

It was Sir John Pringle (1707-1782), later appointed Physician-General to the Army and President of the Royal Society, who did much to improve the health of the soldier. Because he believed hospital and gaol fevers were identical, and that "the more air let into hospitals, the less chance of spreading distempers," he took steps to increase ventilation in army buildings. On the other hand his contemporary, Captain James Lind (1716-1794) the pioneer of naval hygiene, did not subscribe to the view that bad ventilation was the cause of ship fever—as typhus was then called—in the Navy. At one period he suggested that lice carried the disease, but abandoned the idea in favour of putrid body emanations as the cause. He did, however, recommend that sailors be stripped and bathed while their clothes were heated in an oven.

Pringle also carefully described the "Black Assizes" held at the Old Bailey, London, in 1750, and observed that those who sat on the right of the Lord Mayor—the Lord Chief Justice, the Recorder and the London Jury—escaped infection while the Lord Mayor, the rest of the bench and the Middlesex jury which had been seated on the left developed typhus. He was much impressed by this and advised that, before being brought into court, prisoners should be properly cleansed and dressed in clean clothing.

Pringle then recommended that windmill-type ventilators be erected on the roofs of

gaols in order to draw polluted air out of the buildings. When a team of carpenters began to erect this type of ventilator at Newgate courthouse seven out of the eleven men employed on the task died of gaol fever, among them a young apprentice who had been ordered to climb down the shaft of the great ventilator to recover a wig which had been thrown into it. Not only officials and gaolers, but doctors and chaplains were among the principal victims of typhus which at that period was said to be of the "low, putrid nervous type." About this time, also, John Howard (1726-1790) the pioneer of prison reform who did so much to improve conditions in the gaols of England and Wales, regrettably died of the disease.

By the year 1700 medical men were well alert to the menace. In Manchester the pioneer was Dr. Thomas Percival (1740-1804) whose work was soon followed up by Dr. John Ferriar (1761-1815) to whom I shall again refer. In 1773 in Manchester the number of deaths from typhus was just twice the rate for the surrounding countryside. In London, Dr. John Coakley Lettsom (1744-1815) noted that typhus or gaol fever, was a disease of the poor, less prevalent in the more salubrious parts of the city, especially where better housing, cleanliness and good ventilation were available. It was then that Dr. William Cullen (1710-90) the great clinical teacher in Edinburgh, persuaded the medical profession in Britain to adopt the name typhus for the disease. The word had been coined in 1759 in France by Doctor Sauvage of Lyons from the Greek word, "*TYPHOS*," meaning smoke, first used by Hippocrates to indicate clouding of the mind in stupor and coma. During the next twenty years Robert Willan (1757-1812), the founder of English Dermatology, made careful assessment of the typhus epidemics prevailing in London and gave an excellent clinical description of the disease.

In Manchester, Dr. Ferriar was especially concerned, in the last ten years of the century, with the epidemiology of typhus and the new conditions created by the establishment of the cotton industry. There is little doubt that density of population was a factor in the aetiology, for he observed that overcrowding, old houses and narrow lanes were its main sources. The Winter of 1789-90 proved so mild that in the epidemic of that year only 2 of his 90 fever patients succumbed—probably because so many of them had not contracted typhus, but relapsing fever.

In his address to the Manchester Literary and Philosophical Society in 1792 Dr. Ferriar warned that the situation was dangerous—"The poor are indeed the first sufferers from typhus but the mischief does not always rest with them." He also addressed the Manchester Police Committee in the same vein. At one stage Ferriar investigated an epidemic in a village just outside the City and actually traced it to the patients' clothing. It was usual at this time for infected dwellings to be treated by whitewashing the walls and by fumigation. Nevertheless, by 1794-5, outbreaks of typhus in Manchester were again widespread.

This state of affairs led to the founding of the House of Recovery in which patients were to be strictly segregated. This was opened in 1796 in Portland and Silver Streets, and apart from Plague Hospitals, was probably one of the first Fever Hospitals to be established. It was taken over by the Royal Infirmary in 1853. Ferriar also recommended that similar Houses of Recovery be established in every large urban community throughout the country.

In the next 20 years the advent of the French Revolutionary War (1803-15) and the Peninsular Wars (1808-14) brought to Europe a repetition of these severe typhus epidemics, which were undoubtedly a major factor in Napoleon's defeat in his Russian Campaign of 1812. In Britain there was remarkable freedom from the disease except when it was introduced by soldiers returning from abroad as was the case with the remnants of Sir John Moore's Army evacuated from Corunna, many of whom were treated as patients in the Naval Hospital, Haslar. The washerwomen there were soon aware from the foul odour of the clothes when there was an epidemic of typhus. They used to air the dirty linen in the cold, after which it could be safely cleansed. We now know that lice leave clothing which has been exposed in cold places.

The autobiography of Sir James McGrigor (1771-1858) gives a vivid picture of the importance of combatting typhus and of its complications in this period. The London Fever Hospital was opened in 1802, but many citizens opposed the establishment of further hospitals, and in 1818 a Select Committee of the House of Commons took evidence. Some witnesses expressed appreciation of the Manchester House of Recovery and supported it as a means of controlling disease "by destroying its germs and seeds." Others stressed that isolation of patients was unnecessary, since typhus was nursed safely in open wards of the principal London Hospitals.

For the first 40 years of the 19th Century there were three types of epidemic fevers which were readily confused—typhus, relapsing fever and enteric fever. In 1826 Richard Bright (1798-1858) of Guy's Hospital published a description of ulcerated Peyer's patches from the case reports of 10 patients. His paper was profusely illustrated with coloured plates, but of course intestinal involvement was still thought at this time to be a complication of typhus fever. Recognition of enteric fever as a separate clinical entity was due first to an American, William Wood Gerhard (1809-1872) of Philadelphia about 1836 and was later confirmed by the careful observations of Sir William Jenner (1815-1898) at the London Hospital in 1849-51.

The Winter of 1837-38 saw a further typhus epidemic, with nearly 20,000 deaths in England and Wales. A number of contemporary books reflect prevailing conditions, among them Mrs. Gaskell's novel, "'Mary Barton,'" which gives a vivid account of these diseases spreading among the poor in Manchester. The most revealing document however, is Chadwick's "Report of an Inquiry on the Sanitary Conditions of the Labouring Population of Great Britain." Edwin Chadwick (1800-1890) then Secretary of the Poor Law Commissioners, was a pioneer in public health. Much of the evidence in this report was taken in Manchester and showed that many people were living in appalling conditions. Labourers had been regarded merely as units of production and slum houses had been built cheaply without the amenities necessary to maintain reasonably good health. Publication of the two volumes of this report in 1842 excited nation-wide interest but Manchester had already taken steps to put its house in order. A system of sewerage had been started and in 1844 not only was control of housing established but a "Health of Towns Association" came into being. A large reservoir to supply the city with water was begun in 1848; the first to be built in England, it was completed in 1851 but was not filled to capacity until 15 years later (Clark, 1962). However, the city's first M.O.H. was not appointed until 1868.

As epidemics of typhus waned, enteric fevers increased in intensity. In spite of

enlightened improvements in housing and hygiene, England was to suffer yet another severe typhus epidemic just before the middle of the 19th Century. With the Industrial Revolution had come a sharp rise in population and a mass movement of country folk to the cities and towns, so that there was already a great deal of overcrowding when the flood of immigrants from the Irish Potato Famine of 1846, burst upon them. In Ireland the failure of the potato crops was followed by a serious epidemic of typhus and the refugees spread to England leaving a trail of disease wherever they went.

Although the importation of epidemic typhus was to be repeated yet again this time by our soldiers returning from the Crimean War, Britain in 1871 saw the last of the epidemic disease. Thus before the actual cause of typhus was known, improved food and water supplies, better hygiene and living conditions had banished from the scene this acute disease which had plagued England for more than three centuries (Greenwood, 1935).

We had now reached the stage when all the clinical features of epidemic typhus were fully understood. The classical account of the disease is that written by Dr. Charles Murchison (1830-1879), who served for a few years in the Indian Medical Service. This remarkable Scot came to London in 1854 to begin a long series of major hospital appointments, ending with that of physician to St. Thomas's Hospital, where he was considered one of the greatest of clinicians. Although by modern standards he seems to have been rather dogmatic, Sir William Osler called him the model bedside teacher.

But it is Murchison's association with the London Fever Hospital from 1856-70 which afforded him the experience required to write his famous book on *The continued fevers of Great Britain*. Murchsion's account of typhus begins with its sudden onset of high fever, often with rigor, the marked prostration, the flushed face, the dull heavy expression with suffused eyes; the dry tongue covered with brown leathery fur, which splits and bleeds easily. There is also delirium with sleep disturbed by painful dreams. But I must allow you to read Murchison's own words on this score, for he had already suffered two attacks of the disease when he wrote about it. In his series of cases at the London Fever Hospital, more than 93% had shown the typical rash which appears late on the 3rd or early on the 4th day of the disease and exhibits three elements (1) rose-coloured macules (2) petechiae, and (3) subcuticular mottling (Murchison, 1862).

Aetiology of Typhus

You may be surprised to hear that Murchison never accepted that these infectious diseases were due to "germs," but it should be remembered that many of the common micro-organisms had not been discovered by the time he died in 1879. The discovery of the cause of typhus and of its transmission to man makes a fascinating story. It was Howard Taylor Ricketts (1871-1910), working in Mexico in 1906, who first revealed the small micro-organism, now named a rickettsia. Soon afterwards von Prowasek (1875-1915) confirmed the findings of intracellular organisms which had only some characters of bacteria. In the light of present knowledge it is not surprising that both these workers died of laboratory infections.

When in 1916 da Rocha-Lima published the first adequate description of the casual

agent of epidemic typhus, he aptly named it *Rickettsia prowaseki*. Since that time more than 40 related organisms have been found, but only some of them have proved pathogenic to man. Rickettsiae give rise to a number of diseases varying in different parts of the world—with little in common epidemiologically.

The manner in which the classical infection is spread to man was not understood until 1911, when Charles Jules Nicolle (1866-1936) and his team working in Tunis showed that the common body louse, *Pediculus humanus*, was the responsible insect vector. We now know that after the louse has had a blood meal from a typhus patient, rickettsiae multiply in its gut and are passed out in its faeces, surviving some 3-4 days. Infection of man is contaminative, since the louse always defaecates when it bites, and infective faeces are subsequently scratched into the skin. Occasionally infection is reported from the inhalation of dust containing louse excrement. It is perhaps well to remember that lice leave the typhus patient when his pyrexia is high—which may be the origin of the injunction "never sit on a patient's bed." Lice also leave the body when it cools after death. It is when rickettsiae are concentrated in the body of the louse that they are most easily destroyed by physical and chemical means. I can recommend to you Zinsser's book, *Rats, Lice and History*, and if you read it you will feel with him some measure of compassion for the poor louse which swells up and dies of the infection about the 10th day after feeding on a patient (Zinsser, 1935).

In spite of the disappearance of typhus from Britain, areas of endemicity remained in Ireland whence the disease was occasionally re-introduced through the ports of Liverpool and Glasgow. In contrast to this satisfactory state of affairs winter epidemics of typhus continued to occur yearly in Eastern Europe and in the Iberian Peninsula.

The beginning of World War I saw a renewed prevalence in the Balkans but its incidence was maximal in Russia between 1917 and 1922, when more than 10 million cases are thought to have occurred in a population of 120 million, with the fatality rate exceeding 30%. Nevertheless, at this time efforts to prevent lice infestation in the British Army were uniformly successful.

During World War II the disease was so prevalent in Russia and Poland that it played an important part in the failure of Hitler's Russian Campaign of 1941-42, and in spite of strict measures to arrest it, typhus spread back into the concentration camps for prisoners and displaced persons in Germany. By this time prophylactic vaccines against typhus had been developed, but the immunity they conferred was comparatively short-lived.

It was indeed fortunate that in 1942 the Swiss Pharmaceutical Industry reported the remarkable effects of D.D.T. (Dicophane, B.P.) to the Allies. Although first synthesised over 60 years before, once its insecticidal properties were confirmed, simple methods of application quickly replaced the old cumbersome methods of disinfestation.

In 1944 typhus broke out in Italy among the verminous population of Naples and thus created an ideal opportunity for assessing both the lethal effects of D.D.T. on lice and its comparative safety for man. By using D.D.T., this dangerous epidemic was brought to an end, but not before more than 2,000 cases of typhus had occurred

among civilians. The method involved blowing dust containing 10% of D.D.T., into the clothing, thus obviating the necessity for the individual to undress, and by this simple means it proved possible to treat more than 70,000 persons daily. It is most probably significant that only two members of the Forces occupying Naples at that time acquired the disease.

Towards the end of the war, epidemic typhus again occurred in some concentration camps, *e.g.* in Belsen it claimed more than 60,000 victims. Again D.D.T. checked its spread, and very few casualties were suffered by the staff of British Army Medical Units in close contact with the patients.

Pathology of Typhus

Beginning with Pringle, one of the first to introduce regular postmortem examinations, pathologists made many unsuccessful attempts to account for typhus but little that was abnormal was found, since the gross pathology was not distinctive. In 1914, however, Albert Fraenkel (1848-1916) first described the acute degenerative lesions of the smaller arterioles with perivascular infiltration and thrombosis widely distributed throughout the vascular tree .The presence of these characteristic microscopic changes, now called Fraenkel's nodules, was soon confirmed and is the basis of all the clinical manifestations of the disease.

A diagnosis of typhus had always rested on clinical grounds until 1909, when W. J. Wilson (1879-1954) of Belfast detected specific antibodies in the blood of a patient from whom he had isolated a proteus-like organism. Seven years later, during World War I, Weil and Felix observed in epidemic typhus rising titres of agglutination with a type of *Bacillus proteus vulgaris* which they, too, had isolated from a patient. Though its immunological basis is still obscure, the Weil-Felix reaction now using the three special "X" strains, OX19, OX2, and OXK, is still widely used for diagnostic purposes.

Non-Epidemic forms of Typhus

I should now like to consider some of the sporadic forms of typhus which are transferred by chance from animals to man. These primarily are animal diseases or zoonoses, man becoming accidentally infected by means of fleas, ticks or mites.

Murine Typhus: caused by *Rickettsia mooseri* is a widely distributed disease of rats spread from rat to rat and occasionally to man by the rat flea, *Xenopsylla cheopis*, also the arthropod vector of plague. The clinical picture of murine typhus resembles exanthematic typhus and is nowadays seen mainly in Africa and South America.

Tick-borne Typhus: caused by *Rickettsia rickettsi* is a disease of wild rodents spread to man by means of Ixodine ticks. The type originally studied by Ricketts was Rocky Mountain spotted fever of North America. Since then tick-borne has been found to occur in India, Africa, South America and in many other parts of the world. An example in the Mediterranean area is Fièvre Boutonneuse, in which the reservoir of infection is the dog, the insect vector being the common dog tick. Although the clinical picture of tick-borne typhus varies considerably, its relationship to classical typhus is always evident.

Mite-borne Typhus: A type of Japanese river fever was originally described early in the 19th century. When in 1927 the causative organism *Rickettsia orientalis* was

first discovered by Norio Ogata in Japan, more than forty accidental infections occurred in his laboratory staff.

But it is to Lewthwaite (1894-) we owe recognition that this same organism causes scrub typhus of Malaya and many other similar fevers of the Far East. Farmers and soldiers on active operations in the jungle of Malaya are infected from field rats and mice which are the source of infection. The insect vector is a tiny larval mite, belonging to the Genus *Trombicula*, which closely resembles the small red harvest mite seen in Britain. When the infected mite spreads the infection to man it causes a small ulcer or primary eschar at the site of the bite. This is followed by fever, local adenitis and a generalised macular rash, the illness running a course similar to that of exanthematic typhus.

"Q" Fever

In 1937 Macfarlane Burnet (1899-) and Mavis Freeman showed that "Q" fever was caused by a small rickettsia, later named *Rickettsia burneti* by Derrick who first reported the disease in Australia. This organism shows distinctive characteristics such as the ability to resist drying and to survive outside the body longer than other rickettsiae. It is spread to man from domestic animals directly by contact or indirectly by dust, discharges and by ticks.

The resulting acute febrile illness was at first thought to be limited to Australia, but since the war this relatively mild disease has been encountered all over the world. More recently chronic forms of "Q" fever, often accompanied by endocarditis, have been increasingly recognised.

Treatment

Until lately the treatment of typhus was limited to symptomatic measures and good nursing. Nevertheless over the years many other treatments, such as bleeding and hydrotherapy, have been advocated at one time or another. When Murchison wrote "A patient with typhus is like a ship in a storm; neither the physician nor the pilot can quell the storm, but by tact, knowledge and able assistance they may save the ship," he did not forsee that we would one day have a specific treatment for the disease.

It was in 1947 that chloramphenicol, then a newly-discovered antibiotic, was found by Joseph E. Smadel (1907-1963) to be active against *Rickettsia orientalis* in the laboratory. Soon afterwards he went to Malaya where he and Lewthwaite carried out therapeutic trials with early cases of scrub typhus. Although all the patients responded quickly to this form of chemotherapy and some had scrub typhus, others later were found to have typhoid fever. Today, chloramphenicol remains the specific treatment for both rickettsial and enteric infections, reducing the mortality to about one twelfth of the former rate in each of these diseases.

Conclusion

There is today a significant incidence of epidemic typhus in what are known as the developing countries of the world, and the disease is still a potential form of

pestilence, so that an understanding of the problems involved therefore assumes more than academic importance. The rickettsial diseases have without doubt played an important part in the development of modern medicine, especially in its preventive aspects.

The louse still remains mankind's enemy and is now beginning to develop resistance to the newer insecticides. You may remember how its presence in the hair of a woman in church inspired Robert Burns to write his "Ode to a Louse," and I shall—I trust appropriately—conclude with "Rabbie's" pungent lines:—

"Ye ugly creepin, blastit wonner
Detested, Shunn'd by saunt an' Sinner."

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D.Obst.R.C.O.G.	Captain D. R. P. BUSHBY, M.B., Ch.B., R.A.M.C.
	Captain B. CRONIN, M.B., B.Ch., B.A.O., L.A.H., R.A.MC..
	Captain H. MANUEL, M.B., B.Chir., R.A.M.C.
	Captain A. M. TILL, M.B., R.A.M.C.
D.I.H.	Major W. R. O. EGGINGTON, M.B., B.S., M.R.C.S., L.R.C.P., D.P.H., D.T.M. & H., R.A.M.C.
	Major I. C. FRASER, M.B., Ch.B., D.P.H., R.A.M.C.
	Major D. E. WORSLEY, M.B., Ch.B., D.P.H., D.T.M. & H., R.A.M.C.