War Medicine Series

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LOUSE-BORNE TYPHUS FEVER

BY

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When the names "typhus" and "typhus fever" are used without qualification in this article they refer to louse-borne typhus, which is the chief member of a family called "the typhus group of fevers." The other typhus fevers are closely related to the louse-borne disease in being caused by rickettsial bodies, in having the same type of clinical features, and in producing similar pathological changes in the body. They differ sharply in being primarily diseases of lower animals; their viruses are transmitted to man as a secondary incident through fleas, ticks, or mites which are parasites of the infected animals. Because of this essential difference these fevers cannot give rise to epidemics such as readily occur in louse-borne typhus, which is directly transmitted from man to man by a human parasite, the louse. The non-epidemic, or "zootic," typhus fevers are of minor importance as war diseases, but they sometimes cause trouble by being mistaken for the human louse-borne disease, from which they may be indistinguishable by the methods of diagnosis available to isolated medical men.

Louse-borne typhus has a number of synonyms, including typhus fever, epidemic typhus, exanthematic typhus, louse typhus, historic typhus, and classical typhus. It should be noted that when German writers use the name "typhus" without special qualification they refer to typhus abdominalis, or typhoid fever; so also they use the names "pseudo-typhus" and "paratyphus" with reference to typhoid.

Definition.—Louse-borne typhus is a disease caused by *Rickettsia prowazeki*, which is conveyed from man to man by human lice. In most of the cases there is high fever lasting from 10 to 16 days, with early and pronounced nervous symptoms and a characteristic rash. The disease often occurs in epidemics, but it may be endemic or sporadic. Mild attacks which do not conform to the classical type are so frequent and also so important that a detailed definition based on the "typical" form of the disease would be misleading rather than helpful.

History and Distribution

History.—About a hundred years ago typhoid fever and relapsing fever were first recognized as distinct diseases; previously, "typhus fever" or one of the scores of synonymous names served as a designation for any severe epidemic fever other than those that could be recognized by their special characteristics. Since the middle of the fourteenth century there have been many accounts of epidemics of fevers of these kinds in Europe, occurring chiefly in times of war or famine. In some of these accounts typhus can be recognized; others paint a confused picture made up of a mixture of typhus and relapsing fever or of typhus and typhoid. Since 1844 typhus has been recognized as a clear-cut entity, so that Murchison's description in 1862 of epidemics of the disease can hardly be improved on at the present time. The contagious nature of typhus was widely accepted, but vague ideas prevailed about the cause of the disease: for example, Murchison held that a poison was generated spontaneously in the body as a result of overcrowding and bad ventilation. In 1909 C. Nicolle produced the disease in a chimpanzee by inoculating the blood of an infected person; he also transmitted the infection from this animal to other monkeys by lice. The causal organisms were rather vaguely described by Ricketts and Wilder in 1910; Prowazek studied them closely; and in 1916 Da Rocha Lima

described them accurately and called them *Rickettsia prowazeki*. The first agglutination test was carried out by Wilson in 1910: he found that the serum of infected persons agglutinated certain bacteria of the coli group which he had isolated from typhus patients, but he pointed out that the serum response did not prove that the organisms were the cause of the disease. In 1916 Weil and Felix, using a different bacillus, *Proteus* X 19, described the reaction which goes by their names. Recent work has been concerned chiefly with the prevention of the disease, especially by protective inoculation.

Distribution.—The disease is cosmopolitan; it is apt to break out in louse-infested communities in many parts of the world in which cool weather conditions prevail at some season of the year. In tropical countries, for some unexplained reason, typhus is decidedly uncommon except at high altitudes. On the whole it is a cold-weather disease, and although epidemics may occur in hot weather it would appear that cold or cool weather is a necessary preliminary to the widespread transmission of infection. More cases occur in the later part of the cold season and the early hot season than at other times, but there have been many exceptions to this rule. Some countries have remained remarkably free from the disease in spite of the conditions being apparently suitable for the spread of infection; for example, no great epidemics have been reported from India, even from crowded louse-infested communities in which great epidemics of relapsing fever occur at intervals. In the countries of Western Europe, in Canada, and in the United States of America the disease is now rare in times of peace; evidently the reduction in the degree of louse infestation of these countries has brought about conditions in which transmission does not readily occur. Epidemics have been reported in recent years from Poland, Russia, Ukraine, Rumania, French North Africa, South Africa, Korea, Manchuria, North China, and Asia Minor. Cases have also occurred in Mexico, Bolivia, Peru, and the high altitudes of Colombia: Official reports for May and June, 1942, show that severe and widespread epidemics were then raging in Algeria, Tunisia, and French Morocco, and that outbreaks were occurring in many localities in Spain, Hungary, Rumania, and Bulgaria; cases were also reported from Shanghai, Iraq, Iran, Turkey, and Lyons in France. No official reports are now available from Russia or countries in German occupation, but there is plenty of evidence that the disease is causing great anxiety even in Germany itself, where, in spite of elaborate precautions, many groups of cases have occurred among the soldiers engaged in guarding prisoners of war. In one instance 23 of 25 persons employed at a camp near Berlin were attacked.

In the eastern countries of Europe there is a return to the conditions which caused devastating epidemics during and after the war of 1914-18. These conditions were the existence of infection, great movements of population, malnutrition, overcrowding, lack of facilities for personal cleanliness, and louse infestation. In these circumstances typhus fever must be imposing a severe strain on the German and Russian efforts to keep it under control.

In this country the disease still smoulders in some places, and so long as louse infestation is allowed to persist there is need for constant vigilance by the medical profession and the public health services. Persons of all ages and of both sexes are equally susceptible, but attacks in young children are usually mild and so are often missed. So also in endemic areas, adults who have had previous attacks are likely to get the disease in a mild form, and thus infection may persist without being detected.

The Virus

The rickettsiae of the disease have been isolated from the blood of patients during the febrile stage, also in some cases during the last two or three days of the incubation period; the virus usually disappears with or just before the fall in the temperature, but occasionally persists for a day or two in early convalescence. Infection is conveyed from man to man by human lice, chiefly, if not entirely, by the body louse. The louse cannot transmit infection till 5 to 10 days after biting an infected person; it then remains infective for the rest of its life. The rickettsiae are scanty in the human body, but multiply exceedingly in infected lice, chiefly in the cells of the gut. They are small organisms resembling bacilli or cocci;

they stain well with Giemsa's reagent and are Gram-negative. They do not grow in ordinary culture media, but only in the presence of living cells: for example, in tissue cultures or in the yolk sacs of developing chick embryos. In the latter they multiply rapidly, so that suspensions of the yolk sacs may be heavily loaded with rickettsiae a few days after inoculation. Monkeys are susceptible to infection: the virus can be maintained in guinea-pigs for an indefinite number of transfers by intraperitoneal inoculation, but the disease is seldom fatal to the animals and seldom causes scrotal swelling such as results from inoculation with the rickettsiae of flea-borne typhus. White mice are susceptible to inoculation by the tracheal route; the animals get severe pneumonia, and enormous numbers of rickettsiae are found in the consolidated lungs.

The virus is normally transmitted through the skin from infected lice. The exact mechanism of transmission is doubtful; some workers believe that the organisms are not introduced into the body in the act of biting, but rather by the entry of infected faeces or of fluids from the crushed bodies of the insects through the site of the puncture or through scratches. The faeces of infected lice contain enormous numbers of rickettsiae, which can survive for a long time in the dried faeces. It is therefore possible that infection may occasionally be conveyed through contact with the faeces or through the inhalation of dust particles resulting from the drying of the faeces. Some German workers have recently recorded cases in which they held that transmission by the lice themselves could be excluded. These observers emphasize the need for disinfection of the skin and clothing of the patients rather than mere disinfestation by methods which fail to kill the rickettsiae. Another matter of importance to medical attendants is that the blood of the patient is infective, so that if accidentally smeared on the fingers when making blood films it may cause infection. A case has recently been recorded in which the disease was caused by the transfusion of blood from a donor who happened to be in the incubation period of the disease three days before the onset of his attack.

Immunity.—An attack confers immunity, which is complete for a considerable time but gradually wears off, so that a second attack may occur; this is usually much milder than the original illness. Mild or unapparent attacks in persons with partial immunity are believed to be important sources of infection in endemic areas.

Pathology.—The characteristic lesions are tiny nodules in the walls of small blood vessels, especially of the brain, skin, and kidneys: the nodules are made up chiefly of large and small mononuclear leucocytes and of partly necrosed endothelial cells of the blood vessels. Necrosis of the vessel walls at the sites of the nodules is the chief cause of haemorrhages and petechial eruptions. The nodules also cause interference with the blood supply of the brain, heart, and other organs, and so are probably responsible for many of the chief features of the disease.

Clinical Features

Most of the cases seen in severe epidemics conform to a fairly uniform type, though there are wide variations in severity. Sporadic attacks and cases in endemic areas, especially when they occur in children, are often so mild that they are very likely to be missed by medical men whose mental picture of typhus is based on descriptions of "typical" cases. The figures given in parentheses in the following account are based on reports of epidemics; they are not applicable to mild outbreaks. For a detailed account of the symptomatology the textbooks must be consulted.

Incubation Period.—This is usually 8 to 12 days; the extreme ranges are 5 to 23 days. As a rule the longer the incubation period the milder is the attack.

Signs and Symptoms

The chief features of cases seen in adults during severe epidemics are: The onset is usually sudden or rapid, with chill, shivering, or rigor (60 to 80%), severe frontal headache (90%), and pains in the back and limbs. Vomiting frequently occurs (25 to 50%). There is often suffusion of the face with swelling of the eyelids and injection of the conjunctivae. At first drowsiness or mental confusion is present, succeeded by stupor

or delirium in many of the severe cases. Insomnia is frequent (50%). The temperature rises rapidly, reaching its maximum of 103° to 105° F. within two or three days and then remaining high, with daily remissions of 1 to 3 degrees for 8 to 12 days. Occasionally the temperature falls to normal for a few hours before the end of the first week; but, apart from this pseudo-crisis, the fever runs an uninterrupted course in most cases. The throat is often red (30 to 75%), the tongue and mucous membranes of the upper air passages are usually dry, and the latter may be distressingly irritated. Bronchitis is frequent (80 to 90%). Meningism is not uncommon. The spleen is sometimes palpable.

The rash is often the first diagnostic feature; in some outbreaks it has been reported as being absent in about 10% of the cases. In pigmented skins it can only be detected when it is pronounced. It appears suddenly, as a rule between the third and fifth days; in rare cases it is seen on the second day, and it may be delayed till the eighth or ninth day. Often it is preceded by a faint mottling of the skin, then pink or bluish-red macules appear on the sides of the chest, back, and shoulders, rapidly extending to the rest of the trunk and often to the arms and legs. The spots are seldom raised; at first they disappear on pressure, but soon cease to do so; at the same time their colour changes to deep red and then to brown. In severe cases there is often a petechial haemorrhagic point at the centre of each spot; this is surrounded by a brownish mottling. After a few days the spots begin to fade, but brown staining may persist for some days or even weeks. The spots may be few and difficult to detect; usually they are numerous, and in severe cases they may be very profuse. Exceptionally, the eruption is maculo-papular or papular; in severe cases it may consist of purpuric patches of varying size. The distribution of the rash is important in diagnosis. The trunk, especially the sides of the chest or back, is the favourite site; there is extension to the arms and legs in about three-fourths of the cases, but the face is affected in only a few patients (about 4%). The palms and soles are very rarely involved (about 2%). In some recent outbreaks extension to the face, palms, and soles has been relatively frequent.

The pulse soon becomes feeble, it may be slow in proportion to the temperature; the blood pressure falls, so that systolic readings of 80 to 100 are usual. Occasionally there is leucopenia, but a moderate degree of leucocytosis is usual; very high counts of 20,000 or more occur only in very severe cases. The blood tends to become concentrated; the haemoglobin readings and red blood cell counts may be abnormally high even when blood destruction is progressing. Febrile albuminuria is usual; true nephritis is infrequent, but has been reported as fairly common in some epidemics. Red blood cells in varying numbers are found in the centrifugized urine; in severe cases there may be obvious haematuria. The leucocytes of the cerebrospinal fluid are slightly increased in mild cases—considerably so in severe attacks, in which a good deal of albumin may also be present.

The most striking feature of the disease is the rapidly progressing deterioration in the mental and physical condition; before the end of the first week the patient is often in the "typhoid state," with great prostration, low muttering delirium or coma, tremor of the tongue and tendons, and absence of response to external stimuli. Active noisy delirium and great restlessness may occur: in this condition there is an added strain to the already enfeebled heart. The breathing is usually hurried even when pneumonia does not occur; the heart sounds are feeble, especially the first sound, which may be inaudible. Even in relatively mild attacks mental disturbance and physical weakness are conspicuous features; their early onset and rapid progress are in contrast to what happens in typhoid fever. Meteorism is unusual in typhus patients. In recovering patients improvement usually sets in rapidly or suddenly; the temperature falls by rapid lysis or by crisis about the twelfth to the sixteenth day and at the same time the mental condition improves and the appetite returns. At this stage special care is needed because the patient feels so much better that he is tempted to take liberties while his heart is still very feeble. In some cases the mental condition does not clear up till some days or even weeks after the fall of the temperature: slow cerebration, deafness, and tremors of the muscles are the chief symptoms in such cases.

Most of the deaths occur between the tenth and the seventeenth day; it has been stated that the eleventh day is especially critical, but in some epidemics more patients have died after than before the fall in the temperature. A few of the types of temperature curve that may occur are shown in the accompanying chart.

TYPHUS FEVER (LOUSE TYPHUS)

Mild Attacks.—These are far more common than would be gathered from descriptions of the disease that are based on experience of severe epidemics: in many outbreaks severe attacks are quite exceptional. Cases in children and sporadic attacks are often so mild that they are not recognized. In surveys of suspected areas ambulatory cases or even unapparent attacks are sometimes discovered by the Weil-Felix test. The mildest cases that are likely to be recognized in ordinary conditions are those resembling an attack of influenza: the patient has fever, with pains in the back and joints, redness of the throat, headache, and lassitude. There may or may not be a rash. The fever lasts a week to 10 days, the rise and fall in the temperature are often gradual, and apart from a positive Weil-Felix reaction no reliable diagnostic indication may be present. In some outbreaks the cases are more characteristic; they have a general resemblance to the severe attacks seen in epidemics, but the signs and symptoms are all of a milder type, the temperature does not rise so high, and the fever lasts from 10 to 13 days. Complications are rare and convalescence is rapid. Even in groups of cases in which moderately severe attacks occur, the case-fatality rate may be negligible except in elderly patients. In the absence of overcrowding, malnutrition, and very heavy louse infestation the average severity of the disease is by no means great. Brill's disease appears to be a mild form of louse-borne typhus. Although this disease was first described by Brill of New York as long ago as 1897 its true nature has only recently been discovered. Zinsser has shown that the virus is of the same type as that of louse-borne typhus and that more than 95% of the patients had originally come from places in Europe in which typhus fever was endemic. This suggests that the disease may be a late recrudescence of infection which has lain dormant for years in the patients. Although 500 cases have been reported from New York since 1910 there is no record of infection having been transmitted to contacts. Cases of the same kind must occur in other countries, including, in all probability, the United Kingdom. Clinically the disease is mild typhus fever, but it can occur in the absence of louse infestation.

Fulminating Attacks.—At the other end of the scale are the virulent and rapidly fatal attacks. These occur in severe epidemics and usually in elderly persons debilitated by malnutrition. The patient may die within 3 or 4 days of the onset—sometimes before the rash has time to appear, but

more often after the precocious appearance of a haemorrhagic eruption. Clinically the attack resembles one of haemorrhagic small-pox.

Complications.—The most important complication is bronchopneumonia, which occurs in 10 to 20% of cases in epidemics and is often the apparent cause of death. Thrombosis of the femoral vein is not uncommon. Arterial thrombosis occurs in 1 to 5% of cases; it may cause loss of the toes or even of one or both feet. Secondary streptococcal infections are fairly common; otitis media has been reported in as many as 10% of cases in severe epidemics, parotitis in 2 to 4%, occasionally with suppuration of the gland. Bed-sores are frequent in severe cases, especially when nursing arrangements are defective.

Sequelae.—In mild cases convalescence is rapid and there are no sequelae, but after severe attacks the patient slowly regains strength and mental alertness. Weakness, slowing of the mental process, tremors of the hands, and partial deafness may persist for some days or weeks. True relapses are practically unknown, but sometimes there is an irregular rise of temperature for some days after the crisis.

Prognosis

The case-fatality rate varies greatly with age; it is almost negligible in children and is seldom more than 5% below the age of 20. It rises slowly till about the age of 40, when it is from 10 to 15%. It then rises somewhat steeply, reaching about 50% at the age of 50. Few patients of 60 and over recover. These figures refer to severe epidemics, but the risk to life always depends largely on the age of the patient. Persons debilitated by starvation bear the disease badly, and the virulence of the infection is a most important factor. Deaths are far more numerous in severe epidemics occurring in half-starved and crowded communities composed chiefly of adults: in such conditions the death rate may be as high as 40 or even 50%. In outbreaks in endemic areas the average rate may be as low as 5 to 10% if all the mild cases are taken into account. Unfavourable features in individual cases are early onset of delirium or coma, haemorrhagic rash or other haemorrhages, leucocytosis in excess of 20,000, bronchopneumonia, and thrombosis of the large veins.

(The concluding part will appear in our next issue.)

POST-WAR HOSPITAL SERVICES

By arrangement with the Minister of Health the Nuffield Provincial Hospitals Trust has appointed Prof. J. A. Ryle and Dr. A. E. Quine to carry out a survey of hospital services in the North-East of England (Northumberland, Durham, and Cleveland). This will be conducted on the same lines as the surveys now being carried out by officers appointed by the Minister of Health in the London area and in the North-West. This is part of an arrangement under which the Nuffield Trust, with the concurrence of the County Councils Association, the Association of Municipal Corporations, and the British Hospitals Association, has agreed to assist the Ministry by organizing surveys of hospital services in various parts of the country. The areas to be surveyed and the officers to be appointed will be agreed between the Minister and the Trust. The object is to obtain expert advice on the hospital resources and needs of the areas so as to provide a factual basis on which the Government's post-war hospital policy, which was announced by the Minister of Health in the House of Commons on Oct. 9, 1941, can be worked out. The policy, briefly, is to place a duty on the major local authorities, in collaboration with voluntary bodies, to provide a service which will ensure that "appropriate treatment will be readily available to every person in need of it."

Prof. J. C. Drummond, D.Sc., Scientific Adviser to the Ministry of Food, will deliver the Harben Lectures for 1942 on "Problems of Wartime Nutrition" at the Royal Institute of Public Health and Hygiene, 28, Portland Place, W., on Mon., Tues., and Wed., Oct. 26, 27, and 28, at 3 p.m. In his first lecture he will discuss "The Background to the Study of Nutrition in Wartime"; in the second "Deficiency Conditions to be guarded against in Wartime"; and in the third "Measures taken to maintain a Good Nutritional Condition of the People in Wartime." Admission to the lectures is free, and seats may be reserved on application to the acting secretary of the institute.