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SCRUB TYPHUS AS A WAR DISEASE

BY

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When a request was received for a short article on certain aspects of scrub typhus it occurred to me that an outline sketch of some of the chief features of the disease might be useful to medical officers serving in the East. The following notes consist largely of impressions resulting from a study of reports of a considerable number of outbreaks that have occurred during the present war; no mention is made of the names of the authors, partly because several of the reports have not been published, and partly because detailed references would be out of place in an article of so limited a scope.

Relationship of Scrub Typhus to the other Typhus Fevers

A clear mental picture of scrub typhus can most easily be obtained by looking first of all at its relationship to the other typhus fevers, which it closely resembles in aetiology, pathology, symptomatology, and treatment. In these respects all the typhus fevers conform so closely to the same basic pattern that those who know any one of the diseases need pay attention only to the few points in which they differ from each other. But while in the above aspects the typhus fevers form a unitary group, scrub typhus and flea-borne and tick-borne typhus differ so sharply from classical louse-borne typhus in the epidemiological conditions in which they are transmitted to man that they must be placed in a separate subgroup. Louse-borne typhus, being transmitted from man to man by human lice, is a purely human or "demic" disease, so that, in prevention, infected persons and the lice by which they are infested are the chief concern. Scrub typhus—better named "mite-borne typhus"—together with flea-borne and tick-borne typhus, is primarily a disease of lower animals, or a "zootic" disease, and infection is transmitted to man as a secondary incident, so that measures of control are directed against the infected animals and the arthropod vectors which habitually feed on them. For all practical purposes the possibility of transmission of the zootic typhus fevers from an infected person to a contact can be left out of account.

In its epidemiology scrub typhus is more closely related to tick-borne than to flea-borne typhus, whose animal reservoirs live in association with human habitations, whereas the reservoirs of the other two diseases exist chiefly in rural and sylvan areas away from human dwellings. The resemblances between the fevers of the group are suggested by the name "typhus"; so, also, the differences are associated with the arthropod vectors and can most suitably be suggested by a nomenclature based on the names of the vectors. Mite typhus would be a more suitable name than scrub typhus, which implies that the disease is restricted to scrub country and which might even suggest that mite-borne typhus is the only typhus fever likely to be encountered in scrub areas.

Some Special Features of Scrub Typhus

Synonyms and History.—Although the name scrub typhus is of recent origin the disease was described in the third century by a Chinese writer, who attributed it to the bite of a "small red insect," presumably a mite. The classical form of the disease—tsutsugamushi ("small insect") disease—has been well known in Japan for many years, but the widespread distribution

of the fever in the East was not realized till a few years ago because in outbreaks outside Japanese territory the local lesion called the "eschar" was seldom present, and as this was described as an essential feature of tsutsugamushi disease these outbreaks were regarded as being due to "new" fevers, to which many different names were applied. The eschar is now known to be a fortuitous feature, and all the mite-borne typhus fevers are the same as tsutsugamushi disease.

Definition.—Scrub typhus is the fever of the typhus group that is transmitted to man by a mite.

Geographical Distribution.—The disease is suspected of occurring sporadically in the north-eastern parts of Africa, but its definitely known range of distribution is confined to southern and eastern Asia, northern Australia, the islands adjoining these regions, and the Pacific islands. There is therefore a remarkably close association between the distribution of the disease and the areas in the East concerned with the operations of the war against Japan. In India, Ceylon, and the whole eastern theatre of war the disease can be expected to occur; the most dangerous areas are in South-East Asia and the South-West Pacific, where epidemiological conditions are specially favourable for the existence of infection.

Importance of the Disease.—Up to the outbreak of the Japanese War scrub typhus was not of great importance except to labour forces in certain localities. Most of the affected areas were sparsely inhabited and the indigenous populations were largely immune owing to attacks in childhood, so that nearly all the observed cases in these places occurred among the few persons who entered them from outside. Military preparations and operations introduced new conditions: large bodies of troops began to enter the infected areas, and outbreaks, sometimes reaching epidemic proportions, began to occur. Scrub typhus is now regarded as one of the major risks to life and military efficiency in the greater part of the war zone, and it has been found necessary to take drastic steps for its control. In one case hundreds of troops became infected after military exercises lasting a few days in an area where the very existence of the disease had hardly been suspected; in another a large proportion of the staff of a freshly established military hospital were attacked within a short time. Apart from the fatality rate, which may be anything from 1 to 20%, the average period of invalidity is more than three months, so it is not surprising that the disease is being attacked with great energy.

The Cause.—This is *Rickettsia tsutsugamushi*, also called *R. orientalis*, which is closely related to the other typhus rickettsiae in its morphological and cultural characters as well as in the pathological effects produced in the body; the chief difference between the organism and the related rickettsiae consists in the absence of a high degree of cross-immunity after infection.

Transmission of Infection.—The vector is a microscopic larval trombiculid mite; *Trombicula akamushi*, *Tr. deliensis*, and several other species are known or believed to be capable of transmitting infection from animal to animal and from animal to man. These mites bite only once during their lifetime, in the larval stage, so that the same mite cannot both acquire and transmit infection. What happens is that a mite infected by a blood meal can transmit infection through the egg to its off-

spring, which can introduce the rickettsiae into any animal or human being on which they feed. This peculiarity in the life history of the mites has an important bearing on the methods of controlling the disease. The destruction of rats or other reservoirs of infection cannot have much immediate influence in stamping out infection; it may even increase the risk to human beings by depriving the larvae of access to their usual hosts. The mites and the animals from which they derive their infection are most plentiful in places where the ground is damp and covered with grass and other vegetation. Grass, which grows to a great height in the Tropics, is specially liable to infestation; swampy ground, scrub land, and places in which palm trees grow often swarm with the mites. Such places are usually situated near the sea, rivers, streams, or lakes. In dry places and during dry periods of the year the mites are not so active. Infection is often restricted to well-defined areas, but unfortunately it is seldom possible to judge by inspection which places are safe and which are dangerous. Persons who enter mite-infested areas are not likely to be bitten so long as they keep on the move, but the moment they sit or lie down, or even stand still, the mites are attracted and seek out a suitable part of the skin on which to feed. Any part of the body may be bitten, but the favoured sites are those bathed in perspiration and protected from disturbance by friction caused by the clothing. Such parts as the groins, scrotum, axillae, and neck are especially liable to be bitten. The mites when undisturbed remain attached for about two days; they seldom cause pain or irritation, and often the victim does not know that he has been attacked.

Reservoirs of Infection.—Rats and mice are the animals chiefly concerned in maintaining infection among the mites. The complete chain of transmission has only once been clearly demonstrated, but there is convincing circumstantial evidence to support the accepted view on this subject. Analogy with the closely related disease, tick-borne typhus, suggests that infection can persist among the mites for long periods with very occasional refreshing by biting infected animals.

Pathology.—The essential features of the pathology of all the typhus fevers are remarkably similar. Apart from the effects of circulating toxins, special damage is caused to the organs and tissues of the body by interference with their blood supply. The rickettsiae multiply chiefly in the vascular endothelial cells, which become swollen or even proliferated. The walls of the capillaries and small arteries become infiltrated by mononuclear cells, chiefly lymphocytes, and in the tissues immediately adjoining these vessels there are often collections of similar cells. The special nervous and circulatory manifestations that occur in the typhus fevers are believed to be caused chiefly by damage to the central nervous system resulting from obstruction to the blood supply. The heart and other organs doubtless suffer to some degree from similar damage, but the modern view is that the circulatory failure is caused mainly by injury to the vasomotor centres, and to a minor degree by myocarditis. After defervescence a slow but complete return to normal occurs in the great majority of cases; permanent damage to the brain or heart is quite exceptional.

Immunity.—There is complete immunity for a variable period after an attack, and, although this gradually diminishes, second attacks are likely to be less severe. Relapses have not been mentioned in any of the descriptions of the disease.

Clinical Features

The general resemblance between scrub typhus and the other typhus fevers is very striking. Apart from the eschar and lymphadenitis, which are often absent, there is no sign or symptom that can be relied on for the differentiation of a case of scrub typhus from one of classical typhus. The resemblance to tick-borne typhus is even closer, because the local lesion and lymphadenitis occur in some types of that disease.

In making a comparison between scrub typhus and the other fevers of the typhus group account must be taken of the great variations that occur in the virulence of the infection in each fever and also in the age and previous health of the groups of patients concerned. Just as louse-borne typhus may be a relatively mild or a highly fatal disease, so also scrub typhus shows a wide range of severity. The variability of scrub typhus is so important a feature of the disease that it deserves

to be emphasized by giving a few examples based on descriptions of recent outbreaks among troops.

Analysis based on Recent Reports of Scrub Typhus

No. of Cases	Usual Type of Onset	Percentage Incidence of Eschar	Usual Range of Leucocyte Count	Fatality Rate (%)
50	Sudden	6	9,000–12,000	Nil
85	Gradual	80	4,000–6,000	3
626	Rapid	59	3,100–12,000	9.7
756	"	85	Relative lymphocytosis	1
36	"	17	Moderate leucopenia	3

The rash was seen in most of the white-skinned patients, but in very few of the dark-skinned. In the outbreak in which the fatality rate was 9.7% there was only one death among the first 100 patients, but there were 37 in the next 150, who had been greatly debilitated by previous hardship and disease.

The general clinical picture must be viewed in the light of the above statements. Except when otherwise stated, the details can be filled in from any good description of classical typhus occurring among corresponding groups of persons; the average type of the fever, the rash, the symptoms, the complete freedom from relapses, and the convalescence, conform to the same pattern in both diseases.

The incubation period ranges from 7 to 21 days. When the eschar occurs it usually makes its appearance before the onset of the fever; it begins as a papule and soon becomes a round or oval sore, 2–3 mm. in diameter, surrounded by a red raised zone of about the same width. Soon a scab forms at the centre; later this drops away, leaving a punched-out ulcer surrounded by a bright-red zone of skin. There is neither pain nor irritation, so that the patient is seldom aware of the existence of the eschar. Any part of the body may be affected, and the regional lymphatic glands are usually enlarged and tender.

The onset of the fever is as a rule rapid, sometimes with chill, and nearly always with headache of the post-orbital type; pains in the loins and the limbs are common; the conjunctivae are injected, the eyelids swollen, and the face looks bloated. A rapid step-like rise in the temperature follows, and the maximum is reached in two or three days. By the fourth or fifth day there is often a moderate degree of generalized lymphadenitis. The rash appears on the fourth to the seventh day, first as discrete macules on the trunk; soon these become somewhat papular and the rash extends to the limbs. In most of the reported outbreaks the hands, feet, and face are said to have been seldom involved. In pigmented skins the rash can rarely be detected.

The patient's condition steadily becomes worse, and by the end of the first week the same types of mental symptoms as occur in classical typhus are usually observed; there may be excitement or delirium with nocturnal insomnia, or the patient may be lethargic or stuporous. There often is a dry unproductive cough, associated with redness of the throat and bronchitis. The spleen is frequently palpable. The blood pressure falls, and during the second week the systolic reading is often below 100 mm. Temporary deafness, usually partial, is frequently observed, and there is increasing prostration. The leucocyte count may show little change, but a progressive leucopenia with a total or relative lymphocytosis is a common feature in many outbreaks. Leucocytosis, even up to 21,000 total count, has exceptionally been observed, but high counts are usually associated with secondary infections.

On the average the onset is rather less rapid than in louse-borne typhus, and there is a greater average tendency to daily remissions in the temperature curve. Leucopenia and lymphocytosis also are more frequent than in louse-borne typhus, but all these features are so variable that they cannot be relied on to differentiate the two diseases. Scrub typhus is said by some observers to differ from classical typhus in having few haemorrhagic, thrombotic, and septic complications, but these manifestations are equally infrequent in many outbreaks of classical typhus among young and previously healthy men.

The termination of scrub typhus is usually by lysis, which tends to be more gradual than that commonly occurring in classical typhus. The duration and severity of the attacks show the same wide range of variation as occurs in louse-borne

tick-borne typhus; there is also the same tendency to circulatory failure associated with a fall in the blood pressure. With recovery the circulation is gradually restored, and often there is sudden diuresis. Traces of albumin usually appear in the urine, but nephritis is exceptional.

The Weil-Felix Test

Strangely enough, the commonly used laboratory test for scrub typhus is based on the development of serum agglutinins, whose presence is indicated by the agglutination of a bacillus which has nothing to do with causing the disease. This is *Proteus OXX*, a bacillus derived by chance mutation from a strain of *Proteus OX 19*. In classical and flea-borne typhus *OX 19* is agglutinated in rising titre, and the reaction with *OXX* is negative or weakly positive. In scrub typhus these responses are reversed: *OXX* is strongly agglutinated and *OX 19* hardly or not at all. These bacilli thus serve as indicators of the types of the disease, perhaps in a manner analogous to the indications given by various sugars in differentiating the bacilli of dysentery and other diseases.

Carefully selected strains of *OXX* must be used; this organism, itself a mutation strain, is liable to undergo unexplained variations in its agglutination responses, but when standardized suspensions are used the test is as reliable for scrub typhus as the agglutination of *OX 19* is for louse-borne and flea-borne typhus. The rise in titre usually begins about the end of the first week of the fever and reaches its maximum about the end of the second week. The test should be carried out as early as possible and repeated at intervals, because the rising titre is of special significance; an initial negative reaction followed by a titre as low as 1:50 is stronger evidence than a single late reaction of 1:100 or even 1:200. Occasionally the reaction does not become positive till convalescence has set in. In patients who die before the 14th day the reaction often remains negative till death, otherwise it becomes positive in a very high proportion of the cases. False positives are rare when reliable suspensions are used.

As happens in other typhus fevers, the Widal reaction is often positive in scrub-typhus patients who have been inoculated with T.A.B. vaccine.

Complications; Prognosis; Convalescence

Bronchitis is a common complication, but is probably only a manifestation of the disease resulting from the multiplication of the rickettsiae in the respiratory mucous membrane. Bronchopneumonia also is probably a severe rickettsial reaction rather than a secondary infection. Secondary infections with pneumococci and septic organisms are infrequent except among patients who have been debilitated before the onset. Malaria is very prevalent in most of the places where scrub typhus occurs, and must constantly be borne in mind. In all cases of doubt a course of mepacrine should be given.

The average fatality rate in scrub typhus is about 5%. In outbreaks of low virulence among previously healthy young men it may be less than 1%, but in outbreaks of a virulent type in debilitated troops it may be as much as 20%, and in these circumstances elderly patients are more likely to die than to survive. In one outbreak there were six deaths among 13 officer patients, and four of these deaths were in persons over 35 years of age. Most of the deaths occur between the 7th and 21st days.

Convalescence is prolonged after severe attacks, but is usually complete in the long run. The average period of disability is about three months; during this time the circulatory response to exercise is poor, and a return to full duty may have to be delayed much longer. Final invaliding is likely to be necessary only in elderly patients who have had severe attacks.

Diagnosis

Few diseases are easier to diagnose when suspicion has been aroused, yet the all-important first cases in outbreaks have often been missed, with the result that preventive measures have been delayed. Now that the disease has become so notorious the most likely mistake is to make the diagnosis of scrub typhus in attacks of malaria or dengue, or to overlook the coexistence of malarial infection and scrub typhus.

If the eschar is present the diagnosis can be made at the very onset of the fever; otherwise a consideration of the exposure to risk and the early symptoms will often point strongly to scrub typhus, but a confident diagnosis may not be possible till the rash appears or the characteristic agglutination reaction becomes positive. Dengue may be closely simulated in the first few days, but its onset is usually more sudden and the epidemiological conditions in which it occurs are different. Flea-borne typhus may occur almost everywhere in the area of distribution of scrub typhus, but the chief risk of infection is in towns and villages, and outbreaks of considerable size are not likely to arise. The agglutination reaction in the flea-borne disease is of the *OX 19* type; the eschar and lymphadenitis are not present, otherwise the symptoms are very similar to those of scrub typhus. Tick-borne typhus also occurs in many places in the East, but no outbreaks have been reported from the theatre of military operations; the agglutination response is rarely of the *OXX* type, and if cases were mistaken for scrub typhus little harm would be done, as treatment and prevention are on almost identical lines. Louse-borne typhus is remarkably uncommon in the Tropics, even among louse-infested communities, but the disease can be expected to occur in subtropical China, increasing in frequency in the colder parts of the country. In northern China louse-borne and flea-borne typhus may appear simultaneously in one locality and so give rise to difficulties in differential diagnosis because the symptoms and agglutination reactions are the same in these diseases.

Although knotty problems in differential diagnosis may occasionally arise, few mistakes will be made if the epidemiological conditions are considered and serological tests are carried out.

Treatment

Treatment is on exactly the same lines as in louse-borne typhus except that no precautions are needed to prevent the spread of infection from the patient. No drug has yet been found to have a favourable influence on the course of the disease, though para-amidobenzoic acid may turn out to be of value in view of its successful use in some cases of classical typhus. Convalescent serum has had no obvious effect in the few cases in which it has been tried, and the attendant risks in malarious countries deserve consideration.

Careful nursing, preferably in the Fowler position, a generous varied diet rich in vitamins, and an adequate intake of fluid are generally agreed to be essential. At least four pints of liquid should be taken daily; given by the mouth, or if necessary by a nasal tube kept *in situ*, there is little risk of fluid retention such as may occur with the intravenous administration of salines and glucose. Supportive intravenous treatment should be undertaken only when expert laboratory help is available, but plasma may be needed in exceptional cases. The urinary output must be maintained; it should be measured every eight hours in serious cases. Digitalis and adrenaline seem likely to do more harm than good. Oxygen should be given if cyanosis develops. For intense and persistent headache lumbar puncture should be carried out.

The psychological factor in treatment is important. The patient is greatly helped by the maintenance of a cheerful atmosphere; he must not be allowed to receive the impression that his illness is of a mysterious and deadly kind; and care is specially needed to avoid any suggestion that his heart is likely to be permanently damaged. These patients are often fractious, so they must be managed with a judicious combination of firmness and kindness such as is suitable for mental cases. The diet should be varied; "something to chew" is helpful in maintaining the hygiene of the mouth, and when the patient's condition allows he should sit up in bed for his meals. Frequent changes in position and a careful watch for oedema and threatened bed-sores are needed for lethargic and comatose patients. Sulphonamides have not been effective for bronchopneumonia, presumably because this is caused by the rickettsiae rather than by secondary infections. Although penicillin has been disappointing, it is said to have been helpful in one case with bronchopneumonia.

Transfers of patients involving a tiring journey should never be permitted after the first few days. The pathology of scrub typhus should be borne in mind in planning treatment; the disease is essentially a rickettsial vasculitis. The patient must

be warned against exertion till his response to exercise becomes satisfactory.

Prevention

Prevention has to be considered from two points of view—the protection of camp sites and of troops compelled to enter mite-infested areas. When a choice of camp sites is possible a dry area should be chosen. The site should be thoroughly cleared of all grass and vegetation by cutting, oiling if possible, and burning. Indigenous labour should be employed when available. For important camps a bulldozer would be invaluable; the ideal to be aimed at is to obtain a surface covered with earth or sand and completely free from vegetation. When this is impracticable an effort should be made to provide such a surface for occupied quarters and paths, and to prohibit all straying from the prepared ground. The work should, if possible, be carried out under the supervision of an expert entomologist. The protection of troops compelled to expose themselves to risk is a troublesome problem, complicated by the difficulty of designing mite-proof clothing which would be tolerable in tropical conditions. The detailed measures now adopted cannot, for security reasons, be completely divulged, but it is known that mite repellents, such as dimethyl phthalate, have been applied to the skin and clothing, and that intensive study of the whole subject has been carried out by competent experts.

The control of rats and other animal reservoirs of infection must be undertaken with great circumspection, and only under expert guidance, for the reasons already given. Rats should certainly be discouraged from infesting the camp by keeping every scrap of food out of their reach and by seeing that no suitable nesting-places are available for them. The camp should be kept free from animals of every kind; to ensure this a high standard of tidiness is needed, especially in cookhouses and food stores. Rat and mouse holes can safely be treated by cyanide gas; trapping and poisoning may be risky.

Prevention by egg-yolk or animal-lung rickettsial vaccines has been the subject of close investigation by experts, but many difficulties are likely to be encountered in work of this kind. The instruction of all who are exposed to risk must form an important part in the campaign against scrub typhus; success can be achieved only by the intelligent co-operation of everyone. There is plenty of evidence that the disease is being taken very seriously by the Allied Forces in the East, and there are good grounds for hoping that the energetic measures of control now being adopted will reduce the scrub-typhus menace to negligible proportions.

SCRUB TYPHUS: A CLINICAL STUDY

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During the period Nov., 1944, to Jan., 1945, 110 British patients suffering from scrub typhus were treated in a forward Indian general hospital. This paper is a summary of the clinical records of these cases and of impressions gained with regard to diagnosis, prognosis, and treatment. The patients were all drawn from units of a British formation which entered a small "typhus island" in N.E. Burma during the first week of November. The preventive measures now in force had not at that time been adopted, and the onset of symptoms in the first cases occurred on Nov. 17—that is, approximately two weeks after entry into the affected area.

The first group of patients were admitted to the general hospital on Nov. 27, and in the next three days the total number had reached 41 (1 officer and 40 B.O.R.s). In December there were 69 admissions (3 officers and 66 B.O.R.s), most of whom reached us during the first nine days of the month. After this date fresh cases were received only very occasionally, owing to more efficient prophylaxis and to the fact that the main body of the formation had driven beyond the endemic

zone. At first, cases reached the general hospital on the fifth to tenth day of the illness. Later, as forward medical units became more "typhus conscious," the disease was recognized earlier, and patients were evacuated about the third or fourth day.

Clinical Features

The onset was usually sudden, with severe headache and fever, with or without a rigor. The temperature usually reached 103° within the first 48 hours, and was often slightly higher. Thereafter the fever was usually continuous, but a four-hourly chart sometimes showed an intermittent type, a sudden drop to normal or subnormal, accompanied by profuse sweating, taking place in the early hours of the morning. The average duration of fever was 15.7 days (extremes, 5 days and 29 days), the return to normal being by lysis. Twenty-five cases had fever of 10 days' duration or less. Headache was present in 100% of cases from the onset of the illness. It was often frontal or retro-orbital, and of such severity that it was not relieved by the usual analgesics. Sore throat, with injection of the fauces, was present in 54% of cases; it was so severe as to prevent swallowing in 4 cases (3.6%).

Primary Lesion or Eschar.—56% of cases showed typical eschars. The lesion was generally single, but 3 cases each had 2 eschars, and one case had 3. The eschar may be missed if the search is not thorough. In several cases the eschar was found on the scrotum, the perineum, or between the buttocks. The common sites, in order of frequency, were the axilla, the anterior aspect of the trunk, the forearm, the leg, and the back of the chest. The patients were rarely aware of the existence of the lesion, and in only two cases could the men recall having noticed it before the onset of general symptoms. These troops were so inured to jungle sores, however, that it is not surprising that they took little heed of an extra one.

Conjunctival injection and marked flushing of the face were common signs, being observed in 82% and 65% of cases respectively. They were of assistance in the early diagnosis of the disease, since they were present by about the third day.

Adenitis.—Of the cases 98% showed moderate enlargement of the lymph nodes in all areas. The glands were not visibly enlarged except in a small number, but were very readily palpable, discrete, rubbery, and sometimes tender in the first week or so. Enlargement was appreciable by the fourth day of the illness. Except in a few cases, the glands draining the eschar were not noticeably larger than those palpable elsewhere.

Rash.—In 64% of the cases there was a maculo-papular rash—more rarely purely macular—on the fifth or sixth day of the illness. It lasted three to four days and was distributed mainly on the trunk, the face, and the proximal portions of the limbs. One case presented unusual features, in that at the time of the maculo-papular rash, and healing as the latter faded, there were multiple superficial herpes-like erosions of the glans penis, similar lesions of the buccal mucosa, and an oval sloughing ulcer of the lower lip. The Kahn reaction in this case was negative, which answered a suspicion that temporarily occurred to us, and the patient subsequently became the subject of typical typhus necropsy.

Mental State.—There was some definite alteration in 50% of the cases. This varied from a drowsy apathy with mental confusion, in average cases, to restlessness, delirium, and sometimes a "typhoid state" in grave cases. Mild cases showed no mental change other than that caused by the constant intense headache.

Respiratory Signs.—50% of cases had signs of a diffuse bronchitis, and they produced a variable amount of mucoid sputum which was occasionally blood-tinged or rusty. Unless the sputum became purulent or the total white cell count rose above 10,000 per c.mm., we regarded this as a rickettsial bronchitis or pneumonitis—part of the typhus syndrome, and not an indication for chemotherapy. Cyanosis and an increased respiratory rate were observed to be of grave prognostic significance. These signs did not often tally with the physical signs in the chest.

Hiccup was noted in 20% of cases, and was distressing to the medical and nursing staff as well as to the patients affected. It was a symptom of grave prognosis also. Six of our 9 fatal cases were thus affected. In some cases the symptom may be