CHAPTER 5

FEVERS OF THE ENTERIC AND RELATED GROUPS

TYPHOID AND PARATYPHOID

AT the outbreak of war in 1939 the enteric fevers were not thought to raise any serious military problem, owing to the striking success of immunisation. The classic example of the value of immunisation was, of course, the South African war in which the incidence rate was 288 per 1,000. The proof then obtained that this enormous rate could be reduced to negligible level was amply sustained in later experience. During the 1914-1918 war, Australian troops on the Western Front showed an incidence rate of only 0.38 per 1,000, thanks to the adoption of a prophylactic combined vaccine for typhoid, and paratyphoids A and B. Since then much more has been learnt about the antigenic structure of bacteria, and experience has taught the need for using a vaccine which is antigenically potent. The introduction of a "Vi" antigen from virulent strains reduced a small but not negligible death rate from enteric fevers in the British Army in India to vanishing point in the years immediately preceding 1939. During 1939 and 1940 typhoid fever was unknown in the British Expeditionary Force in France, and the same vaccine used for these troops was also used for British troops in the Middle East.

In Australia, when the Second A.I.F. was first being recruited, inoculation was made compulsory. The dosage to be used was then discussed, attention being paid to the severity of local and general reactions and to the degree of protection gained. The vaccine used was the standard "T.A.B." vaccine of the Commonwealth Serum Laboratories, containing in each cubic centimetre 1,000 million *typhosus* and 500 million each of *paratyphosus A* and *B*. The usual doses given by the subcutaneous route were 0.5 c.cm., 1.0 c.cm. and 1.0 c.cm. at weekly intervals. Severe reactions were not unusual, and on the advice of Colonel C. H. Kellaway, Director of Hygiene and Pathology to the Army, these doses were reduced to 0.25, 0.5 and 0.5 c.cm. Even these lower doses produced some sharp reactions, but not to an inconvenient degree, and it was thought that the immune response would be sufficient. Colonel Kellaway suggested the advisability of adopting a detoxicated vaccine, but the staff of the Serum Laboratories preferred the ordinary vaccine. A further question was debated at this time, that of the practicability of using a "cocktail" vaccine combining enteric fevers and tetanus. General Downes, D.G.M.S., during a recent trip overseas had received favourable reports from its use in the French Army and wished to try it in Australia. Later such combined preparations were tested on volunteers, but as the reactions were apt to be unduly severe and the immune response was not always satisfactory, the method was never adopted. It is of course evident that uncomfortable side effects of a vaccine are undesirable, but its effectiveness is vital.

Some doubts were felt in Australia that the lessened doses of "T.A.B." might be insufficient for full protection in countries where the risk was considerable. Tests were made by Colonel Kellaway on three separate groups of volunteers, and these showed that the average range of the agglutinin titre of the blood serum for typhoid O was not satisfactory. These results fell below the standard maintained by the British vaccine, prepared by the Royal Army Medical Corps College. Kellaway therefore advised the administration of an additional dose of 1.0 c.cm. to all members of the A.I.F. overseas.

During 1940 the number of cases of typhoid in the A.I.F. in Palestine and Egypt was not undue, the rate being 0.49 per 1,000. But in 1941 it had risen to 1.05, and 80 cases were reported from an average strength of 76,440 troops. It was shown that the hazard of infection was greater, especially in campaigns in countries like Greece and Syria. In Greece and Crete enteric fevers were relatively common compared with other European countries, and the circumstances of the military actions there made chlorination of water difficult. Up to the time of the evacuation only ten cases were known in the A.I.F. in Greece, but five were fatal, owing at least in part to the exhaustion of the men and the late period at which they reported sick. None of these men had been immunised since the end of 1939. A.I.F. hospitals in Palestine cared for a number of members of the Greek Air Force who had not been inoculated: all contracted virulent infections.

In Syria and the Lebanon too the risk was considerable. The mortality rate among natives was given as 10 to 15 per cent, and among newcomers to the country it was higher. In the large towns water supplies were piped and were usually satisfactory, though the hygiene in certain quarters of the same towns was usually poor and fly-borne infections readily occurred. In the villages water supplies from springs and wells were sometimes polluted, and local epidemics occurred. In Beit Meri, for example, a pleasant hill resort near Beirut, military personnel were quartered in the hotels, and their safety was endangered by a severe outbreak among the local inhabitants of a neighbouring village. But even these risks should not have been sufficient to raise the incidence rate of enteric fevers, which compared unfavourably with that of the British forces, even though the inoculation of the latter was not at the time complete. Instances also occurred of infection among nurses and other members of the staffs of hospitals where patients with typhoid were being nursed. On 12th September 1941 twenty-four patients with proven typhoid or paratyphoid fever were being treated in the 2/7th Australian General Hospital.

Colonel J. S. K. Boyd was asked to carry out mouse-protection tests using the Australian vaccine and comparing it with the British. These showed that insufficient protection was afforded by the Australian vaccine against virulent cultures: it therefore appeared that this vaccine was deficient in Vi antigen. Steps were immediately taken to have a virulent strain sent to Australia to replace that used for production of vaccine.

The strain originally obtained for the purpose had been virulent, but Boyd and Keogh considered that virulence might have been lost by mass culture on media not adapted for the maintenance of the organism for the purpose of antigen production.

One interesting experience, possibly illustrating the same point of the importance of a potent Vi antigen for immunisation, was in connection with Italian prisoners of war in Egypt. Some 700 were attacked by typhoid and paratyphoid in spite of being inoculated and re-inoculated with Italian T.A.B. vaccine. After re-inoculation of the prisoners with R.A.M.C. vaccine the epidemic ceased.

During the time which would elapse before a fully potent vaccine became available from Australia, arrangements were made to give members of the A.I.F. in the Middle East a refresher inoculation of 0.5 c.cm. of the British vaccine. Adequate precautions were advised to ensure maintenance of full antigenic potency of the T.A.B. vaccine for future use. This experience showed the risk of exposure to virulent strains of the enteric group without full immunisation.

In 1942 from an average strength of 41,594, 21 cases of enteric fevers occurred, a case incidence of 0.50—half the rate of the previous year.

The diagnosis of this group of fevers was the subject of a special instruction, stress being laid on the importance of early blood cultures. Tests for rises in agglutinin titres of the serum were of course apt to be misleading in inoculated subjects, in whom they are of little discriminative value in diagnosis. In this work the value of pathological services were great, and in areas like Syria, where an occupying force faced considerable hazard of infection, the presence of a mobile bacteriological laboratory was most helpful. In such areas, where there were no general hospitals, considerable strain was thrown on holding medical units. In the 2/3rd C.C.S. in Beirut, for instance, thirty-three patients were treated for enteric fevers between August 1941 and January 1942, and at one time there were sixteen in the wards. These patients came from sewered and unsewered areas in equal numbers. Four were infected with paratyphoid of various types, and the remainder with typhoid. Three patients died. Considerable benefit was found to occur from the use of convalescents' blood and serum, up to 300 c.cm. serum or two pints of blood.

Before passing on to consider infections by members of the enteric groups of organisms other than typhoid, it is instructive to compare the impact of typhoid fever as a concentrated epidemic attacking an unprotected civil community.

In 1943 an extensive civilian epidemic of typhoid fever occurred at Moorabbin, a semi-urban, semi-rural area near Melbourne. It began with a few cases only, seven being reported in ten days, and two days later with a striking explosion of activity the epidemic began, sixty-nine patients being admitted to hospital in one day. Dr C. R. Merrillees of the Department of Public Health in Victoria investigated the outbreak and soon traced its source to milk from one dairy. It was significant that no cases were traced from a milk-bar in the neighbourhood; the milk came from

another source of supply. The wife of the occupier of the suspected farm was proved to be a typhoid carrier. The prompt closing of this dairy stopped further spread of the disease, but between March and the end of July 1943, four hundred and thirty-three persons were infected with typhoid fever, twenty-three died and thirteen remained carriers. The affected area had a population of 4,500 out of a total of 24,000 in the whole Moorabbin district. During the same period only twenty cases of typhoid were notified from the rest of Victoria.

This epidemic shows clearly the danger of the carrier, and the greater dangers of the careless handling of foodstuffs, and contrasts sharply in its rapidity of spread and its violence with outbreaks in a population with some degree of immunity. The resources of Heidelberg Military Hospital were made available in coping with this epidemic. Numbers of civilian patients were admitted and cared for there, and members of the Australian Army Nursing Service were detailed to help in other hospitals. In the treatment of these patients intravenous injections of T.A.B. vaccine were used, and in the opinion of the medical staff good results were obtained.

Even with the threat of rising rates of enteric fevers in 1941 the numbers were never high, and fell throughout the war years as the following rates for each year show:

A.I.F.	1940	0.49	per 1,000
	1941	1.05	„ „
	1942	0.50	„ „
A.M.F. (in Australia) .	1942	0.14	„ „
A.M.F.	1943	0.11	„ „
	1944	0.03	„ „
	1945	0.10	„ „

During the war in the islands some concern was felt lest "new" strains of enteric organisms derived from the Japanese might infect our soldiers. Investigation of captured documents showed that despite frequent inoculation against typhoid and paratyphoid A, Japanese troops suffered considerably from these diseases. In Rabaul in 1943 paratyphoid A was said to be "the third most prevalent contagious disease". Presumably insufficient protection was conferred by the vaccine they used.

Few proven paratyphoid A or B infections were seen in Australian soldiers, though it is possible that these were more common than was apparent. In 1942 a number of patients in the 113th Military General Hospital at Concord suffered from febrile attacks of diarrhoea with blood and mucus. No organisms were grown but in two instances agglutination of *paratyphosus A* was demonstrated in the serum, up to a titre of 1 in 320, and in two others *paratyphosus B*. One of the former patients died, and ulceration and gangrene of the ileum were found.

In 1943 at Katherine in Northern Territory paratyphoid B appeared, being at first detected in an aboriginal and a civilian. Shortly afterwards a sudden outbreak of "gastro-enteritis" occurred in the wards of the 121st Australian General Hospital. The symptoms were fever, abdominal colic,

vomiting and diarrhoea, though the last-mentioned signs were not always present. The illness was brief, lasting only thirty-six hours. From three patients *paratyphosus B* was grown on culture; one of these men had no diarrhoea, but had an effusion in the knee joint.

SALMONELLOSIS

In New Guinea in the latter part of 1942 enteric-like fevers were being observed which were not due to typhoid or the paratyphoids A and B. Some of these patients were admitted to hospital in the first place for malaria and found to have a continued fever. It soon became evident that another type of specific infection was occurring, and bacteriological examination established that a constant strain of the *salmonella* group was responsible. The occasional presence of metastatic lesions and the recovery of the organism from the blood, the bowel and the local lesions were characteristic of infections by the *Salmonella enteritidis,* which was revealed as the cause by investigations on the mainland.

A considerable degree of toxaemia was a feature of this illness: some of the patients were at first thought to be suffering from typhus. Abdominal symptoms were usually present, chiefly discomfort, distension and looseness of the bowel. An eruption of pink macules was occasionally seen, chiefly on the trunk and lower extremities. Broncho-pneumonia was an infrequent complication: it was found in six out of a series of fifty men studied by Fenner and Jackson.

Three types of infection by *Salmonella enteritidis* were exemplified in New Guinea, a continued febrile illness resembling enteric fever, a gastro-enteritis of short duration with fairly rapid recovery, and a severe septicaemic variety in which metastatic complications were frequent. The second of these is mentioned further in the section on food poisoning and it differs *inter alia* from the continued febrile type in having a brief incubation period. Actually there is no clear distinction between the other two varieties, as metastatic inflammations occurred in many of these infections of the continued febrile type. These were often suppurative and tended to prolong the course of the disease, which was otherwise some two or three weeks. Cystitis was not uncommon, pus appearing in the urine, from which the organism could often be grown. In six of Fenner and Jackson's fifty cases epididymo-orchitis occurred, and in four periostitis or perichondritis. In a few instances subcutaneous abscesses formed, and this suppurative tendency was seen on one occasion in a small abscess at the site of puncture of a vein. The infecting organism was grown also from these lesions. Empyema occurred in two cases of this series, also cholecystitis in two cases, in one of which drainage was necessary Jaundice occurred at times. A relatively slow pulse was usually observed. No striking change was found in the blood cells, the leucocyte count being usually about 8,000 per c.mm. Brachial arteritis was observed in one patient; it resolved after causing threatening symptoms. On one occasion suppurative pericarditis was found, and was successfully treated by Cobley and Wilson with penicillin. Except for these complications the fever

usually resolved in some three weeks, but three men died. Material was available only from one autopsy: no evidence of intestinal ulceration was found. Diagnosis was best made by early blood culture, and agglutination tests were not helpful in this regard except in identifying the organism after culture. An army technical instruction (No. 56) was distributed to inform medical officers that this infection was occurring and to indicate diagnostic methods. An agglutinating serum for *Salmonella enteritidis* (*Gaertner*) was available, thus simplifying diagnosis in the field. This instruction pointed out that the organism could be cultured from the blood, the faeces and the urine, and might persist in the urine for weeks. One soldier who had a complicating cholecystitis continued to pass the organisms in the faeces.

The epidemiology of this infection had some interesting features. It appeared in New Guinea late in 1942 on the Owen Stanley Ranges and early in 1943 at Buna on the coast. A smaller outbreak occurred on the Huon Peninsula in 1944, and other sporadic infections were recognised in various places in the islands. In March 1945 for instance there was an outbreak in Bougainville. Ferris and Hertzberg also described a series of these infections on the Atherton Tableland in Queensland in which the chief presenting symptoms were abdominal pain and diarrhoea not controlled by sulphaguanidine.

In 1944 the disease was demonstrated in natives of New Guinea, in whom it occasionally proved fatal. It had not been previously recognised in New Guinea, although much investigation of febrile diseases in natives had been carried out. It is possible therefore that the infection was introduced to the island during the war years. The most probable method of spread was thought to be by human carriers: in one instance at least the evidence pointed strongly to a human vector. Infection was probably transmitted by food. Rats and mice are known to carry these infections, and this possibly cannot be disregarded. There were plenty of bush rats in New Guinea, though there is no evidence to incriminate them. In the Base Military Hospital in Melbourne in 1944 an epidemic of *Salmonella enteritidis* was recognised among laboratory mice.

Investigation of the cultures from twenty-three patients by Nancy Atkinson at Adelaide showed that the strain was the *Blegdam* variety of *Salmonella enteritidis*. A strain isolated from an outbreak at Atherton was found to be of different antigenic structure, and was thought by her to be a new variant. Six distinct types were recognised in patients on the Atherton Tableland in fifteen months. Antigenic analysis is of great epidemiological importance in these infections, and demands special interest and knowledge, and access to specific diagnostic type antisera.

The importance of this group has been emphasised during the war. Numbers of outbreaks of *Salmonella* infections were reported in civilians: as pointed out in the section on food poisoning, there has also been an increasing incidence among adults during recent years. Draper and others have pointed out the increasing frequency of clinical dysentery, and the seriousness of *Salmonella* infections in infants and young children is

recognised. In treatment no specific was found to be of value in the earlier series. Neither sulphaguanidine nor the soluble sulphonamides affected the course of the disease. The successful treatment of a metastatic pericarditis with penicillin has been mentioned above.

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