A SURVEY OF THE ENTERIC GROUP OF FEVERS

IN

THE MIDDLE EAST,

WITH SPECIAL REFERENCE TO

THE POST-WAR PERIOD,

AND TO

THE INFLUENCE OF IMMUNISATION BY T.A.B. VACCINE

BY

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A Survey of The Enteric Group of Fevers in the Middle East with Special Reference to the Post War Period, and to the Influence of Immunisation by T.A.B. Vaccine.

Introduction

In major campaigns prior to the first World War the enteric group of fevers has been a most serious cause of wastage of Army personnel, because of its high incidence, its prolonged incapacitating effects, and its relatively high case mortality. The introduction of a prophylactic vaccine by Wright and Leishman towards the end of the last century, and its subsequent development, was generally accepted as a prime factor in reducing the incidence of these fevers in the 1914-18 war to almost negligible proportions.

In the second World War the incidence still remained low in Europe, in the Middle and Far East, and in India.

Christian (1947 a) wrote "In past wars typhoid often was more deadly than bullets: now antityphoid vaccination and prompt recognition of cases have reduced typhoid to so small an incidence (as) to be of little importance"

This expresses the view of the majority of medical men at the time it was written, both in civil life and in the services.

In the post-war years a change took place in The Middle East: this group of fevers showed an increase in 1945 which continued on through 1946 and 1947.

During the period 1948-1950 the writer was Consulting Physician to the Middle East Land Forces. A number of large outbreaks occurred, mainly of typhoid and paratyphoid B fever. In some instances a very high percentage of those at risk were infected, and this in spite of the greater proportion of the patients being "protected" by the present T.A.B. vaccine.

The fact that a change in the vaccine was made late in 1943, and by 1945 most troops had been protected by this new vaccine, led to strong suspicions being cast on its efficiency, the more so as the Indian Medical Authorities decided not to adopt the new vaccine, and no increased incidence occurred among British troops there up till the time India was evacuated in 1947.

The number of troops in the Middle East has greatly fallen in the past 3 or 4 years, and there has been a slight reduction in the incidence of enteric fever since 1949, but in 1950 a unit of the Royal Air Force in the Canal Zone of Egypt was stricken by 2 major epidemics of typhoid within a few months.

A larger number of cases occurred than in any recorded outbreak of recent times. The inoculation state of the majority of these patients was up to date.

It is proposed to make comparisons with previous periods, and with certain other countries, and to try to assess the value of immunisation as practiced in the past and in more recent times. It is known that differing views are held by authorities on the subject. Any opinions expressed by the writer are the result of personal observations and conclusions drawn from a review of the facts, and do not necessarily correspond with official opinion.

The one outstanding occurrence during the period under review about which all are agreed, is the discovery of Chloromycetin, and its efficiency in quickly terminating the various salmonella infections. In consequence the case mortality has been reduced to negligible proportions, at least in an inoculated community.

The most advantageous and economical method of using this expensive antibiotic has not yet been assessed, but the large number of cases of typhoid fever treated during 1950 in the Military Hospital at Fayid has given an unrivalled opportunity of trying out various schemes of treatment. As a result one particular scheme has given great promise of overcoming the main disadvantage of this preparation, viz the tendency to produce a high percentage of relapses. The importance of this is obvious when it is stated that the cost of Chloramphenical (chloromycetin) used in this outbreak exceeded £10,000.

Historical.

The Enteric Group of Fevers - Civilian Outbreaks.

A perusal of the literature concerning enteric during the latter part of the 19th century after the time of the discovery of the causative organism by Eberth (1880) shows that a considerable number of outbreaks of appreciable size occurred in England. Some classical examples during that period, and in more recent times, have been collected and recorded by Scott (1934). Instances of these were 'The Outbreak of Enteric Fever at Blackburn' in 1881, 'The Maidstone Epidemic of Enteric Fever' in 1897, 'The Worthing Epidemic' in 1893, 'The Bolton-upon-Dearne Epidemic' of 1921. All these were water-borne. The mortality rates varied considerably, ranging from 7% in one group of cases to as high as 40% in another. An average figure for case mortality was 10-12%. The increasing mortality with age is clearly brought out.

The Outbreak of Enteric Fever at Great Marylebone in 1913, and of Paratyphoid B fever at Chorley in 1924, are examples of milk-borne infections.

The Bournemouth and Croydon Outbreaks.

In more modern times the epidemic of Typhoid fever at Bournemouth in 1936, recorded by Smith (1937), was milk borne, and involved 286 cases with 10% case mortality. Very little publicity was given in the press about this outbreak. By contrast, the water-borne epidemic at Croydon in 1937, which affected 310 persons, with a 13.8% case mortality, provided news in the daily press for a long time. A detailed account is given by Holden (1939). He records many facts which are of interest when comparison is made with the Middle East outbreaks to be described later, where the majority of the victims had been immunised with the recommended dosage of T.A.B. vaccine.

The following features are worth recording about the Croydon Outbreak.

Population at risk:- 40,000 - 45,000

Incidence rate :- 0.75%
(taking the lower figure)

Deaths:- 43 in 310 cases - 13.8%

Age Incidence:- Highest between 10 and 24 years.

Age fatality rate:- One the whole, percentage fatality rate rose with age.

Incubation period:- In 2 cases it was known to be a minimum of 15 and 21 days respectively.

Relapse rate:- 20%

Specific treatment:- Antityphoid serum by Felix from the Lister Institute was given to 69 cases (30.3 cc administered intravenously on 3 successive days).

Result:-			
	No apparent effect	31	
	Some improvement	25	
	Marked improvement	4	
	Died	9	(15%)

Recent Civil Outbreaks.

In modern times a perusal of the Public Health section of the Lancet shows that typhoid and paratyphoid outbreaks continue to occur in Britain, though of smaller magnitude. In this journal (1948 a) an account of a paratyphoid B outbreak is given. The source of infection was apparently pasteurised milk contaminated with water from which a phage type I organism was isolated.

Another outbreak of paratyphoid B fever is described at Kilcreggan (1948 b) where 29 persons picnicing were infected from unsafe water. Again at Pevensey Bay (1948 c) 19 suspected or confirmed cases of paratyphoid B infection occurred among a party of girls who had used water from a stream contaminated apparently by a woman aged 80, who was a carrier, and lived nearby.

Similar small outbreaks of paratyphoid B, and typhoid fever are described at Dewsbury and Salford respectively in 1949.

Enteric Fever in Wars of the Past.

The vital importance of the enteric fevers as the chief casualty producer in war was well illustrated in some of the campaigns of the nineteenth century.

In the Spanish-American War, out of an American force of 107,973 men there were 20,738 cases of enteric fever with 1,580 deaths. Torrens (1922).

In the Russo-Turkish War there were 24,475 cases of enteric fever with 8,900 deaths out of a Russian force of 246,000 men.

In the South African War the British Army employed 557,653 men with an average strength of 209,404. There were 59,750 cases of enteric fever with 8,227 deaths. This is equivalent to an admission rate of 285 with a death rate of 36 per 1,000 of average strength.

Enteric Fever in World War I.

The 1914-18 War shows a very different picture. Anti-typhoid vaccine was introduced early in the war, and later, in 1945 triple vaccine (T.A.B.) came into use.

The following table showing incidence and case mortality in France and Egypt is relevant:-

Table 1.

Theatre of War	Year	Number of Cases	Incidence per 1,000 of Ration Strength	Number of Deaths	Total case Mortality per cent	Ration Strength of Force
France	1915	2,351	4.0	130	5.5	588,000
	1916	2,668	2.0	30	1.12	1,274,200
	1917	1,166	0.61	33	2.8	1,884,100
	1918	334	0.12	20	4.9	2,528,400
Egypt	1916	2,950	17.35	66	2.2	179,000
	1917	505	2.82	22	4.3	179,000
	1918	401	1.87	51	12.7	213,000

The great reduction in incidence in both theatres took place after the introduction of T.A.B. vaccine and there is presumptive evidence of its effectiveness. In Egypt the improvement is not apparent till 1917.

This contention is supported by an incidence of enteric fever of 0.95 per 1,000 among inoculated British troops, and of 10.35 among uninoculated in 1915. The vaccine was prepared from typhoid organisms only at this period.

The following table shows the mortality from proved cases of typhoid on the Western front among inoculated and uninoculated:-

Table 2.

Year	Protected by Inoculation	Unprotected by Inoculation
1915	7.54%	23.2%
1916	1.58%	8.3%
1917	7.73%	12.12%
1918	13.84%	24.0%

These figures suggest that inoculation lowers the death rate.

The progressive increase in the mortality each year after 1916 is difficult to explain. It occurred in all theatres among both protected and unprotected, and is presumed due to lowered resistance resulting from a protracted war.

The mortality from the various members of the enteric group varied greatly

from year to year, but the following figures for proved British cases in France, Italy, Egypt, and Mesopotamia, give a fair average indication over a large series:-

Table 3

	Percentage case Mortality	Number of Cases
Typhoid	9.8	2,472
Paratyphoid A	2.6	2,023
Paratyphoid B	1.55	3,160

The relative frequency of typhoid and paratyphoid fever among British troops in Egypt in 1918 is seen from the following figures:-

Table 4.

	Typhoid Fever	Paratyphoid Fever		Enteric Group	
		A	B		
Number of Cases	31	66	46	285	Ration Strength 213,000
Incidence per 1,000 Ration Strength	0.14	0.30	0.21	1.20	

The high proportion classified under the heading Enteric Group detracts somewhat from the differential value of the figures.

The Enteric Group of Fevers in India

After the 1914-18 War the greater part of the British Army stationed overseas was in India. In many places enteric fever was endemic. It was therefore in this country that most of the cases of the enteric group occurred among British troops. The following figures show the drop in incidence that occurred from 1934 onwards. This coincided with a change in the T.A.B. vaccine. The Rawling's strain of typhoid bacillus previously used for the vaccine was found to have lost much of its virulence and antigenic properties, and in 1933 a new rejuvenated strain was adopted to prepare the vaccine.

British Army in India.

Comparative table of incidence of enteric group of fevers.

Admission Rates per 100,000.

Table 5.

1913	- 230	1935	- 200	1941	- 90
1919 - 1928	- 330	1936	- 150	1942	- 159
(Average over 10 years)		1937	- 80	1943	- 74
		1938	- 90	1944	- 120
1930	- 370	1939	- 110	1945	- 72
1931	- 330	1940	- 120	1946	- 100
1932	- 340				
1933	- 320				
1934	- 170				

It is further pointed out that the figures remained low till the 1939-45 war. But even the increase to 159 cases per 100,000 strength in 1942 is not great in view of the larger numbers of young unseasoned troops drafted to India to meet the menace from the enemy in the East in that year. It should be noted that 1945-46 showed no increase such as occurred in the Middle East at this period.

The T.A.B. vaccine used in India was prepared in the Research Institute Kasauli, and for many years has had a 50% content of a local strain of typhoid organisms. During the last war and subsequently troops arriving in India from home received a booster dose of this vaccine.

The History and Development of Immunisation Against The Enteric Group of Fevers in The British Army.

The first reference to the use of a vaccine against typhoid fever was recorded by Wright (1896). An officer of the Indian Medical Service was given one twentieth of a tube of dead typhoid bacilli followed in a fortnight by three twentieths of a tube, and three weeks later by one quarter of a tube. A second officer received one injection. The reaction was severe. The size of 'the tube' is not stated. In addition to Wright, Semple (1897) and Leishman (1900) collaborated in the work of preparation of a vaccine which could be used for large scale inoculation. Agar cultures killed by heat and preserved in 1% lysol were used.

In 1898 and 1899 British troops of different units in India were inoculated usually with one dose of the vaccine.

A statistical analysis of the effect on the incidence of typhoid and on the death rate is given. It shows that of 2,835 inoculated men 27 (0.95%) contracted enteric fever, and of 8,460 uninoculated 213 (2.5%) developed the infection. The death rate was 0.2% against 0.34% in the uninoculated. A calculation is made which shows that at the same rates inoculation of the whole Army in India would save over 1,000 cases of enteric and nearly 200 lives.

The vaccine was not in general use in the South African War, but a certain number of troops had been inoculated. It has been stated that the morbidity among the uninoculated was 3.2 times as great as among the inoculated. Scott (1939).

Further work was carried out on the vaccine, and Leishman (1905) adopted the 'Rawling's' strain of Bact. typhosum because of its low virulence, also because it gave a smooth suspension. The original culture was obtained from the spleen of a patient who died in The Royal Victoria Hospital at Netley in 1900. This strain was used continuously for the Army Vaccine throughout the 1914-18 war, with the addition in 1915 of Bact. paratyphosum A and B elements.

In the inter-war period there was a general feeling, especially in India, that the Army vaccine was losing its efficiency as shown by the high incidence of typhoid fever. The Rawling's strain was showing rough characteristics. Its loss of efficiency was demonstrated in mouse-protection tests. Grinnel, (1932; Perry, Findlay, and Bensted (1933)(b).

Much valuable experimental work was carried out in the methods of assessing the value of any particular strain for the preparation of a vaccine.

However, it was found possible to rejuvenate the strain by passage through mice, and the Rawling's strain continued to be used for the British

Army Vaccine (Perry et al. (1933 a), (1934), though it was discarded by the American Army.

The effectiveness of this change was reflected in the lowered incidence of typhoid fever in India from 1934 onwards.

Up till this period the most important factors in the strain of organism used to prepare the vaccine were considered to be, (1) consistency in smooth colony formation, (2) richness in "O" antigens, (3) high degree of virulence, (4) efficiency in mouse-protection tests. However, Felix (1934) and his co-workers had discovered a new antigen, which they termed Vi-antigen, this was closely associated with the virulence of the organism. A vaccine prepared from a strain of typhoid organism rich in these antigens produced a high degree of immunity in mice. So this additional factor was considered an essential in the strain of typhoid bacilli used to prepare a potent vaccine. It was later shown by Felix (1941), that paratyphoid A and B bacilli used for vaccine preparation should also be rich in O and Vi antigen.

The general principles of the method of preparation of the vaccine had remained almost unchanged since Wright and Semple's (1897) original account. Cultures of the organisms were grown on Agar at 37°C for 48 hours, washed off with saline, killed by heat at 53°C, and preserved with 0.5% phenol. The vaccine was standardised to contain 1,000 million typhoid bacilli, and 750 million each of paratyphoid A and B bacilli. The standard dose was $\frac{1}{2}$ c.c. for the first injection and 1 c.c. for the second given 10 days later.

The demonstration of the important part played by Vi-agglutinins in the process of immunisation led to further experimental work on the methods of preparation of T.A.B. vaccine; it was shown by Felix (1941) and his collaborators that killing the typhoid bacilli by heat and preserving the vaccine by phenol greatly reduced the Vi-antibody response in the serum of animals and man inoculated with the vaccine, but that alcohol killed and alcohol preserved vaccine did not suffer from this defect. In the case of rabbits inoculated intravenously alcoholised vaccine stimulated the production of typhoid Vi-antibodies, and in the case of human beings a considerable proportion showed Vi-antibody response when inoculated subcutaneously. Furthermore, the local and general reactions to alcoholised vaccine were slight. Another practical point of importance was that in cold storage conditions the alcoholised vaccine still showed Vi-antigen after at least nine months.

The outcome of this work was that towards the end of 1943 the British Army and Royal Air Force adopted T.A.B. Vaccine prepared by the alcoholised method. Owing to the fear of a severe reaction from the injection of the alcohol content of 1cc of vaccine the dose was reduced to half, i.e. 1st dose was 0.25 cc and the 2nd dose after an interval of not less than 10 days 0.5 cc. The improved efficiency of the new vaccine was expected to compensate for the reduced dose. The Royal Navy did not adopt the new vaccine, nor did the Indian Army Medical Authorities.

For a good many years the Indian T.A.B. vaccine had been prepared at the Research Institute in Kasauli. It differed from the phenolised vaccine in that although the rejuvenated Rawling's strain of typhoid organism was used in its preparation, for a number of years there had been the addition of 50% of a 'wild' strain of virulent organisms obtained in India. This wild strain was changed from time to time.

The alcoholised vaccine, though efficient in the laboratory had not yet been tried out in the field. Soldiers posted to India after the introduction of alcoholised vaccine got their initial immunisation at home, and an additional booster dose of the Indian brand of T.A.B. vaccine on arrival in that country.

Further modifications of the home vaccine took place from 1945 onwards. In November, 1945 50% of a fresh strain of S.typhi - strain 240 - was added to the Rawling's strain. In July, 1946 another fresh strain viz strain 272, replaced strain 240, and was itself replaced by strain Ty2 in January, 1947. Finally in May 1947, the Rawling's strain was omitted for the first time in almost half a century.

The new vaccine has since been prepared from 100% of S.typhi strain Ty2, with of course, the added S.paratyphoid A and B elements.

In view of the strong feeling among many workers, especially those in the Middle East, that alcoholised T.A.B. vaccine was less efficient than the previous phenolised preparation which had been completely replaced by 1945, the Army Pathological Advisory Committee decided to commence a trial of phenolised versus alcoholised vaccine. In 1949 an alcoholised vaccine of twice the strength (of organisms) called T.A.B. "A" was prepared, and another similar to the last phenolised vaccine in use, and of a strength comparable with T.A.B. "A", was also made, and called T.A.B. "B". The standard first dose was 0.2 ml, and the second dose, which was to be given after an interval of 3 weeks was 0.4 ml. The number of organisms per dose of S.typhi and S.paratyphi A and B was similar to the old phenolised vaccine. T.A.B. "A" thus had twice the number of organisms per dose the first alcoholised vaccine had contained.

In August, 1949 these vaccines came into use. T.A.B. (A) is given to all ranks with an odd personal number, and T.A.B. (B) to those with an even number. The Royal Air Force has not adopted these vaccines but continues to use the earlier alcoholised type.

It is hoped that eventually an assessment of the relative values of these new vaccines will be possible.

The Inter-War Period.

The Middle East.

Between the first and second World Wars British Troops were stationed in Egypt, The Sudan, and Palestine. Only a few remained in Iraq, and these left about 1924.

The numbers in Cyprus were insignificant. There was a small garrison at Aden. Of these countries Egypt was the principal one in which cases of typhoid and paratyphoid fevers occurred in the British Army. The troops were stationed in permanent barracks with good sanitation and the incidence of these infections was relatively low.

The following table, which includes Malta in the case of the Army, and Kenya in 1937, in the case of the R.A.F., shows the incidence of the enteric group of infections in these two services from 1933 to 1937 and gives an indication of their extent in the inter-war period.

Table 6.

	Army		R.A.F.	
	Cases	Ratio per 1,000	Cases	Ratio per 1,000
1933	13	0.8	-	-
1934	16	1.0	3	0.7
1935	16	0.9	-	-
1936	16	0.6	2	0.3
1937	23	1.2	3	0.6

(Reliable figures for 1938 and 1939 are not available)

It will be seen that the army figures are around 1 per 1,000 per annum, and the R.A.F. little more than half these figures.

The 1939 - 45 War.

The Middle East.

During the 1939-45 war the Middle East was not involved till 1940. The build-up of troops reached its peak in 1942. Figures for 1940 and 1941 are not available but the following table shows the annual incidence of the enteric group of fever for the British Army from 1942 to 1945 and also the Death rate. Comparable figures for the Royal Air Force which are available are given.

Table 7.

		British		R.A.F.	
	Cases	Ratio per 1,000	Deaths in percentage of cases	Ratio per 1,000	Deaths in percentage of cases
1942	281	0.85	13.5	-	13.4
1943	287	0.78	10.8	1.92	13
1944	110	0.55	9.1	1.88	10.6
1945	114	0.81	7.9	1.50	-

The areas involved included North Africa as far as Cyrenaica, and later Tripolitania, also Syria, Iraq, and Persia, in addition to those already mentioned previously.

Large forces were stationed in Egypt, especially in what is now known as the "Canal Zone". The majority were living under canvas in active service conditions.

The incidence of the enteric group in the Army is amazingly low, being even better than the pre-war figures. When one considers these troops were practically all living in tented accommodation, and in many places in Egypt were in relatively close contact with the native community, one feels a considerable amount of credit must be given to the efficiency of the immunity produced by T.A.B. vaccine.

When one compares the figures for the R.A.F. one finds they are about double those for the Army. It is not proposed at this stage to make any further comments on the possible causes of this difference.

Incidence by Commands.

Appendix 2 gives details of the figures. Egypt and Palestine are responsible for the greatest number of cases. It will be seen later that in the post-war years these countries are again responsible for large numbers of cases of enteric fever.

In 1945 the incidence in Palestine is more than trebled, with only a slight drop in 1946.

North Africa - Prisoners of War and Immunisation.

Boyd (1943) gives an interesting account of a comparison of British and Italian vaccines. It was known that in 1940-41 that there was a high incidence of the enteric group of fevers among Axis troops in Libya. During the first Libyan campaign an unexpectedly large number of Italian prisoners were captured, and at first the sanitary arrangements for the camps were make-shift. An outbreak of typhoid fever occurred. It was brought under control by strict application of the usual rules of hygiene, by controlling food handlers, and by T.A.B. inoculation. All prisoners in the affected camp

who could not produce evidence of satisfactory inoculation within two years were re-inoculated with two doses of 0.5 and 0.1 cc of British T.A.B. vaccine; others were given 0.5 cc only. In other camps those producing evidence of inoculation within nine months were not done.

The incidence of the enteric group remained low until May; by June there was a large outbreak of typhoid and paratyphoid infections which lasted till September.

Further inoculation of all prisoners was done in June 1941 by vaccine of Italian origin. This had little effect on the course of the outbreak. In August the affected camps were inoculated with 2 doses of British T.A.B. vaccine. After this the outbreak came to an end. (Boyd is careful to say that the termination of the outbreak was not necessarily the result of the inoculations).

Subsequently all new Axis prisoners, many from El Alamein, received British T.A.B., and little enteric developed except among those freshly captured, and within a very short period after capture.

In the Summer of 1942 a R.A.M.C. officer who was captured by the enemy was in administrative and medical charge of British and other prisoners in a camp with a strength which varied from between 24,000 and 16,000. This was at a period when the incidence of enteric might be expected to be high. He was able to report later that though the sanitation of the camp was crude and flies abounded, and there was an enormous outbreak of dysentery, yet no cases of enteric were diagnosed. The Italian medical officers admitted to this latter infection being present among their troops.

The obvious inference from the above is that the British T.A.B. possessed immunising properties far ahead of that used by the enemy.

Boyd then reports the results of mouse-protection tests using the British preparation and two captured Italian vaccines. It is shown that the British T.A.B. gave results expected from a vaccine made from virulent organisms, the Italian vaccines had such limited powers as might be expected from a vaccine made from non-virulent organisms.

This paper is a most important one, as it is the only one in modern terms which records what amounts to a field trial of different types of T.A.B. vaccine. Although precise statistical data could not be given, the general indications could lead only to the conclusion that the high incidence of the enteric fevers among the enemy was closely linked with the relative inefficiency of their vaccine.

An Outbreak of Typhoid among Immunised Personnel.

British Liberation Army.

At this point it is appropriate to pass from the Middle East to Germany to refer to the only outbreak of appreciable proportions that occurred during the war on the Continent of Europe.

It is by way of contrast with the previous section. It is the first occasion when doubts were cast on the efficiency of the British Army T.A.B. vaccine.

Jordon and Jones (1945) give an account of this epidemic of Typhoid (Phage Type "E1") which occurred among 230 men of one unit in Germany who fed from the same Mess; 34% of those at risk developed the disease. The cases occurred within a period of four weeks. In spite of careful examination of cookhouse personnel, and bacteriological testing of food milk and water, the source was not traced.

The important feature of this epidemic was that all the 79 men attacked were up to date with their T.A.B. inoculations, with one exception, and he was only a fortnight over due. On an average just over 6 months had elapsed since the last inoculation. They had all had at least 3 inoculations at yearly intervals, and the majority had had 4 or 5.

Unfortunately in this outbreak there was doubt about the type of vaccine last used. Although in only 2 cases was there positive evidence that their last dose was of this new alcoholised T.A.B. vaccine, it is highly probable that a large proportion of the unit had had this type of vaccine for their last inoculation, as the outbreak occurred in the Autumn of 1944 and the vaccine was first introduced late in 1943.

The outbreak was a severe one, but only 2 cases died.

The writers make the comment "No comparable outbreaks of typhoid have been recorded among British troops during this war, although armies have been employed in endemic zones all over the world".

It will be shown later that outbreaks of a comparable nature occurred repeatedly in the post war-years in the Middle East.

The Shallufa Outbreak of Typhoid Fever.

One large outbreak of typhoid fever occurred in a R.A.F. unit at Shallufa in the Canal Zone in June and July 1945. It has been well described by Anderson and Richards (1948).

Out of 747 persons who fed from the same mess 110 contracted the infection-

an attack rate of 14.7%. 100 of the 110 had been incoulated within a year. In about 75% the most recent inoculation was by alcoholised vaccine. 35% of the cases were severe and 29% moderately severe; 26% were mild; 9% relapsed.

On analysis there was no evidence that the severity of the infection was inversely proportional to the number of T.A.B. inoculations a patient had received. The case fatality was 10%. The last inoculation date of the cases who died was satisfactory. Here then is a change from the views held in the first world war, where it is recorded that the severity, as well as the incidence, was reduced as a result of inoculation. The cause of the outbreak was definitely traced. A number of carriers were found during the investigation, and one of these, an Egyptian dish-washer, was shown to be excreting in his urine typhoid organisms of the same phage type as those isolated from the patients, viz Craigie type Di.

The authors conclude that as the attack rate was 14.7% the protection afforded by T.A.B. vaccine cannot be of a high order.

The Post-War Period.
1946 - 1947.

The Middle East.

It has been seen that the incidence of enteric fever during the war years remained more or less constant.

Appendix 2 which is a graph of the monthly incidence among British Troops shows this clearly. Incidentally the curve indicates that the seasonal increase runs concurrently with the hot weather, and in the early months of the year reaches its lowest level. The year 1945 showed a slight increase, but in 1946 a very definite change took place; not only were there many more cases, but the incidence was extended over a greater part of the year. The situation became even worse in 1947.

The following table shows the actual numbers of admissions and the annual ratios per 1,000 strength of British troops with the Enteric Groups of Fevers.

Table 8.

	1945	1946	1947
Cases	114	256	390
Ratio per 1,000 strength	0.81	1.48	2.44
Deaths as percent of cases	7.9	8.9	7.7

It will be seen that the figures 0.81 per 1,000, which is only slightly above the average figure (0.71) for the previous 3 years, is almost doubled (1.48) in 1946, and trebled (2.44) in 1947. Incidentally the case mortality is much the same each year being about 8 to 9 per cent.

It is of interest to look at the following table which gives the proportion of typhoid, paratyphoid, and clinically diagnosed cases, and their incidence by quarters for the year 1947. (British troops). The annual figures for 1946 are given for comparison.

Table 9.

1947	Typhoid	Paratyphoid A, B, & C.	Clinical	Total cases	Quarterly ratio per 1,000 strength
1st Quarter	17	2	21	40	0.27
2nd Quarter	88	2	22	112	0.67
3rd Quarter	74	6	69	149	0.91
4th Quarter	21	59	9	89	0.59

	Typhoid	Paratyphoid A, B, & C.	Clinical	Total cases	Annual ratio per 1,000 strength
1947 Totals	200	69	121	390	2.44
1946 Totals	153	55	40	248	1.44

It will be seen that there are approximately 3 times as many cases of typhoid as there are of paratyphoid; it may be accepted that the clinical cases probably represent typhoid and paratyphoid in the same proportions.

The above table is representative of the seasonal distribution of these infections; the bulk of the cases occur during the 2nd and 3rd quarters, but outbreaks are liable to occur in the 4th quarter also; Appendix 3 shows more precisely the monthly incidence of British troops and of all troops in the Middle East. The non-British are locally enlisted Mauritians, East Africans, and Cypriots mainly. The years 1946 and 1947 are covered by the charts.

The following table indicates the distribution of the Enteric Groups of Fevers in the different theatres among British personnel in 1946. The figures are the annual ratio per 1,000 strength.

A comparison is made with the Royal Air Force.

Table 10.

	British Army	Royal Air Force	Remarks
Middle East	1.44	1.42	Immunised with alcoholised vaccine commencing end of 1933
Central Mediterranean Force.	0.28	-	
British Army of the Rhine.	0.06	-	
South East Asia Land Force.	0.25	-	
India	1.00	0.61	Phenolised vaccine are in use in India.
Forces Abroad	-	0.96	All forces overseas except BAOR alcoholised vaccine as above.

The Middle East clearly tops the list. With the exception of those in India, troops and airmen would have been immunised with alcoholised T.A.B. vaccine. In India a booster dose of phenolised Kasauli - made T.A.B. vaccine

would have been given on arrival, and each subsequent booster dose would have been with the same type of vaccine.

The next table shows the distribution of the Enteric Fevers in Middle East by Commands among British Troops. The figures are ratios per 1,000 strength with actual admissions in brackets. 1945 is shown for comparison with 1946.

Table 11.

	Command	1945	1946
	Egypt	0.55 (42)	1.66 (125)
	Cyrenaica	0.31 (1)	0.36 (1)
	Tripolitania		2.41 (9)
	Palestine	1.43 (49)	1.00 (57)
	Syria	1.00 (11)	1.48 (7)
	Cyprus		
	Sudan and Eritrea	0.43 (1)	1.40 (3)
	Malta	-	-
	Aden	-	-
X	P.A.I.C.	0.99 (10)	3.19 (10) (Iraq)
	Greece	-	1.28 (37)
	Total M.E.	0.81 (114)	1.44 (249)

X Persia and Iraq.

Taking these Commands with more than 10 cases it will be seen that Egypt Palestine and Greece show the highest incidence.

Mortality: 13.72% of the cases of typhoid fever in the British Army died, and 2.5% of these diagnosed clinical enteric; there were no deaths from paratyphoid fever.

The year 1947 beat all records for its high incidence of enteric fever. There was a total of 562 cases among all categories of troops, as we have seen, 390 of these were British. The following table shows the distribution of admissions by diseases in the Chief Commands affected, and the types of infection involved:-

Table 12

	Total Middle East	Egypt	Palestine	Cyprus	All Other Commands
Typhoid	302	168	68	38	28
Paratyphoid	79	14	61	2	2
A, B and C Clinical Enteric	81	92	17	65	7
Total	562	274	146	105	37

Brig. C. G. Parsons, Consulting Physician in the Middle East during 1947, reported over 50 outbreaks in the 18 month period commencing in the middle of 1946. These outbreaks accounted for a considerable proportion of the cases, but numerous sporadic cases also occurred. A total of 650 cases of enteric fever occurred in the Army during that period in this theatre.

Many of the outbreaks were small.

Mortality: The overall mortality was just under 10%, but in certain individual epidemics it was very high indeed. In one small outbreak of typhoid fever among British troops at Port Said 6 out of 9 cases died. In another in Palestine 5 out of 31 died. In this particular outbreak there were 60% of relapses after apparent recovery.

Typhoid fever was responsible for most of the deaths. The percentage mortality from the cases among British troops (30 cases) in 1947 was 14.50% clinical enteric accounted only for 0.83% of deaths, (1 case), and no patient with paratyphoid fever died.

During 1947 the death rate in the Middle East from typhoid fever was exceeded only by that from injuries. In the majority of cases the inoculation history was satisfactory.

Influence of T.A.B. Vaccine.

Parsons concluded that T.A.B. vaccine as then used (alcoholised), though it afforded some degree of protection, in no way modified the course of the disease or the mortality rate. Here again we find an authoritative opinion contrary to the views expressed on T.A.B. in the 1914-18 war, but in keeping with the views of Anderson and Richards after the Shallufa outbreak in 1945.

Appendix 5 refers to British units only. It shows how a considerable proportion of the cases of enteric are accounted for by outbreaks of various sizes, the stations where the outbreaks occurred, and the type of organism responsible, also phage type where this was known.

Comparison of Enteric Fever in Inoculated and Uninoculated Persons.

In Cyprus an opportunity occurred for a rough comparison of the severity of enteric infection in the inoculated troops, and the uninoculated illegal Jewish immigrants. Many thousands of the latter were in camps on the island, and were involved in outbreaks at the same time as British troops. There was no apparent difference in the severity of the infection, the course of the disease, or the mortality rate in the immunised troops. In all fairness however, it must be pointed out that the Jewish immigrants, most of whom came from central Europe, were of all ages, and must have been pretty well 'salted' with enteric infections in the past, and had probably acquired some degree of natural immunity. Most of the troops were in their early twenties - an age at which

susceptibility to the infection is at its highest.

A trial of the Intensive Penicillin - Sulphathiazole therapy.

The urgent need for a specific treatment of typhoid had led to various trials of a combination of penicillin and sulphathiazole. The synergic action of this combination against typhoid organisms, demonstrated by Bigger (1946), gave promise of success. McSweeney (1946) gave a most optimistic account of the results of a very intensive course - 10 mega units given each day in two-hourly intramuscular doses of 200,000 units together with 1 gm of sulphathiazole three-hourly by mouth over a period of 4 days. After a two day interval the course was repeated. In addition each course was preceded by 1 gm sulphathiazole intravenously.

Parsons issued a directive to medical specialists in the Middle East on the subject, and a number of groups of cases of typhoid fever in different hospitals were treated with a similar combination of penicillin and sulphathiazole, although the precise method of McSweeney was not used in most instances. This can hardly be the cause of the failures, for in some cases very large doses of penicillin were given. It had already been noted in Middle East hospitals that minor trauma to ill typhoid cases had an adverse effect, producing a drop in blood pressure. There is no doubt that the frequent injections must have had a very damaging influence on the patients. There was little enthusiasm for the treatment among Medical officers and nursing staffs, and some very severe criticisms were made by them. Parsons (1948) published the results later. His comments in an official report were made in stronger terms than those published. He has described the treatment as cruel, and so little effective as to be valueless.

Anti-Typhoid Serum.

About this time the Army Medical Authorities at home decided that a trial of Felix's Typhoid Anti -O and -Vi Serum prepared by The Lister Institute should be made. The development of this serum followed the original experiments on mice, Felix and Pitt (1934). It was greatly improved later, and tried out in various outbreaks at home and overseas with, on the whole, favourable reports. However, reference to the cases treated in the Croydon outbreak already mentioned in this survey show no reason for optimism. (Holden 1939). It took some months to prepare the serum, and it was not ready for trial till 1948, as will be seen later.

The Period 1948 - 1950.

Early in 1948 the writer was sent as Consulting Physician to the Middle East to relieve Brig. C. G. Parsons. The most important preventable disease was the enteric group. The authorities were much concerned at the high incidence.

The first quarter of the year produced few cases. The incidence was lower than in any corresponding quarter since 1945, being only 14 admissions among all troops - British and non-British - in the Middle East.

The Acre Outbreak.

This quiet spell was not to last however, and during the second quarter of the year there was one of the most remarkable outbreaks of the enteric group of fevers of recent times in military history. The following account is largely based on the report of the epidemic by Captain A. Batty Shaw and Captain H. A. F. Mackay.

In the spring of 1948 the Palestine episode was coming to a close, and preparations were afoot to evacuate all troops from that country via the Port of Haifa. It was necessary for tactical reasons to maintain a Company of The Middlesex Regiment, 107 strong, at a hutted camp in Acre. A detachment of 64 Palestine Police were stationed in quarters about 800 yards distant. The water supply to these camps was from the same source.

There were active hostilities between the Jews and the Arabs at this period, and the town of Acre was full of Arab refugees; in consequence public services were greatly disorganised. It transpired later that enteric fever existed among the civil population, but to what extent was unknown.

On 26th April a soldier was admitted to the military hospital at Haifa with a condition clinically indistinguishable from a severe attack of blackwater fever. The illness had started 3 days previously. The patient was febrile and passed dark urine, which showed the bands of oxyhaemoglobin and methaemoglobin when examined by a simple spectroscope. There was also evidence of haemolysis in the blood. Not unnaturally the physician attending this patient at first thought he was suffering from blackwater fever. However he took blood for culture, and soon got the true diagnosis - typhoid fever. A second very similar case was admitted on the following day, he also was proved to be suffering from typhoid. This method of onset is distinctly rare. The writer who has seen a large number of cases of enteric group in various tropical countries had not encountered it previously. It is mentioned in few standard text books, but the older editions of Osler's Principles and Practice of Medicine, and its latest edition by Christian (1947 b) refer to it.

These two cases were followed up by Batty Shaw (1951) who attended them, and it has since transpired that one of them was in fact suffering from a familial type of haemolytic anaemia, apparently activated by the attack of typhoid - a very remarkable coincidence in view of the second case of toxic haemolytic anaemia occurring at the same time.

As a result of investigation of other patients recently admitted to the hospital from the same unit further cases of typhoid were picked up. Cultural investigations of the new admissions from this unit showed that in addition to typhoid there were also cases of paratyphoid B infection. What was even more astounding was the detection of both S.typhi and S.paratyphi B in cultures from the blood of the same patient in a number of instances. These cultures were originally carried out in the laboratory at the hospital at Haifa. In every case they were confirmed at the Central Pathology Laboratory at Fayid in the Canal Zone of Egypt.

In addition to the cases from the Middlesex Regiment patients admitted from the Palestine Police detachment in an adjacent camp were found to be suffering from typhoid fever.

Finally by 14th May a total of 65 British soldiers and 11 members of the Palestine Police had been admitted to Haifa Military Hospital from Acre, 44 suffering from typhoid, 3 from paratyphoid B infection, 27 from a combination of both, and 2 were diagnosed clinically.

64 of the 65 soldiers belonged to the Company at Acre, one belonged to another company. He had been on escort duty in the vicinity on 13th April and had obtained some food from the Acre company. He was admitted to hospital about a fortnight later.

No such outbreak has ever occurred previously in the British army so far as is known, though one instance of mixed infection with typhoid and paratyphoid organisms is reported by Dawson and Whittington (1916). During life paratyphoid A organisms were isolated from the blood, and after death typhoid bacilli were cultured from many organs.

The very high attack rate among Army personnel is unprecedented, being approximately 61% of British troops at risk. Among the Palestine Police the attack rate was only 17%.

Source of Infection.

Although the source of the infection was not proved bacteriologically, circumstantial evidence points to the water supply. The Company of The Middlesex Regiment involved, and the detachment of the Palestine Police, lived in separate camps, but had a common water supply. Without warning and without notification to the consumers, the authorities ceased to chlorinate the water when they ran out of cylinders of chlorine for the water purification plant. This occurred about the 7th of March.

The source of the water was in the hills many miles distant; from there it was conveyed to Acre by an ancient Roman aquaduct, which was exposed over

the greater part of its length. The aquaduct had also been damaged in places by Jews and Arabs during the previous fighting.

It was thought that all the primary cases had been infected between the 9th and the 13th of April. When the Army Hygiene authorities investigated the water soon after the onset of the outbreak no pathogens were isolated, but there was evidence of heavy faecal contamination - a count of 180 B.coli per ml was obtained. Presumably the source of infection had ceased to exist.

The very high infection rate is most extraordinary in a water-borne outbreak; the only explanation of this is that an exceptionally heavy contamination must have existed for a short time - possibly deliberate gross contamination with faeces. The double infection could thus be explained.

Immediate steps were taken to ensure that the water was rendered safe for use, but the damage had been done.

Inoculation State of Exposed Personnel.

The type of vaccine in use at home since the end of 1943, and in the Middle East since 1945, was the alcohol killed alcohol preserved T.A.B. vaccine. The initial dose was 0.25 ml, and the 2nd dose at 10 to 14 days interval was 0.5 ml. Subsequent booster dosage was 0.25 ml annually. In addition troops on arrival in Middle East had an extra booster dose.

Of 10 soldiers who had had at one period the type of T.A.B. vaccine in use prior to the alcoholised i.e. the phenolised, 5 were affected.

The inoculation state of the Palestine Police was of a different standard. They were inoculated every two years. Many had had previous immunisation in the Army with phenolised vaccine. The latest vaccine used for their inoculations was uncertain, but was probably alcoholised.

The following table shows the proportion of the troops affected according to their inoculation state. The figures are based on documentary evidence, and it can be taken that through probable omission of entries in their documents the numbers protected may be somewhat greater than shown:-

Table 13.

At Risk	Protection State	Attacked		Not attacked
107	Protected 96	57	60.8%	39
	Less protected 11	8		

The corresponding figures for the Palestine Police are as follows, but the accuracy of the protection state figures is less certain.

Table 14.

At Risk	Protection State	Attacked		Not attacked
64	Protected 41	6		35
	Partially protected 21	5	17.2%	16
	Not protected 2	-		

Relationship of Severity to Inoculation State.

All degrees of severity were met with, from the patient who complained of nothing more than a headache, and whose temperature was little over 99°F and lasting only a day or two, to the gravely ill case in the typhoid state.

Undoubtedly a number of the milder cases would have been missed, but for the fact that every man in the affected units who complained of the slightest ailment had his blood cultured for the Salmonella group.

27 of the 76 patients were classified as severe, including 12 dangerously ill, 25 were mild, and the rest were of moderate severity.

The following table gives a good indication of the relationship between the severity of the illness and the inoculation state:-

Table 15.

2nd Middlesex Regiment.

	Severe	Moderate	Mild	Total
Fully inoculated	22	11	22	55
Partially inoculated (All degrees between 1 inoculation and full inoculation)	2	1	1	4
1 inoculation only and that within the last year	0	2	2	4
	24	24	24	63

Table 16.

Palestine Police.

	Severe	Moderate	Mild	Total
Fully inoculated (Inoculated in one of the Services previously and in P.P. within 2 years)	1	1	4	6
Partially inoculated (Inoculations at 2 yearly intervals only)	2	2	1	5
	3	3	5	11

As regards the Army personnel, there is little to indicate that inoculation could have afforded appreciable protection; the very fact that over half of those whose T.A.B. inoculation state was up to date acquired the disease is evidence of that. Admittedly the proportion of those attacked among the unprotected - 8 out of 11 - is higher than with the protected - 57 out of 96 - but with the small numbers concerned this is of little statistical significance.

In water-borne outbreaks the attack rate among those at risk is low as a rule, because of the dilution of the organisms. There is no record of any previous outbreak with an attack rate approaching the present one.

It is improbable that in any water-borne outbreak the individual could get an overwhelming dose of infecting organisms; admittedly the immunity produced by T.A.B. vaccine is not claimed by immunologists to be able to withstand enormous doses of the infecting organisms.

When we come to the Palestine Police the lower morbidity rate - 17.2% of those at risk can be explained by two factors.

1. The average length of service overseas for the whole detachment was $5\frac{1}{2}$ years, being 3 years for those affected, and 5 years for those unaffected. In the case of the Company of The Middlesex Regiment the corresponding figures were 11 months, 8 months, and 17 months.

2. The average age of the army personnel was $20\frac{1}{2}$ years, that of the Palestine Police 26 years, of those army personnel affected 20 years, and of the affected Police $24\frac{1}{2}$ years. These figures emphasise the well known facts that liability to infection diminishes with increasing age, and with length of service overseas in an endemic area.

It is therefore impossible to assess the influence of T.A.B. inoculation in the case of the Palestine Police. A perusal of the tables showing the relationship of the state of inoculation to the severity of the illness does

not give much help in indicating that the previous inoculation lessened the degree of illness, unless one considers that the very mild cases might have been worse but for the T.A.B. immunisation. It is possible, however, that the mortality rate was influenced as only 3 deaths occurred, these were all soldiers. A 4% mortality is low considering that 27 cases were classified as severe, and 12 of these were on the dangerously ill list.

Transfer of Patients during the Outbreak.

Owing to the evacuation of the troops from Palestine in June all the patients had to be transferred to the Canal Zone of Egypt. This was done by hospital ship to Suez, thence by ambulance to El Ballah, a road journey of approximately 28 miles. The patients stood the journey remarkably well, and in no instance did any apparent deterioration take place as a result, in spite of the fact that many were seriously ill at the time. All the cases were seen by the writer the day after their arrival in Egypt.

Clinical features and Complications.

In Appendix 6 there is a comparative summary of the principal features in the various outbreaks during the period under review. The frequency of the various symptoms, signs, and complications will be seen there. The high proportion of patients presenting with headaches, especially frontal, dizziness, cough, backache, abdominal discomfort, and anorexia is noteworthy. The rarity of haemoglobinuria seen in 2 cases on admission has already been commented on. Only a fifth of the patients had diarrhoea as an early symptom, and this was of a mild degree.

As regards the early signs, a furred tongue with clean edges was common, and enlargement of the spleen was detected in 55%. Rose spots were seen in 60% of the cases, in some the distinctive characteristics of the paratyphoid B rash could be made out, and in one case of double infection the two type of exanthem could be seen in different crops. The length and character of the pyrexia showed great variation. Some of the milder cases with a pyrexia of less than 100°F for only a day or two would never have been detected had they not been associated with an epidemic. Double infection with typhoid and paratyphoid did not necessarily make the patient more ill.

Among the complications deserving comment were haemorrhage from the bowel in 3 cases, one being fatal, splenic infarcts in 3 cases, and femoral thrombosis in 3. Among 18 cases with epistaxis one required a blood transfusion.

Among the various central nervous system complications were mild sensory peripheral neuritis in 6 cases, tender toes in 9, tremor in 13, and increased reflexes in 13. Most of the ill patients had evidence of toxic effects on the higher centres.

Deaths. 1 from bowel haemorrhage
2 from toxaemia

All were up to date with their inoculations.

Diagnosis.

In the Middle East previous experience had shown the importance of blood culture as opposed to serological tests in the diagnosis of the enteric group of fevers. Stool and urine cultures were of value in a limited number of cases.

In the Acre outbreak, as a result of the skill and persistence of the pathologist at Haifa, Captain H.A.F. Mackay, bacteriological proof of the infection was obtained in 74 of the 76 cases - a record which the writer has not known to have been beaten. 73 were by blood cultures.

The following table gives the distribution of the infections:-

Table 17.

	2nd Middlesex	Palestine Police	Total
Typhoid Fever (Phage type T)	36	8	44
Paratyphoid B Fever	3	0	3
Typhoid and Paratyphoid	25	2	27
Clinical Enteric	1	1	2
	65	11	76

On investigating this outbreak bacteriologically the pathologist was able to show that the chances of isolating the organisms from the blood were greatest during the second week, and that a high percentage of positive cultures could be obtained in the third week, especially in very severe cases. It is interesting to observe that positive cultures were sometimes obtained from patients with temperatures as low as 99°

The Aerosporin Trial.

The news of the occurence of an outbreak of enteric fever at Haifa quickly leaked out, and as a result of a B.B.C. news bulletin, a leading member of a well known Research team offered for trial a supply of the new antibiotic "Aerosporin", a polymyxin. This was accepted and arrived by air at the Medical Directorate Middle East on the same day as a large consignment of Antityphoid "O" and "Vi" Serum which had been prepared for a controlled therapeutic test.

The writer decided in favour of a trial of the new antibiotic for the following reasons:-

1. A controlled trial of both was not a practical proposition.
2. The previous accounts of the results of Felix's Serum were not very impressive.
3. The Serum has to be given intravenously and it is liable to produce an unpleasant reaction at times. Painful procedures and severe reactions have a

very adverse effect on ill typhoid patients, and unless some very definite therapeutic gain is anticipated from the treatment it is not worth giving.

4. The accounts in the literature of Aerosporin were encouraging.

In vitro, aerosporin was shown by Brownlee and Bushby (1948) to be bactericidal to certain gram negative bacilli including Salmonella. It had been tried out in whooping cough in children with a certain degree of success by Swift (1948). He gave 10 children aged 1 month to $2\frac{1}{2}$ years intramuscular aerosporin in a dosage of 0.4 mgm four or three hourly for 5 days with beneficial results and only mild toxic effects.

The earlier preparations were found to have a toxic effect especially on the kidneys - a drawback in many of the antibiotics of bacterial origin. However this disadvantage was said to have been removed in the preparation of aerosporin supplied for trial.

The suggested dosage was 0.2 mgm per kilo body-weight, given intramuscularly every 4 hours for 5 days. If this was ineffective the dose was to be doubled. The writer had high hopes for this antibiotic, and a scheme for a controlled trial was sent off by air to Haifa with a good supply of aerosporin.

The alternate case method of control was not used, but cases as nearly comparable as possible were paired off, one to be given the specific treatment, the other not. The more severely ill cases were chosen to begin with. Owing to the outbreak being well under way by the time the trial was started it was not possible to pick out early cases. Altogether 13 cases were given aerosporin, some in Haifa, and others after transfer to El Ballah.

It was possible to select only 10 comparable controls.

Immediate Effects.

At first a series of seven patients were treated. The injections were painful and resented by some patients. There was an increase in vomiting and anorexia, and the patients generally became more ill than their controls. Headache became more severe, and the pyrexia was not lessened. Four became delirious, but none of the controls did so. Slight swelling of superficial lymph glands was noted.

Late effects.

There was definite improvement after the treatment was stopped and the pyrexia fell to a lower level in five cases.

A further six patients were treated with 3 controls only. In three of these cases there was some clinical improvement, and the temperature came down five days after the aerosporin was stopped. One very ill case improved to a greater extent than could have been anticipated.

Of the total of thirteen cases the ultimate assessment was that eight showed no improvement. One patient who was given 26 mgm four-hourly, (double

the original recommended dosage) became so ill with severe circulatory collapse and diarrhoea that the drug had to be stopped after four doses. Eleven of the thirteen showed some evidence of renal damage with the appearance of albumen and casts between the 3rd and 5th day; but in only one instance was the damage considered to be severe. In one case where albuminuria was present before starting aerosporin it became more marked later.

Effects of aerosporin on a fit person.

The pathologist at Haifa gave himself one injection of 13 mgm of aerosporin. Within one hour he had a rigor with vomiting, faintness, sweating, and pallor. Some hours later his systolic blood pressure had dropped to 90 mm!

Deaths.

Two of the thirteen treated cases died, and one of the controls.

Effect of Aerosporin on Blood Culture.

Blood cultures for S.typhi taken on the 2nd, 4th and 6th days after treatment commenced were positive in most instances.

Cases treated at other hospitals.

A few more cases of typhoid fever were treated with aerosporin at the military hospitals at Tel El Kebir and Fayid with the same unsatisfactory result.

Assessment of Aerosporin.

It was difficult to assess the true value of aerosporin with such a small number of cases, but unless a non-toxic preparation became available it was thought that further trials were not worth while, as a much larger dosage would obviously be required to control the infection.

The total admissions for the enteric group of fevers during the 2nd quarter was 94, representing a ratio per 1,000 of 0.57. The high figure was largely due to the Acre outbreak.

During the 3rd quarter the admission rate was still high being 0.67 per 1,000 owing to many scattered sporadic cases, chiefly in the Canal Zone of Egypt. During the 4th quarter the ratio dropped to 0.20 per 1,000.

The Shubra Outbreak of Paratyphoid B Fever.

In June cases of paratyphoid B fever began to be admitted to the Military hospital at Fayid from 109 M.U. of the Royal Air Force stationed at Shubra in the Canal Zone. There were a few admissions from 205 Group also.

This outbreak lasted till August. It was of a mild character, and there was difficulty in assessing the exact numbers of cases involved, as at this time of year many undiagnosed, or undiagnosable, pyrexias are admitted to hospital, and positive blood or other cultures are the only certain means of diagnosing paratyphoid fever. This is especially the case when a rash is absent.

The final figures were 52 bacteriologically proven cases, 49 being R.A.F. and 3 army attached personnel. A further 87 cases were investigated for paratyphoid by repeated blood urine and faeces cultures.

Two cases of typhoid fever were admitted from the same unit at this time.

The numbers at risk in the whole unit were about 2,500. One airmen's mess was suspected as being the source of the infection, and the strength at risk here was about 750. The source was thought to be active between the 27th June and the 13th August.

Extensive investigations were carried out to try to track down the origin of the infection, and 3 urinary carriers were found among locally employed cookhouse workers. Unfortunately the organisms isolated in no case tallied with the phage type of the S.paratyphi B causing the outbreak. This was phage type 3ai. The carriers were excreting S.typhi phage type G, S.typhi untypable, and S.paratyphi A respectively. One Y.M.C.A. worker in the unit was found to be a carrier of S.paratyphi B type 3ai, but he was considered to have had no connection with the cause of the epidemic.

Inoculation State.

Most of the cases had had alcoholised T.A.B. vaccine within six months, and all within a year.

Comments on Clinical Features.

In most cases the syptoms were mild and the pyrexia was not high. Its duration varied from 1 to 29 days. There were no deaths, but 5 cases relapsed, only one being proved bacteriologically. Slight headache anorexia and coated tongue were the most frequent presenting features. Malaise and constipation were the next most frequent early complaints. Abdominal pain, nausea, vomiting, and diarrhoea were much less common. Sore throat, backache, and stiff neck were complained of by a few. Only one case showed a rash, one had a palpable spleen, and one had epistaxis.

Diagnosis.

It is clear that in such an outbreak, bacteriological proof is essential for diagnosis.

Of 42 positive blood cultures 36 were obtained within the first 8 days of the illness.

The other 10 cases were proved by culturing pooled urine in faeces, a positive growth being obtained between the 11th and 22nd day of illness.

Sporadic Cases of Typhoid Fever in the Canal Zone.

By no means all the admissions for the enteric group are the result of epidemics, and a short account is given of a group of 29 cases of typhoid fever in Fayid Military Hospital during the 3rd and 4th quarters of 1948.

Of the 29 only 2 were not sporadic; they had been infected during an outbreak of 15 cases at the Military Hospital, Tel El Kebir.

Severity.

There was considerable variation in the severity of the illness: 16 were severe, and of these 6 were very ill. 13 were moderately ill or mild cases.

Deaths. There were 2 deaths, one from perforation, and one from bowel haemorrhage.

Relapses. Only 2 cases relapsed.

Comments on Clinical Features.

The commonest early features were headache, anorexia, and furred tongue, next came constipation, abdominal pain, diarrhoea, palpable spleen, and bronchitic signs. Nausea, vomiting, and rigors were less common. Only a few complained of stiff neck and joint pains. One had epistaxis, and one a sore throat.

Seven developed rose spots which characteristically appeared in crops over the abdomen and chest.

The duration of the fever varied from 10 to 86 days.

Complications. 5 cases showed tachycardia, 4 developed broncho-pneumonia; there was femoral thrombosis in 1 case, periostitis in 1 case, and a number showed thining of hair.

Diagnosis. This was by blood culture in 26 cases, 6 being positive by the 8th day. One was positive as late as the 25th day of illness. Two were diagnosed by faeces culture. One was diagnosed clinically.

Phage types. The following S.typhi phage types were identified:

N.(4), G.(4), A.(2), C.(2), O.(1).

Inoculation State.

22 patients had been inoculated within a year; most of these had had a booster dose on arrival, or within six months of arrival, in Middle East. Of these, 2 were severely ill, and one died. Three had not been inoculated within a year, one of these had refused inoculations, 2 of the 3 were very ill. One case whose inoculation history was unknown died.

It is difficult to make any assessment of the influence of T.A.B. in this group. Rather less than 80% were fully protected. This figure is a lower one than usual.

Other Outbreaks.

A number of lesser outbreaks of typhoid and paratyphoid fever occurred during 1948. Most of these were in the Canal Zone of Egypt. One is worth recording.

Outbreak of Typhoid Fever at the Military Hospital Tel El Kebir.

27 cases of typhoid fever originated among patients in the hospital at Tel El Kebir. Some developed the disease after they had left for another station. One British officer and 14 British other ranks were affected. The others were non-British. The source was not traced.

Inoculation State.

One had refused T.A.B. since April, 1946.
One had had only one dose in April, 1946.
One was a month overdue.
Three, though within one year of last inoculation, had had no booster dose on arrival in Middle East.

Thus 2 were quite unprotected.
The severity of the disease was mild or moderate. There were no relapses and no deaths.

The clinical features.

Apart from the general slightness of the symptoms in most cases, there was little of note worth recording. Rose spots were uncommon.

Complications. There were no perforations and no marked bowel haemorrhages. There were however 2 instances of lower limb thrombophlebitis, and one small pulmonary embolism.

The only 2 cases with delirium were patients on whom aerosporin was tried; One had visual hallucination of 'little men'.

It is of interest to mention that one case of acute cholecystitis was operated on at this time. There were pigment calculi in the gall bladder, and

the bile yielded a pure culture of S.typhi phage type N. This case was not a food-handler.

Diagnosis.

There were 19 positive blood cultures of S.typhi phage type N, and the case just mentioned with a positive bile culture.

In addition the Widal reaction showed a very appreciable rise in T.O. titre in 7 cases over a period of 4 weeks, e.g. from 1/50 to 1/5000.

Paratyphoid Fever among Army Personnel.

Small outbreaks and sporadic cases of paratyphoid A and B fever have occurred among army personnel in addition to the R.A.F. Shubra epidemic. Paratyphoid B was slightly more prevalent. Paratyphoid C is rare among service personnel. In 1948 only 2 cases were reported.

The following table shows the Quarterly Incidence of The Enteric Group of Fevers among all classes of Army Personnel during 1948.

Table 18.

	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Total
Admissions	14	94	84	22	214
Ratio per 1,000 of strength	0.06	0.57	0.67	0.2	1.50
Deaths	-	3	1	1	5

The following table gives the Quarterly admission by diseases.

Table 19.

	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Total
Typhoid Fever	6	62	49	10	127
Paratyphoid A) B) C)	4	25	27	9	65
Clinical Enteric	4	7	8	3	22

In comparison with previous years the relative incidence of paratyphoid to typhoid fever is slightly higher; the figures do not include the R.A.F. personnel in the Shubra outbreak of paratyphoid B which would further raise the ratio.

The higher incidence in the 2nd and 3rd quarters is again marked. The much lower proportion of patients diagnosed clinical enteric gives great credit to all concerned in the investigation of cases of this group of infections.

The mortality is also exceptionally low. If we exclude the paratyphoids among whom there was no fatal case, and add to the typhoids the proportionate number from the clinical enteric group, say one third or 7 cases, we are left with 5 deaths in 134 cases of typhoid and presumed typhoid, giving a mortality rate of less than 4 per cent.

It is reasonable to attribute some credit to T.A.B. immunisation as we are not concerned with one outbreak only, but with several outbreaks, and a considerable number of scattered sporadic cases.

1949.

This was indeed a notable year in the story of enteric fever in the Middle East. For the first time the new antibiotic chloromycetin became available to Britain.

In 1949 also there was an extensive epidemic of typhoid fever in East Africa, involving a large number of East African as well as British troops. This was the first of its kind, certainly within the last 30 years.

During the first quarter there were only 6 cases of enteric fever in the Middle East. The usual increase in incidence of the infection commenced in The Canal Zone in May, and a number of small outbreaks of typhoid and paratyphoid B fever occurred, as well as sporadic cases. Out of the small Officers' Mess of an R.A.S.C. Car Company four were admitted with typhoid, and a fifth with a short pyrexia of unproved origin. The source of the infection was not discovered.

The Royal Air Force Units in the same neighbourhood were also getting a number of cases. Their hospital at Fayid is a small one, and most of the infectious cases are eventually treated at the Military Hospital.

In 1948 a personal note from Brig. A. Bennett, Consulting Physician to the Far East Land Forces, had brought advance information of the work of Woodward Smadel and others (1948) in applying chloromycetin, which originally had been isolated by Erhlich (1947), to the treatment of Scrub Typhus, and of treating a case successfully which eventually proved to be typhoid fever.

The writer sent a request for a supply of this antibiotic, but it was not available to Britain till 1949, after a process of synthesis had been discovered by the manufacturers. This preparation, now named chloramphenicol, was received in the Middle East in June. Owing to its cost, and to the limited amount available, it was decided to restrict its use at first to severely ill cases of typhoid fever only. The following is an extract from the writer's first report on chloromycetin issued during the third quarter of 1949:-

> "Many of the cases of typhoid fever were extremely ill, and an excellent opportunity presented itself to try the efficiency of chloromycetin. One case was treated at El Ballah, one at Tel El Kebir, and the rest at Fayid. The trial is still in progress but sufficient information has been obtained to confirm the efficiency of this antibiotic, reported mainly in American literature. The preparation was used only in very ill patients, irrespective of the stage of the disease. The dosage employed was 50 mgm/kilo body weight by mouth initially, followed by 0.25 gm two hourly till the temperature reached normal; then the same dose was continued 4 hourly till the temperature had been normal 5 days.

In some cases, especially those treated early in the disease, the headache was relieved and the patient felt better within a matter of hours. The temperature reached normal within 3 to 5 days approximately. There was evidence of marked lessening of the toxaemia during this period, and in the cases treated early the patient felt quite well by the time he was apyrexial. In those profoundly toxic with dry tongue, delirium, and incontinence of, the change was more gradual, and although their temperature fell to normal or slightly above, the effects of the toxaemia on their cardiovascular and nervous systems took many days to pass off. Slight mental confusion and incontinence, persisted, especially at night, and slowly lessened over a period of one to two weeks. There was a tendency for the heart rate to be increased during this time in some instances. It must also be remembered that the intestinal ulcers take time to heal, and the risk of haemorrhage and perforation exists till this process is complete.

The above brief account does not convey adequately to the reader the truly dramatic change seen in the patients' condition by those handling the cases. To all of us who have had a long experience of ill typhoid patients it seems almost miraculous that a substance has been found which can be given by mouth and literally snatch patients from the jaws of death, even late in the disease.

Certainly with two of the Fayid cases this happened, as before starting chloromycetin they seemed to have practically no hope of recovery. One developed a very severe bowel haemorrhage the day after treatment started, and on the following day there were signs of bilateral basal pneumonia.

At one stage he was pulseless and comatose, even after parenteral fluids and some blood had been given. Altogether 4 pints of blood were transfused and 100,000 units of penicillin injected intramuscularly 4 hourly in addition to the chloromycetin by mouth, and recovery eventually resulted."

Toxic effects. None were seen in any case.

Blood cultures. These became negative after starting chloromycetin.

Relapses. Out of 9 cases treated during the quarter 3 are known to have relapsed subsequently in the 2nd or 3rd week after the temperature reached normal. Two of these had started the initial course of treatment in the first week of illness. The blood culture again became positive. The response to a second course of chloromycetin was as effective as in the first instance.

During the 3rd and 4th quarter of the year further cases of typhoid were treated with chloromycetin with results similar to those described. At Tel El Kebir 4 cases had no relapse. They were given a larger total dosage, viz

30 gm.

An excellent detailed account of a series of 14 cases treated at Fayid has been reported by Cook and Marmion (1949).

One case each of paratyphoid A and paratyphoid B infection have been treated with chloromycetin with equally good results.

The constancy of the effect on the pyrexia in all cases of the enteric group treated was remarkable, irrespective of the stage of the disease at which treatment started; however, a 14 day period in bed after the temperature has reached normal has always been insisted on.

Unfortunately the relapse rate has been high - 3 in 14 cases. At this time we strongly suspected that chloromycetin by its action might interfere with the development of natural immunity. However, the relapses have all responded to a second course, and there have been no deaths.

The Mackinnon Road Outbreak of Typhoid Fever.

Mackinnon Road is a recently constructed hutted military station situated in the 'bush' in Kenya. There is a large East African garrison, and a smaller British garrison. Typhoid fever was said to be prevalent in Kenya among the native community at the time.

The first admission to hospital was an African patient on 20th April, the first British admission was on 27th April. The outbreak continued through May and June until 19th July. There were 61 Africans with 7 deaths (mortality 11.5%), and 35 British with 2 deaths (mortality 5.1%). Chloromycetin was not available till the latter part of the outbreak when the cases were recovering. The outbreak came at a difficult time for the hospital and staff, as they were in the process of moving to a new site. The laboratory staff were overwhelmed with the amount of work, as this laboratory was a much less well equipped one than the permanent Central Laboratory at Fayid.

The Source of Infection.

The origin of the British cases was probably an African carrier from a Military Construction Unit who had been with an African fatigue party assisting in washing dishes in the British cookhouse; but there was no bacteriological proof.

The exact source of the African cases was not traced, though in the earlier part of the outbreak they all belonged to a construction unit which was disbanded later.

Inoculation state.

92% of the British cases and 94% of the Africans were protected by T.A.B. inoculation within a year.

Severity.

About a third of the cases were severe, proportionately more Africans than British being in this group.

Diagnosis.

Two factors caused delay in diagnosis in a number of cases. Malignant tertian malaria parasites were found in the blood of 11 British and 9 African patients, and bacillary dysentery was prevalent at the time. Three British and 10 African cases presented with typical dysenteric stools.

Bacteriology.

S.typhi was isolated from the blood in a far smaller percentage of cases than in any other outbreak of typhoid fever in the Middle East. Positive cultures were obtained in 60% of the British, and in only 18% of the Africans.

Clinical features.

Headache was present in the majority of cases; it persisted throughout. Unlike other outbreaks diarrhoea was the next commonest symptom, being present in about half the cases. The frequency of dysenteric symptoms has already been referred to. Although microscopically these stools showed typical "bacillary exudate" no dysentery organisms could be cultured, nor did sulphaguanadine relieve the symptoms. A typical coated tongue which later peeled at the edges was characteristic. Sore throat was not uncommon. Neck stiffness without rigidity was also met with early. Anorexia nausea and vomiting were uncommon. Constipation was less common than usual. Abdominal distention was rare. Enlarged spleen was detected in only a fifth of the cases. Rose spots were present in 9 British cases only; in 2 of these there was 'cropping'. The course of the pyrexia was variable, but in general the British cases ran a continued fever. Sometimes a case which commenced with a low pyrexia and which remained low for a time, suddenly developed into a full blown case of typhoid with high fever. This was seen in a number of cases in the Acre outbreak also. A number of patients showed an intermittent temperature. In some cases there was a residual low fever lasting for a considerable time though the patient felt well.

Relapses. 2 British and 3 African cases relapsed.

Complications. Bronchitis was not uncommon among either British or Africans. Pneumonia followed in a number of cases. Hyperpyrexia of 106°F and over occurred in 5 Africans: only one of these died. One African case died of perforation, and one British patient had a fatal bowel haemorrhage. Pericarditis with heart failure was the cause of death in one African. Other complications met with were meningitis, maniacal symptoms, tender toes, pruritis, boils, carbuncles, and thining of the hair. There were 2 cases of thrombophlebitis.

During 1950 a British soldier who had had typhoid in this outbreak was operated on for cholecystitis. S.typhi were cultured from his gall-bladder.

Blood Counts.

This is one of the few epidemics where white cell counts were done. In the British cases the majority fell between 5,000 and 6,000 per cmm, only two were below this range and five were above it. In the Africans there was a much wider scatter, the figures varying from 3,800 to 9,200 per cmm.

In 1947 most specialists had decided that W.B.C. counts were not of great help in the differential diagnosis of the enteric group.

Comments.

The disease ran a somewhat different course in African patients. The mortality was double that of the British. Immunisation could have had little influence on either the incidence or the severity in the Africans.

The following tables show the Quarterly Incidence of The Enteric Group of Fever for 1949.

Table 20.

All Classes of Army Personnel.

	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Total
Admissions	7	121	25	38	188
Ratio per 1,000 of strength	0.08	1.30	0.24	0.41	2.02
Deaths	1	7 (4 African)	4 (3 African)	1	13

Table 21.

British Army Only.

	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Total
Admissions	7	53	11	35	106
Ratio per 1,000 of strength	0.12	0.94	0.19	0.62	1.88

The following table shows the number of typhoid and paratyphoid and Clinical cases.

Table 22.

	All Troops	British Troops only
Typhoid Fever	121	64
Paratyphoid A)		
B)	19	19
Clinical Enteric	48	23

It will be seen that the principal difference between the total figures and those for the British Army only is due to the African troops affected in the outbreak at Mackinnon Road in the 2nd and 3rd Quarters.

The very large numbers of clinical cases in the 2nd quarter is due to the same cause.

There were no cases of paratyphoid C fever. Paratyphoid A and B occurred in about equal numbers. One small outbreak of 7 cases of paratyphoid A fever which occurred at Geneifa in the Canal Zone is of interest as it is one of the few outbreaks in which a urinary carrier of S.paratyphoid A was discovered among food-handlers. As soon as he was removed the outbreak stopped. It is reasonably certain he was responsible for the outbreak. The mortality during the year was again low, being 6.9% of all cases. There were no deaths from paratyphoid fever.

Chloromycetin undoubtedly played a part in reducing mortality. Although it was used only in a very limited number of cases - about 30 in all, the most severely ill cases were selected. The higher death rate among Africans at Mackinnon Road (11%) has raised the total figure somewhat. The British figure is only 4.7% of those attacked.

1950.

During the past two years there has been at least one notable outbreak of the enteric group each year in the Middle East. In the present year the incidence of these infections among army personnel was lower, but the Royal Air Force at Fayid in the Canal Zone suffered from two outbreaks in one unit within the space of a few months; together they far exceeded any of the previous Service epidemics this century.

There were only 2 cases of enteric fever in the Army during the first quarter, and 21 in the second.

First Abyad Outbreak. 109 Maintenance Unit R.A.F.

In 1948 there was an outbreak of paratyphoid B fever at Abyad. The name of the place at that time was Shubra. This epidemic has already been described. Between 6th April, and 2nd May, 1950 the first outbreak of typhoid fever occurred in the same Unit, indeed in the same mess! Those infected all fed from one airmen's mess which catered for about 686 persons, including 29 attached army personnel. Altogether there were 96 suspects; of these, 65 were eventually treated in the Military Hospital Fayid, including 4 proved army cases. In addition 3 men, including one soldier, developed typhoid after arriving at other stations from Abyad. A further 4 cases at the R.A.F. Hospital were confirmed bacteriologically.

Excluding the unproved suspects, about 10 per cent of those at risk were infected, and 14 per cent including all suspects.

Source of Infection.

In addition to the routine investigation of an outbreak, an immense amount of work was done in culturing many specimens of urine and faeces from over 200 food-handlers and potential food-handlers in the station. Although 3 urinary carriers and one presumed carrier were discovered, none was actually employed in the airmen's mess or considered responsible for the outbreak.

Inoculation State of the Unit. This is shown in the following table.

Table 23.

The First Abyad Outbreak of Typhoid Fever.

Months since last T.A.B. inoculation	1 - 6	6 - 12	12 - 24	No record
Army	Nil	2	1	1
R.A.F.	32	26	1	2
Total	32	28	2	3

60 out of 65 (92%) were thus protected. The R.A.F. had received alcoholised vaccine, the Army the new T.A.B. (A) (alcoholised), or T.A.B. (B) (phenolised).

Severity of Outbreak.

3% were very severe, 19% severe, 50% were moderately severe, and 28% were mild. It is thus clear that the outbreak was not an unduly severe one. Chloramphenicol was used in all but 5 cases.

Clinical features.

The principal early symptoms were headache, anorexia, feverishness, malaise, and constipation. Abdominal discomfort, pain in the neck, and backache were the next most frequent complaints; limb pains, dizziness, nausea, and catarrhal symptoms of the upper respiratory type came next. Isolated patients complained of drowsiness, chest pains, diarrhoea, flatulence, dysuria, and epistaxis. More than half the cases had a coated tongue, the spleen became palpable later in 41 per cent. Cough became more obvious, some showed signs of bronchitis, and a few had sore throats. About a quarter had epistaxis later. A third showed rose spots. Abdominal discomfort, sometimes with pain and distension, become more noticeable, and a few more cases had diarrhoea, and some had vomiting. Some had tenderness over the gall bladder. Several showed mental disorder and retention of urine.

Complications. These were few. One patient had haemoptysis, one venous thrombosis, one pleural effusion, and one peripheral neuritis; one was mentally deranged, and one showed evidence of chloride deficiency. During convalescence thrush stomatitis occurred in some cases.

Mortality.

There were no deaths. It can be stated that this was the result of chloramphenicol. Indeed up till this time no British case of typhoid and paratyphoid fever who had been treated with cloramphenicol since its introduction in the summer of 1949 had died. It had been used in about a hundred cases by now.

Relapses.

The incidence was approximately 20%. One patient had 2 relapses. It became clear in 1949 that chloramphenicol greatly increased the relapse incidence; this was amply borne out in this the first Abyad outbreak, and will be referred to later when the second Abyad outbreak is dealt with.

Diagnosis.

Combining the figures from the R.A.F. Hospital at Fayid with those from the military hospital, we get a total of 71 cases confirmed by culture of S.typhi. There were 58 positive blood cultures; 12 faeces and one urine culture were also positive. The phage type of S.typhi isolated was J.

Other Small Outbreaks and Sporadic Cases.

During the same quarter a further 8 cases of typhoid fever occurred in military units at El Ballah in the Canal Zone and one in Fayid.

There were 8 sporadic cases of paratyphoid in the area.

The Second Abyad Outbreak of Typhoid Fever.

While the patients from the first outbreak were still convalescing, a second and more devastating epidemic smote the same R.A.F. unit.

Source of Infection.

The source of infection was in the same airmen's mess as the first, although there had been a complete change over of food-handlers.

Very extensive investigations from all possible angles failed to trace the origin of this outbreak. The abrupt and extensive nature of the outbreak suggested a water-borne infection, but although the original source of the water - the sweet water canal - is exceptionally foul, its subsequent filtration and clorination, which are most carefully supervised and checked, ruled that out. In any case only one mess was concerned. It was considered that heavy contamination of food or distributing receptacles must have been the cause.

Here again we have an unprecedented occurrence in the history of typhoid in the Services. This outbreak extended from 15th July till 15th August, between that date and 26th August there were 3 further isolated cases.

The outbreak was of an explosive character, and the admission rate peaked on the 4th day when 24 cases were admitted to the military hospital at Fayid; by the 8th day there were 93 cases in hospital apart from a considerable number in the small R.A.F. hospital under investigation or awaiting transfer. This was the primary wave, and it was rapidly succeeded by a secondary wave. By the 15th of August a total of 226 cases were in the military hospital, and 3 more were added during the next eleven days making 229. Fifteen of these were from the attached 27 army personnel.

In spite of the strain on the limited hospital staff and on the Central Laboratory, full advantage was taken of the unrivalled opportunity to carry out research work, and much valuable information should be forthcoming when all this work is completed.

Numbers at Risk and Attack Rate.

In Abyad I outbreak approximately 686 persons were at risk, 657 being R.A.F., the remainder army personnel attached.

In Abyad II outbreak approximately 657 were at risk, 630 being R.A.F., and the remainder army personnel attached.

Between the two outbreaks there had been a changeover of approximately 200: rather more than that number left, and slightly fewer arrived at the station.

Therefore in Abyad II outbreak about 33% of those R.A.F. personnel at risk were infected, and 55% of the army personnel.

Inoculation State.

The R.A.F. were protected mainly by the original alcoholised vaccine, but various others such as vaccines prepared by The Lister Institute and by certain private firms were also used, the army by either the new alcoholised, TAB 'A', or the new phenolised T.A.B. 'B'.

The following table indicates the inoculation state of the men of both services who contracted typhoid.

Table 24.

The Second Abyad Outbreak of Typhoid Fever.

Months since last T.A.B. inoculation	1 - 6	6 - 12	12 - 24	More than 24	No Record
Army	8	6	1	Nil	Nil
R.A.F.	83	104	12	2	13
Total	91	110	13	2	13

All army personnel but one were protected, i.e. 93 per cent. At least 187 R.A.F. personnel were protected out of 214, i.e. at least 87 per cent of those attacked. Unfortunately the inoculation date of those at risk but not attacked is not available.

Cases infected in Both Outbreaks.

It is of great interest to note that 5 convalescent patients from Abyad I outbreak contracted typhoid again in Abyad II outbreak; 4 of these were proved bacteriologically.

Severity of Outbreak.

In general terms it can be stated that in comparison with Abyad I outbreak this was much more severe. There were approximately twice the percentage of very severe and severe cases, and less than half the percentage of mild cases,

the proportion of moderate cases was about the same in each outbreak.

The following are the figures:-

Table 25.

	Abyad II		Abyad I
Mild	27	(12%)	(28%)
Moderate	105	(48%)	(50%)
Severe	73	(34%)	(19%)
Very severe	13	(6%)	(3%)

Clinical Features.

The most frequent presenting symptoms were headache, pain in the back of the neck, malaise, and anorexia. Constipation, abdominal pain, feverishness, backache, nausea, and cough came next in order. Limb pains, vertigo, abdominal discomfort and flatulence, sore throat, vomiting and diarrhoea were less frequent a few had epistaxis, chest pains, and drowsiness.

Later, furred tongue was commonly seen. An exanthem appeared in 40 per cent of cases, and the spleen was palpable in 38 per cent. Evidence of abdominal distension, and signs of bronchitis, were not uncommon, but pneumonia was infrequent. A number had tenderness over the gall bladder. A few showed mental disorder and incontinence.

Among the rarer features were deafness, earache, conjunctival injection and haemorrhage, stomatitis, glossitis, and herpes labialis. Diarrhoea of a dysenteric type, with stools containing fresh blood and mucus, occurred on 3 occasions.

Complications.

A greater number of complications were met with than in Abyad I outbreak, even so the incidence was much less than could have been anticipated had chloramphenicol not been used.

Sixteen patients showed evidence of hypochloraemia, some were severely ill requiring intravenous therapy for a time.

There were 5 cases with severe meteorism.

Four patients developed pneumonia.

There were 2 instances each of bowel haemorrhage, haemoptysis, venous thrombosis, peripheral neuritis and mental disorder. Two patients had doubtful bowel perforations. One case of perforation which was operated on died. There was one example each of spontaneous pneumothorax, haematemesis, external popliteal nerve palsy, and a doubtful typhoid spine.

During convalescence a number of minor septic skin infections occurred. Some of the more ill patients had a varying degree of alopecia.

Diagnosis.

The percentage of cases in which bacteriological proof was obtained has equalled the Acre outbreak. Of 229 cases, blood cultures were positive in 206, faeces cultures in 11, and urine culture in 1, giving a total of 218 or 95 per cent positives. Five were diagnosed by agglutination, leaving 6 in whom the diagnosis was uncertain. S.typhi isolated was phage type E.1.

Deaths.

One resulted from a bowel perforation.

One occurred from toxaemia, and was thought to be an example of a 'toxic crisis' following chloramphenicol. A mortality of less than one per cent is unprecedented in an outbreak of this magnitude and severity.

Chloramphenicol.

In addition to the two Abyad outbreaks during the 2nd and 3rd quarters of 1950 there were a number of sporadic cases, also a small outbreak of 8 cases from El Ballah treated at Fayid Military Hospital. This gave an unrivalled opportunity to try out various schemes of treatment to try to find some method of reducing the relapse incidence following the use of chloramphenicol. In 1949 owing to the scarcity of this antibiotic a minimum was given, and most of the patients had about 21 gm total dosage. Only the seriously ill cases were given the benefit of this antibiotic at that time.

In 1950 there was not the same need to restrict its use. It still remains a very expensive preparation however. The rule was that a case of enteric fever must be diagnosed bacteriologically before it could be started, the only exceptions being patients who were suspects and were sufficiently ill to require specific treatment.

The total dosage was increased also in 1950. Of the different courses tested out only 4 will be referred to here, as, of the first series of trials, they represented the schemes which gave the lowest and the highest relapse incidence respectively.

Course C.

(Loading dose 3.5 gm) followed by 3 gm per day in divided doses (4 or 8 hourly) for 9 days, then 1.5 gm per day for 5 days. Total 34.5 gm in 14 days (minimum). The loading dose was omitted in later cases.

Course D.

(Loading dose 3.5 gm) followed by 3 gm per day in divided doses until the patient is afebrile for 2 clear days with a minimum of 15 gm. Then an interval of 7 days. Finally (a loading dose of 2 gm) followed by 1.5 gm per day in divided doses to a total of 10 gm. The loading doses were sometimes omitted

in later cases, but the minimum total dosages remained unaltered. Total 25 gm minimum.

Those of us who saw the effects of chloramphenicol in 1949 considered that the most obvious explanation of the increased relapse incidence, was the bacterio-static action of the antibiotic interfering with the normal development of immunity during the course of the disease. It had been suggested in 1949 by Sir John Taylor (Special Report) that the addition of T.A.B. vaccine might be of value in treatment. T.A.B. treatment alone of course, had been used by a few medical officers 20 or more years ago in the army, but fell out of use because of unsatisfactory, if not dangerous, results.

In 1950 there was much divergence of opinion as to the possible value of T.A.B. vaccine plus chloramphenicol. However, the writer considered it was worth trying, and empirically decided on 0.02 ml, i.e. a tenth of the usual first immunisation dose, to be given daily subcutaneously for 10 days, commencing at the same time as chloramphenicol. This was started when the 2nd Abyad outbreak was well under way in August. The preparation used was T.A.B. (B).

The one fear was that there might not be a sufficient number of new cases to test out the new treatment!

The different courses of treatment were given in different wards to avoid any errors. The T.A.B. course was then added to scheme C and also to scheme D.

The following table shows a somewhat unexpected result:

Table 26.

Course	Number on Course	Relapses Blood Culture +	Relapses Blood Culture −	Total	Percentage relapsing
C	52	6	3	9	17.3
D	103	32	12	44	47.6
C + T.A.B.	36	4	2	6	16.7
D + T.A.B.	24	1	0	1	4.2
Total	215	43	17	60	27.5

Unfortunately for the trials (though fortunately in every other respect) the epidemic came to a close before 50 cases could be treated by Course D + T.A.B.

Treatment of Relapses.

Up till Sept. 25th all relapse cases received the same treatment as in their initial attack, after that date they were given either Course C or C + T.A.B. The response to treatment was as satisfactory as in the initial attack.

It is clear from the table that the T.A.B. vaccine added to the Course which previously gave the lowest relapse rate, i.e. Course C, with 17.3% relapses, had little influence, the relapse rate being practically the same 16.7%. However, when the vaccine was given with Course D the relapse incidence fell from 47.6% to 4.2%. Even with as few cases as 24 this figure is of statistical significance.

Criteria for a Relapse.

These were very rigid. Every unexplained pyrexia of 48 hours or more during convalescence was considered a relapse.

But the difficulty in deciding on what is a relapse is seen when it is stated that positive blood cultures were obtained from some symptomless convalescents, and from some with only a low fever for a day or two, as well as from the clear cut case.

The above result would suggest that to obtain the benefit of the immunising effect of T.A.B. vaccine during treatment, it is of advantage (1) not to give more chloramphenicol than is necessary to control the infection, (2) to give the T.A.B. during a phase when no chloramphenicol is being administered.

Perhaps next summer in the Middle East it may be possible to test out this tentative hypothesis.

Reactions from T.A.B. Vaccine treatment.

Although most patients made no complaint about the effects of the daily T.A.B. injection, the local reactions in a number of cases were quite severe, and equal to the full dose in a fit person.

No severe general reactions were seen. It would be inadvisable, however, to increase the size of the individual dose.

Double relapses.

Altogether 6 cases were known to have had a second relapse, 4 having been bacteriologically proved. Five of these relapses were in cases treated both in primary attack and first relapse by Course D, one received Course C.

The Duration of Fever after Chloramphenicol was started averaged between 3 and 4 days over a large number of cases, irrespective of the stage at which treatment commenced. This is similar to the findings in 1949.

Toxic Effects of Chloramphenicol.

It was considered in 1949 in the Middle East that chloramphenicol produced no toxic effects. With the large numbers treated in 1950 it became clear that certain toxic effects could be produced. The precise assessment of the prevalence of these was difficult, because in many cases they correspond closely to symptoms which are commonly present in typhoid fever.

The toxic crisis considered by some to be due to extensive release of endotoxins from the lysed organisms was thought to have occurred in at least one case who died with vascular collapse. There is a considerable literature on the subject, but one of the most complete articles was written by Mollaret and others (1950) who support their contention by experimental work on mice.

It was thought advisable latterly to do away with the loading dose. This certainly made no difference on the influence of the antibiotic in bringing down the temperature to normal.

Serious effects from the administration of chloramphenicol are so rare, and the beneficial effects are so consistent in the majority of cases, that from the practical point of view the administration of chloramphenicol in all cases of typhoid fever, especially severe typhoid, should be a routine procedure. After all, we know that in the past certain cases who were only moderately ill could very suddenly show signs of acute toxaemia, and die with peripheral, and probably central, cardio-vascular failure.

Other conditions considered to be produced by chloramphenicol in a small number of patients were nausea, anorexia, abdominal discomfort, soreness of the mouth and throat, superficial glossitis, dysphagia, angular stomatitis, vomiting, diarrhoea, drug fever which ceased when the chloramphenicol was withheld, various skin eruptions, urticarea, and in one instance only a scaly lichenoid type of skin lesion. Several patients had disturbance of accommodation. Granulocytopenia was not encountered. The literature contains many references to toxic effects of chloramphenicol, but authorities like Perin Long and others (1950) give a list which is somewhat shorter than the above.

Method of administration of Chloramphenicol.

In certain very ill patients difficulty in administering the preparations was occasionally met with; it was felt that a parenteral preparation for initial use in such cases would be a great boon. Administration by stomach tube was required in only a few instances. Rectal administration was unsatisfactory owing to the doubtful absorption, and the local irritation produced.

Effect of Chloramphenicol in S.typhi in the body.

It is not proposed to go into any bacteriological details, but by an ingenious series of cultural experiments Archer (1950) was able to show that the action of chloramphenicol tended to be bacteriostatic. This is in accord with the generally accepted view. By a series of blood cultures taken at short intervals after a dose of 3.5 gm of chloramphenicol had been administered by mouth, Goffe (1950 a) showed that the blood was sterile after 40 to 60 minutes.

Resistance.

There was no clinical evidence to suggest that the salmonella develop chloramphenicol resistance. No laboratory studies were carried out along these lines however.

Carriers.

Three cases from Abyad II outbreak continued to excrete the organism in the faeces for many weeks during convalescence. A trial of large doses of chloramphenicol by mouth was unsuccessful. 6 gm per day or more produced vomiting. A report has just been received by the writer since he left the Middle East to the effect that, two of the three carriers ceased to excrete the organism after a combined course of chloramphenicol, T.A.B. vaccine,and sulphamezathine, but no details are available. One persistent excretor was left (December, 1950).+

This carrier is the only known one out of the Abyad outbreaks; sufficient time has not yet passed to say whether or not he will become a chronic carrier. In past years it has been rare to hear of a carrier being picked up from cases returned to England from Middle East, certainly not more than an occasional one has been.heard of.

The incidence must be only a fraction of one percent. Ames and Robins (1933) analysed some New York figures by Agar, and in the 20-29 age group, out of 579 cases there were 12 carriers, a 2.1 per cent incidence. Possibly the carrier rate is less in an inoculated community. Certainly, though treatment with chloramphenicol appears to interfere with the development of natural immunity, it does not seem to have increased the already low incidence of carriers from service cases of enteric fever.

Re-immunisation of Chloramphenicol treated cases.

It was decided both by the R.A.F. and the Army Medical Authorities to give all cases which had received chloramphenicol one booster dose of T.A.B. vaccine of the type they had previously received, before discharging them from convalescence.

Clearance Tests.

At present in the army before an enteric case is discharged from hospital and considered free from infection, he must have had three negative urine and faeces cultures each week for two weeks. The R.A.F. insist on fourteen negative urine and faeces cultures.

General Principles in the Treatment of Enteric Fever.

Although chloramphenicol has a specific effect and greatly shortens the illness, it is essential to remember that typhoid fever in particular, is a dangerous disease. The earlier the treatment is started the less the risk. A very few cases appear unresponsive to chloramphenicol, in others the diagnosis

+ The third carrier has now ceased to excrete S.typhi.

may be uncertain or delayed, with the result that it may be several weeks from the onset of the illness before the specific antibiotic is started. It is also important to realise that where bowel ulceration has occurred it must take some little time to heal. The disease is most frequent during the hot weather, therefore fluid loss from the body is much greater than in temperate climates, and dehydration readily occurs. In acute infections, and particularly in typhoid fever, the blood chlorides tend to be reduced, if there is much sweating, and especially if vomiting and diarrhoea are added, dangerous hypochloraemia may occur. The clinical features of these conditions, so well described by Marriott in his Croonian lectures (1948), and summarised by Anderson (1949), may easily be mistaken for typhoid toxaemia with disastrous results.

In the recent Abyad outbreaks a number of such cases were seen, and correctly diagnosed. Fluid intake and output charts, coupled with the testing of urine for chlorides by Fantus' method enabled the symptoms of these conditions to be recognised for what they were, and appropriate corrective measures taken.

In the most severely ill cases, it was necessary to retain a Ryle's or similar tube as a trans-nasal intra gastric drip for administration of fluids etc. - and in some instances of persistent vomiting, for gastric suction. Intravenous solutions of glucose or saline, according to requirements, had also to be given for considerable periods in one or two cases.

Diet. In the early stages a soft or semi-fluid low residue diet with adequate protein and plenty of fluids was given, the quantity of food depending on the condition of the patient. Later a soft mixed diet of about 3000 calories sufficed. Once the chloramphenicol had begun to take effect there was no difficulty in getting patients to take a sufficient amount of a convalescent diet, as they often showed an exceptionally good appetite, even before their temperatures were normal.

It must be remembered that even after chloramphenicol is started, some of the graver complications may occur, and instances of haemorrhage and fatal perforation have both been experienced. However, it is pointed out that the risk of these rapidly diminishes with time after the antibiotic treatment is started.

It is advisable to add to the diet a preparation rich in vitamin B in view of the tendency to deficiency of this vitamin in chloramphenicol therapy.

Bed rest.

Perhaps the strict rule of keeping patients in bed till the temperature has been normal for two weeks is over cautious, but one Medical Officer in charge of a group of wards is Abyad II outbreak considered that those patients who did not obey the rules and moved about earlier, were more liable to get febrile attacks during convalescence.

Physiotherapy.

It is important that during this prolonged spell in bed appropriate physiotherapeutic measures are adopted, and bed exercises should be given, especially for the lower limbs. These help to maintain muscle tone and to lessen the risk of venous thrombosis.

Air-Conditioned Wards.

Sufficient air-conditioned wards were not available to cope with this large epidemic, but it was arranged that all the very ill cases were admitted or transferred to these wards. Quite apart from adding to the comfort of the patient it reduced considerably the risk of dehydration and hypochloraemia.

Standard of Nursing.

It is hardly necessary to add that the highest standards of nursing are still necessary, though not for such long periods as in the past, thanks to chloramphenicol.

Perforation of Typhoid Ulcers.

One such case which was fatal has already been referred to. Perforation occurred while under treatment with chloramphenicol. At times there is considerable clinical difficulty in deciding whether or not a leaking ulcer is present. In two doubtful cases the patient was carefully watched and chloramphenicol continued: both recovered. One was so gravely ill that a laparotomy would almost certainly have ended fatally.

At the same period a patient was admitted to the R.A.F. hospital Fayid as an acute perforated ulcer - thought to be a peptic ulcer. At laparotomy the true diagnosis was apparent, and with the help of chloramphenicol the case recovered. An Asmara, Eritrea, a typhoid case under treatment suddenly showed signs of bowel perforation. He recovered after laparotomy under a local anaesthetic. Chloramphenicol was continued, and penicillin given in large doses. Streptomycin was used also.

In 1950 the case incidence of perforation was somewhat under one per cent, and the mortality 33%; both figures are lower than might have been anticipated.

Paratyphoid fever.

Besides these large epidemics a certain number of sporadic cases of typhoid and paratyphoid fever continued to crop up in the Middle East, chiefly in the Canal Zone of Egypt, Earlier in the year there had been a small outbreak of paratyphoid B infections in one unit, contracted in Tripoli. The unit was about to move to Malta, and immediately on arrival there a number of men were admitted with pyrexia. S.paratyphi B was cultured from the blood of three, but almost certainly several other admissions to hospital from the unit were

also clinical infections of the same type. The illness was very mild.

In September and October an outbreak of 6 proved and one clinical infection with paratyphoid A occurred at Suez. These were rather more ill, and two required intravenous therapy. All responded to chloramphenicol.

During October 5 proved and 5 clinical cases of paratyphoid B infection occurred in a unit in the Canal Zone. They also responded well to specific treatment. It has been observed however, that during treatment with chloramphenicol the pyrexia came down more gradually in paratyphoid than in typhoid.

In no instance was the source of the infection traced.

One case of paratyphoid C infection was reported in 1950. This occurred in a British soldier in East Africa. This is the third only in the whole of the Middle East since the beginning of 1948 among army personnel.

Enteric Infections among Nursing Staff.

Although a large proportion of the R.A.M.C. nursing orderlies employed in Military Hospitals are National Service men with a very short training and experience of nursing, remarkably few of those employed in nursing enteric cases have contracted the infection. The occasional case has occurred, but in the two large Abyad outbreaks of typhoid fever there was no instance of infection among any of the nursing staff, either sisters or orderlies.

The inoculation state of the staff was of course maintained at the highest standard, but of even greater importance were the hygienic precautions adopted in the wards and annexes. These were such as to leave as little risk as possible to the staff handling the patients and dealing with discharges and excreta.

One pathologist did contract a paratyphoid A infection at this time. There were a few cases of paratyphoid A in hospital during this period, but he had handled no material from these. He was dealing only with S.typhi. It was his first year overseas!

Discussion

Epidemiology of The Enteric Fevers.

From what has been written it is clear that of all the countries in the Middle East Theatre where service personnel are stationed, the incidence of enteric is highest in the Canal Zone of Egypt. Numerous outbreaks of all sizes, besides considerable numbers of sporadic cases, have continued to occur, especially since 1945. The possibility of occasional outbreaks elsewhere is shown by the extensive Mackinnon Road epidemic in East Africa.

Enteric fever in the Civil population in Egypt.

The true extent of enteric among the civil population of Egypt is difficult to assess; only a proportion of the severely ill cases ever reach a hospital. The admissions to one of the large Cairo hospitals for infectious diseases average over a thousand a year. Details of the number proved bacteriologically are not available. Over a long period the mortality rate has been around 12% El Ramli (1950).

Much recent research work on enteric fever has been done by the British Naval pathologist attached to the Naval American Medical Research Unit, which is adjacent to the Cairo Isolation Hospital.

Miller (1949) has carried out a survey of a village of 5,000 inhabitants which may be taken as similar to numerous other Egyptian villages.

An assessment of the proportion showing Vi - agglutinins in the serum of a titre considered significant, gave the high figure of thirty per cent. Out of 200 such individuals with a 'positive' Vi-titre, 12 apparently healthy persons were excreting typhoid organisms, 2 paratyphoid A, and one paratyphoid B. Of these, 10 were urinary, and 4 faecal excretors, the other was both a urinary and a faecal excretor.

As a result of further investigations, including a serological survey and history taking of over 3,000 of the inhabitants, Miller concluded that during the previous 2 years 38 had had enteric fever. Six were still excreting the causative organism, and in addition, 2 cases of active infection were identified. He considered that just over half had been typhoid, about 40 per cent paratyphoid A, 5 per cent paratyphoid B, and 3 percent paratyphoid C.

It is obvious that Egypt is a country where enteric fever is exceptionally prevalent. The high proportion of carriers, estimated by Miller at approximately 3 percent of the community, and especially the high proportion of young men who are urinary carriers, makes the Egyptian employee a potentially dangerous one.

In the Canal Zone many thousands are employed, and a considerable proportion are in one way or another associated with food! The turnover per annum is high also. The urinary carrier is recognised as much the more dangerous type. The proportion of urinary carriers among Egyptians is high.

The Army Health Authorities and Pathologists consider that potential food-handlers can be screened by cultural examination for the Salmonella group of three specimens of urine before employment. Care is taken to ensure that the specimens produced are actually passed by the individual concerned, a most important essential in a country where known non-infected specimens have a market value! The names and photographs of detected carriers are circulated to units with orders.

It might be asked why stools are not examined also. From the practical point of view it is considered much less essential, and it just could not be done in the Army with the reduced numbers of technical personnel at present available. The Royal Air Force, however, being a very much smaller service, are able to examine three stools as well as the three urine specimens: they also do three-monthly bacteriological checks on food-handlers.

The following figures show the numbers of urinary carriers picked up by these routine screening tests at the Central Pathology Laboratory (Archer (1950 a). They are rather lower than Miller's figures for the native village.

Between 15th October 1949 and 11th September, 1950, specimens of urine from 5337 Egyptians potential food-handlers were cultured, and 54 carriers detected (1%). The proportions of the different organisms isolated were as follows: S.typhi 7, S.paratyphi A 21, S.paratyphi B 1, S.paratyphi C 22, unidentified 3.

The high proportion of S.paratyphi C is of interest. There is no C component in the vaccine used by the Army and Royal Air Force, yet only 3 Service cases of this infection have been reported in the past three years in the Middle East.

Egyptian Carriers and Schistosomiasis.

The reason for the high proportion of urinary carriers in Egypt is considered to be the high incidence of urinary schistosomiasis. It is generally estimated that 60% - 70% of Egyptians acquire this latter infection.

The typhoid organisms apparently find the urinary system damaged by schistosomiasis a suitable nidus to continue their existence protected from the antibodies circulated in the blood: although, strange to relate, if the urine of a carrier is tested for agglutinins of the enteric group they can usually be detected in the specimen! Archer (1950 b).

Work is at present in progress on this very subject, both in the Central Pathology Laboratory in Fayid, Archer (1950 c), and at the Naval American Medical Research Unit in Cairo, Miller (1950 a). Attempts are being made to cure Egyptians suffering from Schistosomiasis who are also carriers of one of the Salmonella infections, to see if they subsequently cease to excrete the organisms. The results are not yet available.

Egyptian Chronic Carriers.

It is generally considered that chronic enteric carriers excrete the organisms intermittently. Investigations are in progress at the Central Pathology Laboratory Fayid on a group of Egyptian employees who were found to be urinary carriers of S.typhi, S.paratyphi A, and C. It has been shown that more than half are persistent excretors. These men have been under observation for a year. Goffe (1950 b).

The numbers of organisms in the urine is very high in some instances. One carrier excretes 60 million S.typhi to the ml!

When we come to survey the results of the very extensive and complete investigations carried out in all enteric outbreaks, we find very little of help in the findings obtained. Thousands of specimens of urine and faeces have been examined from food-handlers from messes where outbreaks have occurred in the past three years, and in only a very few instances has the individual causing the outbreak been detected. In this present survey only two cases are quoted. Frequently urinary carriers are detected among Egyptian food-handlers, perhaps carriers of S.paratyphi and S.typhi of the wrong phage types in a typhoid outbreak, or S.typhi in a paratyphoid outbreak.

Transient Carriers and Mild Clinical Infections.

Are these carriers who are picked out chronic carriers? Some may be, probably most are not. If they are not they must have acquired the infection immediately before, or at some period subsequent to, their employment and be temporary carriers, perhaps they suffer from a very mild infection at the time. This is quite possible. The endemicity of the disease is so high in Egypt that many inhabitants must acquire a considerable degree of immunity. They may get a mild clinical infection, possibly not producing sufficient symptoms to put them off their work, yet they will excrete the organism for a time. Even among service personnel we find cases during an epidemic who have positive blood cultures and show practically no symptoms or signs. This was well brought out in the Acre outbreak. It is the writer's opinion that the Egyptian employee who gets a very mild clinical attack of enteric and goes undetected is the greatest danger.

Failure to trace the Source.

The mechanism for investigating an epidemic cannot commence for at least two weeks after the actual infection of the food in the mess concerned has taken place, owing to the comparatively long incubation period of the disease. By this time the Egyptian employee responsible has ceased to excrete the organism and goes undetected.

Practically all the outbreaks have been of the same pattern, certainly all the major ones have been connected with a single mess, with the exception of the Acre outbreak. Here of course, the circumstantial evidence was so strong that the water supply could be clearly credited with the responsibility.

Other possible factors.

The question of the possibility of sabotage has been suggested; the writer thinks it is quite unnecessary to look to such an unlikely factor as a cause.

In considering the water supply in the Canal Zone it has only to be mentioned that this, though foul at its source, is so carefully controlled before issue to the consumer, that infection by that vehicle is practically impossible. The distribution of the cases in an outbreak rules it out as it is a piped supply. It could only be a factor if secondarily infected by a food-handler after it had been drawn from the tap.

Milk comes under the same category, it is either tinned or reconstituted except in a few cases such as that of families for whom a limited amount of fresh milk is available. It would have to be contaminated at the time of distribution in the mess affected by an infective food-handler.

The house fly is well known to be able to carry the enteric organisms, and certainly can be responsible for sporadic cases, but is unlikely to be directly the cause of large outbreaks.

The seasonal factor has a very strong influence. No large epidemic has occurred in the cold weather (see appendix 2). The Egyptian incidence is very similar to that observed in the Services. The early summer and the late autumn produce the highest figures among the local inhabitants El Ramli,(1949). The reason no doubt is that the climatic conditions are such as to favour the survival and growth of the Salmonella group outside the human body during these periods.

Discussion on Factors Influencing Immunity. The Role of T.A.B. Vaccine.

Age.

It has long been established that among adolescents and adults the younger age groups are more susceptible to enteric fever. In any large epidemic where this question is investigated the answer is always the same. It has been demonstrated in the Acre outbreak; it was shown in the official report on Abyad I outbreak. Hill (1950). Holden (1939) showed that the highest incidence in the Croydon outbreak was in the 10-24 age group.

Length of residence in an Endemic Area.

It has also been recognised that a new arrival overseas is much more likely to contract the infection than the older resident, other things being equal. This was also demonstrated in the Acre and Abyad outbreaks.

Previous attacks.

Although absolute immunity does not occur after an attack of enteric, a high degree of immunity must be produced. Second attacks are uncommon but may occur. But the writer knows of no series of cases similar to the five men who participated both in the first and second Abyad outbreaks, a fact strongly suggesting interference with natural immunity by chloramphenicol, as they were all treated with this antibiotic in the first outbreak.

T.A.B. Vaccine.

One of the chief factors to which all medical personnel of the services in particular, have pinned their faith, has been the artifically produced immunity resulting from inoculation with antityphoid and antiparatyphoid vaccine.

Very early in the history of the vaccine, when it contained only the antityphoid element, figures were produced to show that in India at the end of last century the incidence of the disease was lower in the inoculated. A statistical analysis by Greenwood and Yule (1915) of the figures of the Anti-typhoid Committee of 1913, showed a definite reduction of the incidence of typhoid fever in the inoculated. The first two tables quoted in the earlier part of this Survey show the reduction not only of incidence, but also of the mortality rate in inoculated as compared with the uninoculated.

It has been accepted by all authorities that the experiences of the 1914-18 war proved the great value of the vaccine, at least of the typhoid element.

When the incidence of typhoid rose and remained unduly high among British troops in India in the inter-war period the blame was placed on the vaccine, and an enquiry into this showed that the strain of organism used had 'aged' and

lost certain properties which were considered essential. Grinnel (1932); Perry, Findlay, and Bensted (1933).

The rejuvenation of the strain was brought about, and following this, the incidence of typhoid fever in India fell and remained low. See Table 5. Indeed it remained relatively low right through the 1939-45 war into the post-war period, until all British troops were evacuated from that country. In the report on 'The Health of the Army in India for the Year 1942' it is stated, "The British Army owes a great debt to the laboratories at Millbank and Kasauli for the provision of such a potent vaccine".

The second part of the quotation from The Principles and Practice of Medicine, Christian (1947 a), given in the introduction to this Survey is repeated, "Now antityphoid vaccination and prompt recognition and isolation of cases have reduced typhoid to so small an incidence (as) to be of little importance".

The experience of Boyd (1943) in the Western desert with the British vaccine, when compared with Axis' products, forms a strong case for the efficiency of the T.A.B. vaccine as then used. The low incidence among troops in the Middle East up till 1944-45 supports this case.

This weight of opinion and evidence for the efficiency of the British T.A.B. vaccine up till the period 1944/45, and of the vaccine used in India after the rejuvenation of the Rawling's strain, is too strong to be set aside.

No one would deny that other factors such as a good standard of hygiene, satisfactory refuse and excreta disposal, and good living accommodation, all played their part, though the last factor must have been absent in most active theatres of operations overseas during the war.

The reason for the low pre-war incidence of enteric in the Royal Air Force suddenly increasing during the war, and remaining considerably greater than the Army incidence in the Middle East is uncertain (Tables 6,7). Possibly the inoculation state was less satisfactory. The standard of hygiene may have been below that of the pre-war period.

Doubts concerning the degree of efficiency of T.A.B. Vaccine.

The first real jolt to be received concerning the efficiency of the vaccine was the outbreak in Germany in a Guards' Unit, when 34 percent of those at risk contracted typhoid fever. It occurred in 1944, and it is most unfortunate that owing to active service conditions it was uncertain with what type of vaccine most of the unit had last been inoculated.

The next outbreak of typhoid to shake one's faith in the vaccine was in an R.A.F. Unit at Shallufa in Egypt in 1945. Here apparently 75% had had the new alcoholised vaccine last, and 14.7% of those at risk were infected. The case mortality was 10%. There was no evidence that the severity was reduced in

those whose inoculations were up to date. As time went on and more Service personnel became protected by the new alcoholised vaccine, so the graph of incidence rose during 1946 and 1947, and remained above the low war-time level (Appendices 2,3, and 4). It is little wonder that the medical personnel on the spot who dealt with the outbreaks began to lose faith in the new vaccine. The pathologists said little. The immunologists at home, who could perhaps take a more dispassionate view, were divided in opinion.

What other factors could have caused this very real increase in the incidence in enteric fever in Middle East, and not in India? It will be recalled that India continued to make her own vaccine at The Research Institute at Kasauli, and that it was a phenolised vaccine with a rejuvenated Rawling's strain plus a 'wild' strain which was changed from time to time.

Apart from changing the method of production of the home vaccine in 1944 the dose was halved. Here was a possible additional factor.

1948 brought the Acre outbreak with over 60% of those at risk contracting enteric fever. This surely is a peak record for an epidemic of this size. There were, however, differences in this outbreak from the previous ones. Whereas it was considered that the vaccine in no way influenced the severity of the disease, the mortality in the Acre outbreak, which was by no means a mild one, showed cases with all degrees of severity down to the patient with a temperature of 99°F, and only a slight headache for a day or two. The mortality also was only 4%. Admittedly, the standard of nursing was exceptionally high on this occasion, but this fact in itself could not account for the marked reduction in the death rate compared with the previous higher average mortality.

It would seem that the views about T.A.B. vaccine having some influence in lessening severity and mortality held in the 1914-18 war, and subsequently reversed in 1946-47, should once again be supported.

The Acre outbreak did little to suggest that the resistance to the invasiveness of the typhoid and paratyphoid organisms was in any way increased in those at risk by their having been immunised previously with T.A.B. vaccine. Naturally acquired immunity as seen in the Palestine Police was far superior to that produced artifically: only 17.2% were affected compared with 60.8% of the troops.

Next came the Shubra outbreak of paratyphoid B. The percentage affected of those at risk is difficult to estimate, as the precise number of clinical cases was uncertain, but there were 52 proved cases, and even more than that were suspected in addition out of 750 at risk, making an incidence of about 14%.

The inoculation state was good. The degree of severity was mild.

The group of 29 sporadic cases of typhoid fever at Fayid were not so well protected: less than 80% were up to date with inoculations. On the whole the

illness was moderately severe, and the mortality 7%. The 27 cases of typhoid in the hospital at Tel El Kebir with over 80% protected were relatively mild, and no deaths occurred.

The outstanding feature, therefore in 1948 was the comparatively low overall mortality - less than 4%. It is a reasonable assumption that as this figure was from a number of outbreaks and sporadic cases it is improbable that it is a chance occurrence. The writer considers T.A.B. vaccine must have had some beneficial influence on the course of the disease, though it did little to prevent its occurrence.

The Mackinnon Road Outbreak in 1949 was moderately severe with a 6% British mortality and 11% African. The inoculation state - taking the 12 month period - was over 90%. The difference in death rate between British and Africans is probably due to the better resistance of the British to infections in general. The British mortality rate remains relatively low.

The graphs in Appendices 2 and 3 show the slight general downward trend in the incidence of enteric among British troops after 1948/49 until 1950. The significance of this may be that as a result of the frequent outbreaks and the consequent drive to improve hygiene generally in the Canal Zone, the risk of infection has become less.

One can hardly credit the lowered incidence to the T.A.B. vaccine.

The new T.A.B. (A) and (B) vaccines. In Aug. 1949, of course, the new T.A.B. (A) (alcoholised) vaccine of double the previous strength, and T.A.B. (B) (phenolised) of similar strength, were introduced for a comparative trial. One might almost have attributed these new vaccines with some of the credit, but for the two Abyad outbreaks of 1950, in which a small number of Army personnel were at risk and a large proportion of them went down with typhoid!

Turning to Appendix 3 again, one sees the erratic course of the graph of incidence of enteric in the Royal Air Force. This is explained by the smaller numbers in the total strength, and the magnitude of the outbreaks. 1947 and 1949 were good years. 1950 is the blackest year the R.A.F. have ever experienced as regards enteric infections.

The two large Abyad outbreaks of typhoid originated in the same mess on each occasion. This was the mess which was involved in the Shubra outbreak of paratyphoid B in 1948. The name 'Shubra' was changed to 'Abyad' in 1949. The attack incidence of 14% for the R.A.F. in the first outbreak is relatively high, but the 33% attack rate in the second is almost a record for an epidemic of this magnitude. It will be observed that the attack rate for the British, 'protected' by the two new vaccines T.A.B. (A) and (B) is up to 56% in the second outbreak. The majority of the R.A.F. were protected by the original alcoholised T.A.B., but several other proprietary vaccines such as those supplied by the Lister Institute were also used.

The proportion of both British and R.A.F. who were protected, taking the twelve month's figures, was good on the whole, although the fact that only 87% were protected for the second outbreak, might be criticised. But the Army personnel with 93% 'protected' showed up very badly. The high incidence says little for the two new vaccines.

In view of the free use of chloramphenicol in the Abyad outbreaks, it is impossible to give any indication of the influence of inoculation on severity and mortality.

Other Factors which might have played a part in the High Incidence of Enteric since 1945.

Keeping qualities of the vaccines. It is possible that the keeping qualities of the alcoholised vaccine were poorer than was anticipated, and their immunising efficiency might have dropped. It is unlikely however that more than half of those at risk would be inoculated with vaccines nearing their allotted span of usefulness. The incidence in these outbreaks is so high, that even half the incidence would have been excessive. Incidentally the official life of the vaccine was cut down to as little as six months.

Miller (1950 b) has carried out mouse-protection tests on current and out of date T.A.B. (A) and T.A.B. (B) vaccine, and these lost little of their efficiency in protecting the mice many months after the official expiry date. How far the protection of mice corresponds to the protection of humans is a moot point, but the analogy is accepted by the immunologists. Perry, Findlay, and Bensted (1933 c) state that in default of actual field experiments, we are in agreement that the mouse protection test affords a most valuable laboratory procedure for the determination of the resistance to infections afforded by a typhoid vaccine.

The following suggestions have been put forward mainly by others - mostly pathologists and immunologists - to account for the increased enteric incidence since 1945:-

(1) The youth of the new arrivals in Middle East, and the rate of turn over of new troops. But surely during the war years very large numbers of young troops kept arriving out after 1941 at frequent intervals, and in their first year would have been as susceptible as the present day soldier.

(2) There were fewer Egyptian food-handlers in contact with the army personnel during the war. The writer made enquiries on this point from the Director of Pioneer and Labour, Middle East, and got the reply that the British Army employed numerous Egyptians as food-handlers during the war.
Incidentally the post-war camps are of a more permanent nature than the war-time ones.

(3) The standard of hygiene during the war was much higher in Egypt than it was after that period on the Canal Zone. The Army Health Authorities in the Middle East should be required to answer this point, but it is considered they would not agree! They would probably be right.

(4) The types of enteric organisms in Egypt have become more virulent. The type of virulent Salmonella typhi used in preparing T.A.B. vaccine during the past four years has been Ty2, phage type E1. This was the type of organism which caused the Abyad 2 typhoid outbreak!

(5) The possibility of an increased incidence among the civil population. It is impossible to get accurate statistics. The only figures the writer has been able to obtain indirectly are the number of typhoid and paratyphoid admission and case mortality in an Egyptian Infectious Diseases hospital from 1943 to 1947.

Table 27.

Year	Typhoid Fever	Deaths	Paratyphoid Fever	Deaths
1947	826	102	293	9
1946	1218	169	397	23
1945	1228	135	466	36
1944	1073	128	398	18
1943	1112	150	341	10

+ This shows a fairly consistent incidence during the period when the Service cases increased. Unfortunately more recent figures are not obtainable.

Views on T.A.B. vaccine.

The writer concludes that while some of the other factors mentioned may have had a slight influence in increasing the enteric fever incidence since 1945, the most probable factor is the loss in immunising properties of the T.A.B. vaccine used since 1944.

The reasons for this are not clear. Theoretically, and by mouse-protection tests, both the original alcoholised T.A.B. vaccine and the double strength new T.A.B. (A), and also the new T.A.B. (B) phenolised vaccine should be more efficient than the phenolised vaccine in use up till 1943/44. The new T.A.B. (A) and (B) vaccines have been introduced too recently to be assessed, but both showed up badly in Abyad II outbreak. The number of cases was very small however. How far the mouse injected intraperitoneally or even subcutaneously, with a dose of virulent S.typhi is comparable to a human being swallowing a dose of the same organisms, the writer is not prepared to discuss, but can only say in its favour that S.typhi found virulent for man is comparably virulent for mice!

The writer is absolutely convinced that there must be some factor missing

from, or present in inadequate quantities, in all the vaccines made since 1943/44, which was present in the previous phenolised vaccine. After all, the Kasauli-made Indian T.A.B. vaccine was not changed in 1943/44 and the incidence of the enteric group of fevers in India among service personnel did not materially vary (Table 5).

The writer considers that the alcoholised vaccine used after 1943/44 is of some value, it appears to have lessened the mortality after 1947. It must also have some antigenic properties to have produced a lower relapse incidence when used in treatment with chloramphenicol in the interrupted course of treatment of typhoid fever.

What it apparently lacks is a potent anti-invasive factor, an as yet undiscovered antigen - an Ai-antigen! In the earlier part of this survey the development of T.A.B. vaccine was given in some detail. The most noticeable observation is the not inconsiderable number of changes of one sort or another made in the preparation of the vaccine and in the strain of organisms used in the last 6 or 7 years. Perhaps some of these changes have been responsible for the elimination of, or reduction in, this hypothetical Ai-antigen.

Discussion on Certain Features brought out in the Summaries of the Outbreaks.

Appendix 6 (a) (b) (c) and (d).

Diagnosis.

The key to early and accurate diagnosis is Blood Culture. The earlier blood is taken for culture in a febrile condition of uncertain origin, the quicker will a diagnosis of one of the salmonella group be made if the case is enteric. It is pointed out that the older teaching that the organism is most easily isolated in the first week does not necessarily hold good to the same extent with modern cultural methods. It is sometimes easier to isolate the organisms in the second week, and positive cultures may be obtained for the first time quite late in the disease. This points to the necessity for repeated blood cultures. Where a well equipped laboratory with well trained staff is available, the diagnosis should be proved bacteriologically in over 90% of cases; cultures may be positive where there is little or no pyrexia, and few if any symptoms.

Urine and Faeces cultures need only be persisted in for diagnosis where the blood culture is repeatedly negative, and the case is considered enteric fever. Agglutination is of little help in an inoculated community, and comes far behind cultural methods as an aid to diagnosis. The serial rise in titre must be very great indeed to be of real value. It is not worth doing as a routine in the Army.

Rose spots. In one case of paratyphoid B infection the organism was isolated from a rose spot on the abdomen!

White cell counts. These are frequently within normal limits and are not of much help; they are of greater value as a negative point if a high polymorph leucocytosis is found. A large proportion of undiagnosed pyrexias in the

tropics have a normal or slightly low white cell count.

The differential diagnosis of the paratyphoids from typhoid must in the long run depend on culturing the organism. Clinically in an outbreak of paratyphoid only, one can suspect new cases, but in a country where typhoid and paratyphoid A and B so often occur at the same time, the causative organism must be isolated by blood culture or by other means to arrive at a correct diagnosis.

The Early Temperature Chart.

Although the classical step-ladder onset of typhoid may occur, it is often absent. The temperature chart varies enormously in different outbreaks, and also in the same outbreak, and by itself is not a great help in diganosis. It is important to realise that there may be a preliminary pyrexia of a few days and then an apyrexial period, or a low running temperature for about 10 days, followed by an abrupt onset of the real major attack. It is also important to remember that one can get an intermittent temperature perhaps up to 104° or 105°, and often with a double daily peak in the 4-hourly chart. Intermittency was a feature of many of the Abyad II cases. Again, the writer has seen a steady high temperature resembling a lobar pneumonia chart in a proved case of typhoid without evidence of chest involvement.

Pulse rate.

The relatively slow pulse is often seen in the earlier stages, while a persistent tachycardia may remain during the first part of the convalescent period.

Early symptomatology.

This varies somewhat in different epidemics, but is often relatively consistent in any one outbreak. Headache is the most constant symptom in all cases. Digestive symptoms come next, either anorexia or abdominal discomfort or both, also nausea. General malaise is usual. Constipation is quite common, and diarrhoea is much less frequent at an early stage. Stiffness of the neck is fairly common, also joint pains and backache. The classical symptom of epistaxis varies greatly in its frequency. Sore throat and coryza also vary in incidence. Once an epidemic starts, the pattern of the early symptomatology is of great help in picking out and isolating new suspects at an early stage. Among the rarer clinical features at onset, dysenteric-like stools, and haemoglobinuria, have been mentioned.

Signs.

The earliest and most frequent sign is the furred tongue. Splenic enlargement is a later manifestation. It appears in less than half the cases.

Exanthem. The relative infrequency of rose spots is somewhat surprising, the average is probably not more than a third of the cases, though individual outbreaks vary. The extent of the rash also varies greatly in any epidemic.

Exceptionally it is as profuse as that of measles, and extends beyond the trunk to all the limbs. It is of no prognostic value.

The type of eruption does not often help in distinguishing the paratyphoids from the typhoids. In the Shubra outbreak of paratyphoid B, only one case had a rash, and one a palpable spleen.

Complications.

The enteric group can probably produce a greater variety of complications than almost any other infection. One has only to peruse any new or old textbook to appreciate this. The list given in appendix 6 (d) is by no means complete even for the Middle East, and in some of the smaller outbreaks, and in sporadic cases, others were met with. For instance, cases of cholecystitis due to S.typhi and to S.paratyphi B have been operated on, calculi removed, and the organisms isolated from the gall-bladder. One case of liver abscess which failed to respond to emetine was found at operation to be due to S.paratyphi B!

Summary.

As a background to the present survey, and for purposes of comparison, a brief historical account of the enteric group of fevers is given. Reference is made to a number of civil outbreaks.

Figures are quoted showing the high incidence in some of the older wars, including the South African War. An account of the history and development of the British Army antityphoid and anti-paratyphoid vaccine is included. Evidence is produced to show its effectiveness in reducing the incidence and mortality, especially in typhoid fever, in the 1914-18 war.

Its deterioration during the inter-war period is commented on, and the steps taken to investigate the cause, and to rectify successfully the defect by rejuvenation of the Rawling's strain of Bact. typhosum are referred to. How far this was successful was shown by the immediate drop in the incidence of typhoid in India - at that time the main source of enteric cases in the Army.

Before the 1939-45 war the Indian Medical Service took over the preparations of its own vaccine at Kasauli Research Institute. It was somewhat different in constitution from the home vaccine in that it always included a local 'wild' strain of typhoid organism. It remained basically unchanged during the war years and after, likewise the incidence of enteric in the army in India remained low throughout.

The British T.A.B. vaccine proved its efficiency once more during the 1939-45 war in the Middle East. Here also the incidence of enteric among the large bodies of troops at the base in Egypt, and engaged in the battles in North Africa, remained comparatively low.

During this time Boyd was able to compare the British T.A.B. vaccine with that used by the Italians and Germans, and to show how poor were the protective qualities of the Axis' vaccine, both for men and for mice!

As a result of Felix's discovery of Vi-antigen, and its better preservation by using alcohol as the killing and preserving medium in the preparation of the vaccine, a new alcoholised vaccine was introduced into the Army late in 1943. By 1945 most of the Army had been immunised by this preparation. It contained only half the number of organisms of the previous vaccine. In the Middle East from the latter half of 1945 the incidence of enteric steadily rose. In B.A.O.R. also, in 1944, one unit had an outbreak with a high proportion of those at risk contracting typhoid. Unfortunately there was some uncertainty as to which vaccine had been used in their latest inoculations.

During 1946 and 1947 the incidence in the Middle East continued to rise, due partly to numerous outbreaks, but also to many sporadic cases. The death rate was relatively high.

A number of outbreaks are described; in some a large proportion were infected among those at risk; an instance is the Acre outbreak of combined typhoid and paratyphoid B fever in 1948, with a 61% incidence. This occurred

in spite of the very large proportion of the cases having had a satisfactory inoculation record.

Several other outbreaks with unusual features are recorded, in all of which the inoculation state was satisfactory. A noticeable reduction in the mortality took place from 1948 onwards, apart from any specific treatment. There was a very slight drop in the incidence of these infections in the Army after 1948.

Since August 1948 practically all the cases in the Middle East have occurred in the Canal Zone. The epidemiology of enteric in Egypt is discussed, and the possible reasons for its high post-war incidence stated.

In order to test if the alcoholised type of vaccine was inferior to the older phenolised T.A.B., two new vaccines were prepared, T.A.B. (A) an alcoholised vaccine double the strength of the previous one, and T.A.B. (B), a phenolised preparation which was not quite comparable to the previous phenolised vaccine.

These were introduced in 1949 and given to men according to their personal numbers. Although sufficient numbers of cases from among those inoculated have not yet contracted enteric fever to assess T.A.B. (A) and (B), there appears to be little difference between them. In one of the outbreaks affecting men protected by these vaccines, over 50 percent of those at risk were attacked!

The course of enteric in the Royal Air Force in the Middle East is also traced. Their incidence rose somewhat during the war, but more so afterwards. The culmination was the two large outbreaks of typhoid fever at Abyad in the Canal Zone in 1950, when over 300 cases occurred from the same mess, in spite of a reasonably high inoculation state with alcoholised vaccine.

The various specific forms of treatment tested in the Middle East are referred to; finally in 1949 chloramphenicol was introduced, and exceeded even the highest expectations in its efficiency, cutting short the disease, and reducing the mortality to negligible proportions.

The one disadvantage of this new antibiotic is its apparent interference with the natural development of immunity, and a consequent marked increase in the relapse incidence. After trying different schemes of treatment one was at last found which greatly reduced the number of relapses. It consisted of a combination of small daily T.A.B. injections with an interrupted chloramphenicol course.

For purposes of comparison, and to stress the points of interest which have been brought out in the various epidemics in the Middle East, a tabular summary of the principal outbreaks of typhoid and paratyphoid fever which occurred during the period under review is set out in an Appendix. The relative frequencies of the various features are shown as percentages.

The diagnosis, the early clinical features, and the complications, are then discussed briefly.

In conclusion, the writer maintains that this survey indicates how essential it is that research on the qualities necessary to improve the antigenic properties of the T.A.B. vaccine should continue.

If outbreaks akin to some of those described occur in the future, perhaps among much larger concentrations of men, they might indeed have very serious consequences.

In the mean time every possible step must be taken to safeguard food during its preparation, cooking, distribution, and serving, also crockery and cutlery during the process of collecting, washing, and re-issue. A substitution of British food-handlers for those locally employed would solve the problem in the Middle East, but it has to be accepted that this is not a practical proposition at present, owing to man-power shortage. More than ever it is essential to maintain the very highest hygienic standards in everything pertaining to food and water in the Services.

Appendices.

1. Incidence of Enteric Fever among British Army Troops in Middle East by Commands. 1943 - 1946. Annual Rates per 1,000 Strength.

2. Incidence of Enteric Fever among R.A.F. and British Army Troops in Middle East, 1945 - 1950. Annual Rates per 1,000 Strength.

3. Incidence of Enteric Fever in Middle East, 1946 - 1947. Monthly rates per 1,000 Strength.

4. Incidence of Enteric Fever among British Army Troops in Middle East, 1943 - 1950. Monthly Rates per 1,000 Strength.

5. Outbreak of Typhoid and Paratyphoid Fever among Units of the British Army in 1947.

6. Summaries of Main Outbreaks of Enteric Fever in Middle East. 1948 - 1950.

   (a) General Features.
   (b) Symptoms.
   (c) Signs.
   (d) Complications.

APPENDIX I

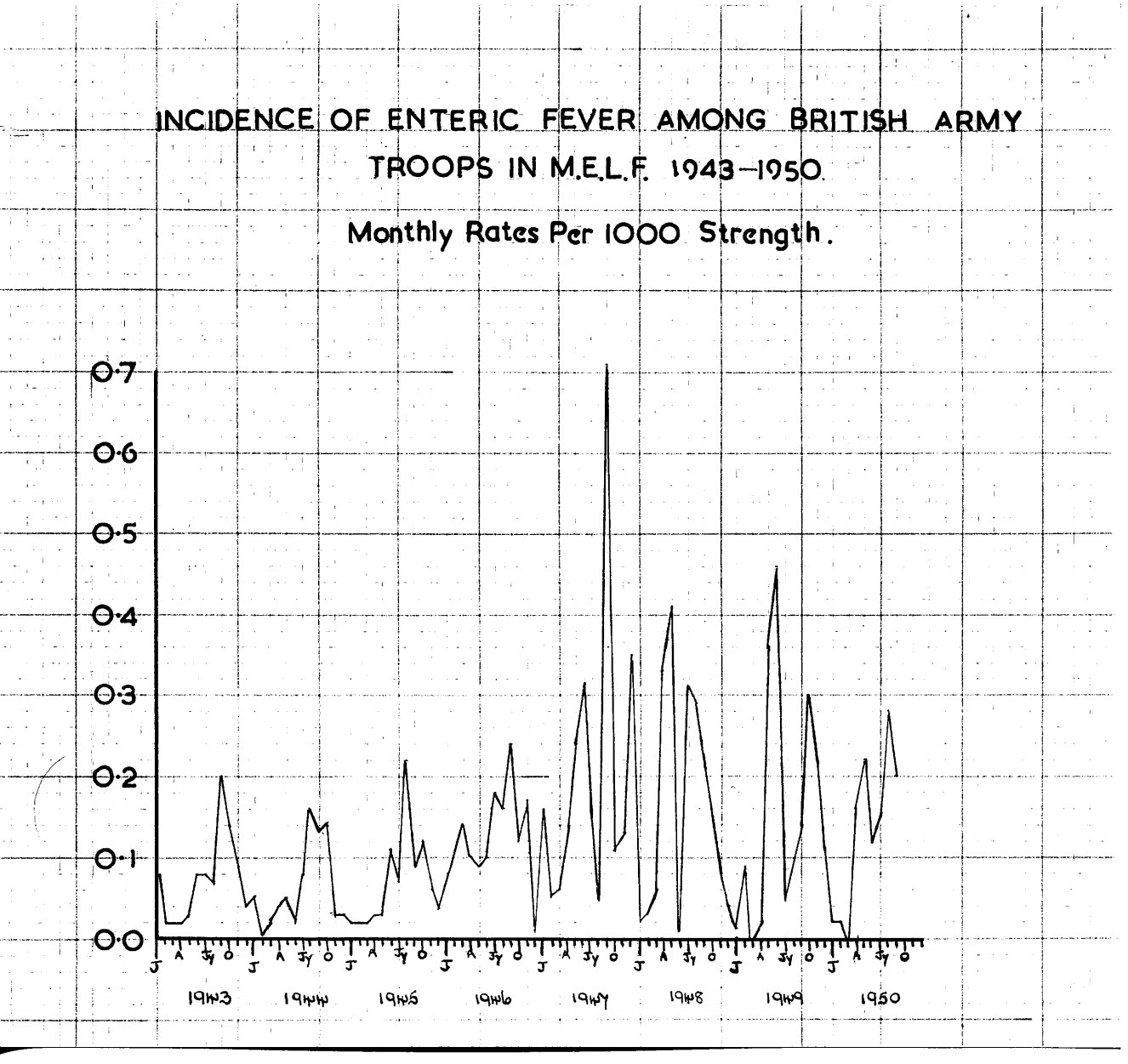
Incidence of Enteric Fever among British Army Troops in M.E.F. by Commands

Annual Rates per 1,000 Strength

	1943	1944	1945	1946
Egypt	-	0.58 (71)	0.55 (42)	1.66 (125)
Cyrenaica	0.87 (237)	0.41 (3)	0.31 (1)	0.36 (1)
Tripolitania	-	0.22 (1)	-	2.41 (9)
Palestine	0.38 (15)	0.42 (17)	1.43 (49)	1.00 (57)
Syria	0.55 (17)	0.07 (14)	1.00 (11)	1.48 (7)
Cyprus	1.08 (4)	-	-	-
Sudan and Eritrea	1.99 (7)	0.73 (2)	0.43 (1)	1.40 (3)
Malta	0.49 (7)	-	-	-
Aden	-	3.57 (2)	-	-
P.A.I. Force	-	-	0.99 (10)	3.19 (10) (Iraq)
Greece	-	-	-	1.28 (37)
Total M.E.F.	0.78 (287)	6.55 (110)	0.81 (114)	1.44 (249)

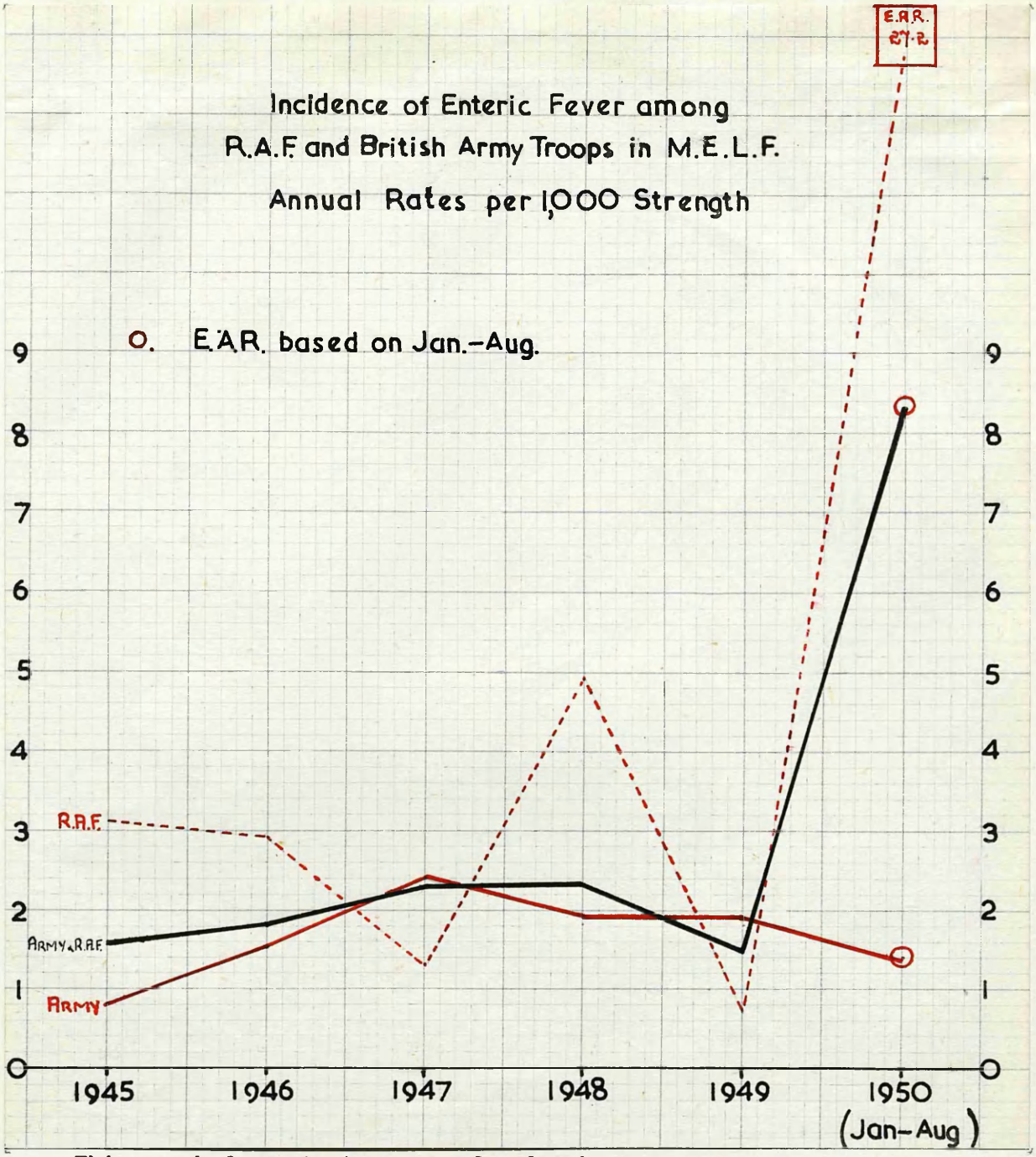
This table shows that Egypt and Palestine are responsible for the largest number of cases. Egypt shows a three fold increase in 1946 over the previous figures. Palestine shows a corresponding increase in 1945, which drops slightly in 1946. The somewhat high figure for Cyrenaica in 1943 is possibly an aftermath of El Alamein and the heavy fighting that followed.

Appendix 2



This graph shows the seasonal incidence of the enteric group of fevers among British troops in the Middle East. The figures are lowest during the first quarter and at the end of the year. The peak periods occur during the second and third quarters.

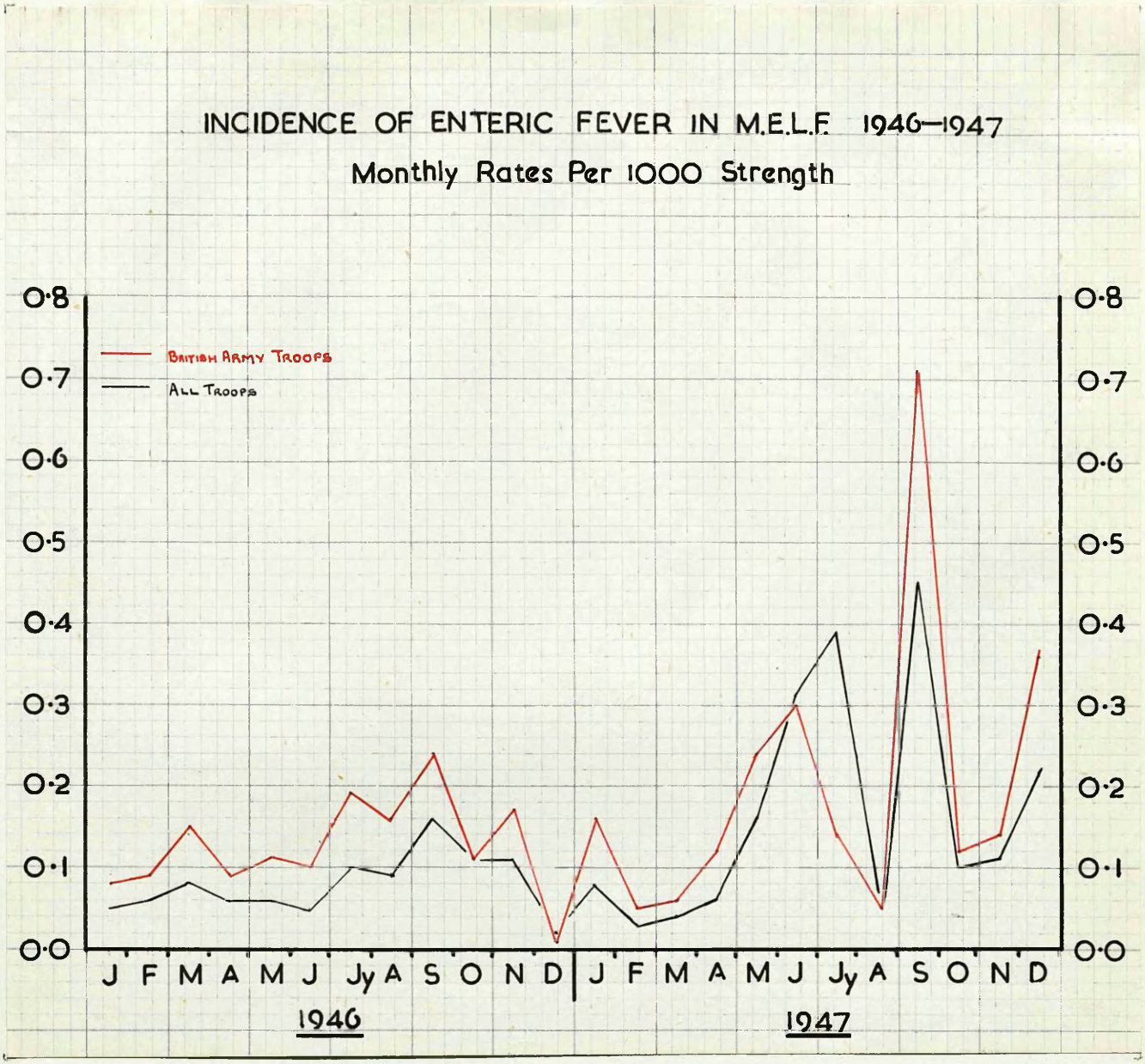
Appendix 3



This graph demonstrates more clearly the same trend as Appendix 2. The Royal Air Force Incidence and the total incidence are shown for comparison. The much greater annual variation of the R.A.F. figures is well brought out. The figures depend more on large outbreaks among a much smaller total strength than that of the Army.

The very high peak in 1950 of 27.2 per 1,000 is due to the two typhoid fever outbreaks at Abyad.

Appendix 4



This graph shows a comparative monthly incidence of enteric fever for British troops, and for British plus locally enlisted troops. The incidence among the latter is so slight that it hardly alters the nature of the graph.

The multiple peaks in 1946 give an indication of the fact that the incidence was made up of many outbreaks.

APPENDIX 5

Outbreaks of Typhoid and Paratyphoid Fever among Units of the British Army in 1947.

	Month	Type of Organism	Station	Number of Cases
1.	Jan - Feb.	B. typhosum type "F"	Alexandria	20
2.	March	" "G"	Tel El Kebir Egypt (Canal Zone)	6
3.	March	" "B2"	Port Said	9
4.	April	" "Imp VI"	Fayid Egypt (Canal Zone)	5
5.	May	" "E"	Lamli Sarafand (Palestine)	29
6.	May	" "Imp VI"	Fayid	6
7.	May	" "A"	Famagusta (Cyprus)	15
8.	June	" "Imp VI"	Tunisia	3
9.	June	" "E"	Shandur Egypt (Canal Zone)	5
10.	June	" A typical 2	Salonika	11
11.	Sept.	B. paratyphosum A	Nicosia (Cyprus)	87
12.	Sept.	B. typhosum type "C"	Qassasin Egypt (Canal Zone)	4
13.	Sept.	B. typhosum	Jerusalem	24
14.	Sept.	B. paratyphosum B.	Gaza (Palestine)	5
15.	Nov.	"	Palestine	10
16.	Dec.	"	Nazareth	40
			Total Cases	259

The large outbreak of Paratyphoid A in September was exceptionally mild. Out of the 87 cases 49 had no abnormal signs.

APPENDIX 6

(a) (b) (c) (d)

Comments on figures in Summaries of Larger Outbreaks in Tabular Form

In certain instances it has not been possible to give precise figures, e.g. the exact number of cases in the Shubra outbreak with negative cultures for S. paratyphi B which were clinical paratyphoid.

Where percentages have been worked out they have been given to the nearest whole number, except in Abyad I and II Outbreaks, as whole numbers are adequate for comparison.

In dealing with inoculation states and with clinical features only percentages have been given.

Appendix 6 (a)

Summary of Larger Outbreaks of Typhoid and Paratyphoid B Fever

	Acre, Palestine April-June, 1948 Typhoid and Para B.		Shubra, Egypt June-August, 1948 Para typhoid B.		Fayid, Egypt July-November 1948 Sporadic cases - Typhoid	Mackinnon Road April-July, 1949 Typhoid		@ Abyad I April-May 1950 Typhoid		@ Abyad II July-August, 1950 Typhoid	
	Army	Palestine Police	R.A.F.	Army	Army	British	Africans	R.A.F.	Army	RAF	Army
Approximate Numbers at risk	107	64	750	-	-	300	-	657	29	630	27
Source	Presumptive evidence of water supply.		Not definitely traced.		-	Not traced.		Not traced.		Not traced.	
Number of Cases	65 61%	11 17%	49 7%	4	29	35 12%	61	92 14%+	4 14%	214 34%	15 56%
Total	76		53		29	96		96 X		299 Ø	
								61 Ø	4		
Diagnosis:											
Blood Cultures	+ 71 93%		42 79%		26 90%	21 60%	12 20%	59 Ø) 95%		206)	)95%
Faeces "	3 4%		)		-	-	-	3 Ø		11)	
Urine "	-		) 10 19%		2 7%	-	-	-		1)	
Clinically	2 3%		Many doubtful suspects		1 3%	14 40%	54 89%	3 Ø		6 +5 agglut	
Phage types	T		3ai		N,C,G,O,A.			J		E1	
Severity Mild	30 39%		Practically 100%		)	13 37%	29 48%	28%		27	12%
Moderate	17 23%				) 13 45%	12 34%	13 21%	50%		105	48%
Severe	29 38%				16 55%	10 29%	24 39%	22%		86	60%
Relapses	Nil		5 9%		2 7%	2 6%	3 5%	Relapses varied from 47.6% to 4.2% according to treatment.			
Deaths											
Toxaemia	2) 4%	Nil	Nil		-	1) 6%	4) 11%	Nil		1)	
Bowel Haemorrhage	1)				1) 7%	1)	-)			-) 1%	
Perforation	-				1)		1)			1)	
Other causes	-				-		2)			-	
Inoculation State:											
T.A.B. within 12 months	100%		X 86%		79%	92%	94%	95%	2	87%	93%
" " 6 %	88%		60%		21%	-	-	52%	-	39%	53%
No record			7 cases					2	1	2	-

+ S. typhi 44
S. paratyphi B. 3
Both S.typhi and S.paratyphi B. 27

X Excluding suspects

@ Previously named Shubra

Ø Numbers treated in Military Hospital, Fayid.

APPENDIX 6 (b)

Summary of Presenting and Early Symptoms

	Acre Typhoid and Para.B.	Shubra Para.B	Fayid Sporadic Typhoid	Mackinnon Road Typhoid		Abyad I Typhoid	Abyad 2 Typhoid
				British Majority	African Majority		
Headache	99%	98%	90%	-	-	79%	62%
Dizziness	92%	-	-	-	-	6%	10%
Cough	76%	10%	21%	-	-	28%	19%
Backache	76%	2%	-	-	-	14%	19%
Abdominal discomfort or pain	73%	21%	-	-	-	22%	15%
Anorexia	73%	81%	69%	)Uncommon but		40%	38%
Nausea	55%	)	17%	)anorexia more often		16%	14%
		) 17%		)met than other		[illegible]	[illegible]
		)		)symptoms			
Vomiting	4%	)	14%			13%	13%
Insomnia	54%	37%	-	-	-	-	-
Malaise	-	10%	90%	-	-	40%	41%
Neck stiffness and pain	39%	-	10%	17%	5%	16%	39%
Joint and Muscle pains	-	-	7%	-	-	10%	13%
Constipation	36%	33%	31%	26%	11%	32%	25%
Coryza	34%	-	-	-	-	5%	2%
Sore throat	-	12%	3%	17%	5%	11%	4%
Diarrhoea	19%	16%	28%	49%	44%	9%	6%
Dysenteric symptoms	-	-	-	9%	15%	-	1%
Epistaxis	11%	4%	3%	9%	2%	21%	7%
Nightmares	5%	-	-	-	-	-	-
Frequency or Dysuria	-	2%	-	-	-	2%	-
Retention of urine	-	-	-	-	-	3%	-
Haemoglobinuria	3%	-	-	-	-	-	-
Shivering	-	2%	-	-	-	-	-
Rigors	-	-	14%	-	-	-	-

APPENDIX 6 (c)

Summary of Signs

	Acre	Shubra	Fayid	Mackinnon Road		Abyad I (Before Chlor.) started	Abyad II (Before Chlor.) started
				British	African		
Tongue coated	Majority	67%	76%	Majority	Majority	5%	63%
Spleen enlarged	59%	2%	28%	20%	18%	41%	37%
Rose spots	60%	2%	24%	26%	-	8%	40%
Pyrexia	1 day to over 12 weeks	1 to 29 days	10 days to over 12 weeks	11-46 days average 25.7	Up to 48 days average 21.7	The pyrexial period depended almost entirely on the day of illness chloromycetin was commenced.	
Meteorism	(Unknown)	-	(Unknown)	rare	rare	8%	15%

Appendix 6 (d)

Summary of Complications

	Acre Typhoid and Para.B	Shubra Para.B	Fayid Typhoid	Mackinnon Road Typhoid		Abyad I Typhoid	Abyad 2 Typhoid
Number of Cases	76	53	29	35 Br.	61 Af.	65 (in BMH)	229 (in B.M.H.)
Intestinal haemorrhage	4%	-	-	3% (1 case)	-	-	1 case
Intestinal perforation	-	-	-	-	2% (1 case)	-	1 case
Splenic Infarcts	3%	-	-	-	-	-	-
Cholecystitis or tender gall-bladder	-	-	-	3% (later)	-	3% (2 cases)	4%
Stomatitis	-	10%	-	-	-	-	6%
Glossitis	-	-	-	-	-	3%	2%
Venous thrombosis	4%	-	1%	3%	2%	3% (1 femoral) (1 cerebral)	1% (2 cases)
Pericarditis	-	-	-	-	2%	-	-
Tachycardia	-	-	11%	-	-	-	-
Haemoglobinuria	3%	-	-	-	-	-	-
Epistaxis	20%	-	-	-	-	21%	7%
Pharyngitis	8%	-	-	-	-	11%	8%
Bronchitis and	) 21%	-	)	23%	14%	8%	12%
Bronchopneumonia	)		) 9%	3%	6%	-	1%
Pleural effusion	-	-	-	-	-	2% (1 case)	-
Haemoptysis	-	-	-	-	-	2% (1 case)	-
Tremor	17%	-	-	-	2%	-	-
Increased tendon reflexes and clonus.	17%	-	-	-	-	-	-
(Depressed tendon reflexes)	-	-	-	-	-	-	-
Peripheral neuritis	-	-	-	-	-	-	1%
Paraesthesia and hypoaesthesia	8%	-	-	-	-	-	1%
Pruritis	-	-	-	-	3% (2 cases)	-	-
Nystagmus	1%	-	-	-	-	-	-
Deafness	)	-	-	-	-	-	1%
	) 14%						
Slurring of speech	)	-	-	-	-	-	-
Tender Toes	12%	-	-	3%	2%	-	-
Meningitis	-	-	-	-	3%	-	-
Acute mania or mental disorder	-	-	-	-	5%	5%	3%
Otitis media	4%	-	-	-	-	-	-
Thining of hair	)late	-	2%	3%	-	-	-
	)compli-						
Boils or carbuncles	)cation, %	-	-	-	5%	-	-
	)not available						
Conjunctival haemorrhage	-	-	-	-	-	-	1 case
Periostitis	-	-	2%	-	-	-	-
Hyperpyrexia	-	-	-	-	8%	-	-

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ADDENDA

Abyad II Outbreak of Typhoid Fever.

i. Since this Survey was written further reports have been received which show that in addition to the five cases treated in the Military Hospital Fayid who contracted typhoid fever in both outbreaks about twice that number were ill in both; these were treated in other hospitals.

This adds further support to the views expressed regarding the probability that chloramphenicol interferes with the development of natural immunity.

ii. A complete analysis of the inoculation state of the R.A.F. personnel at risk in the outbreak, the types of T.A.B. vaccine used, the age of the vaccine, and length of time from the last inoculation to the period of the outbreak has been made by Group Captain J. Hill.

Though the precise figures cannot be quoted here, there is nothing in the analysis to indicate that the factors analysed had much effect on the incidence of the infection. This all tends to confirm the opinion expressed regarding the inefficiency of these vaccines.