Typhoid and paratyphoid fevers / prepared by the Standing Medical Advisory Committee for the Central Health Services Council and the Ministry of Health.

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Great Britain. Standing Medical Advisory Committee.
Central Health Services Council (Great Britain)
Great Britain. Ministry of Health.

Publication/Creation

[London] : Ministry of Health, 1965.

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TYPHOID AND PARATYPHOID FEVERS

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Prepared by
The Standing Medical Advisory Committee
for the
Central Health Services Council
and the Minister of Health

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MEMORANDUM ON TYPHOID AND PARATYPHOID FEVERS

Summary

There was a dramatic fall in the number of deaths due to typhoid and paratyphoid fevers in England and Wales from 1871 to the early 1930s, associated with improved water supplies and sanitation generally. The introduction of chloramphenicol as a specific form of treatment in 1948 further reduced mortality. Typhoid fever is now mainly sporadic in England and Wales and about half the cases acquire infection abroad.

Typhoid or paratyphoid fever should be considered as a possible diagnosis in any person who has had unexplained pyrexia for three days or more; if the patient has recently been abroad it should be considered from the first day of illness. The Medical Officer of Health should be notified, preferably by telephone, immediately a case is suspected. Culture of blood, faeces and urine and a Widal test should be done immediately; early diagnosis is vital from both epidemiological and clinical points of view.

Two or three per cent of persons contracting typhoid fever may expect to become permanent carriers and the likelihood of this increases with age; women over 40 are particularly vulnerable. Treatment of the carrier is still unsatisfactory but a prolonged course of ampicillin in high dosage together with probenecid has yielded promising results.

Effective T.A.B. inoculation is recommended for all persons going abroad and will normally be done by their own doctor.

TYPHOID AND PARATYPHOID FEVERS

Although undoubtedly of considerable antiquity it was not until the early 19th century that typhoid fever was recognised as a separate clinical entity. In 1880 Eberth discovered the causative organism and in 1896 Achard and Bensaude first distinguished typhoid and paratyphoid fevers. Typhoid fever and enteric fever are notifiable under the Public Health Act, 1936. Enteric fever comprises typhoid fever and paratyphoid fevers A, B and C.

Incidence

During the half century prior to 1930 there was a dramatic fall in the number of deaths due to typhoid and paratyphoid fevers associated with improved water supplies, sanitation and standards of

hygiene generally. Since 1930 the fall has been much more gradual, signifying that by then improvements in sanitation had probably had their maximum effect in controlling the disease.

Typhoid and paratyphoid fevers have been separately reported to the Registrar General's office since 1941. Table 1 sets out the total yearly corrected notifications, deaths and fatality ratios due to typhoid and paratyphoid fevers in England and Wales since that time. Reduction in fatality ratios from 1948 onwards was undoubtedly associated with the introduction of chloramphenicol as a specific form of treatment.

There is evidence that in recent years about half the number of cases of typhoid fever occurring in England and Wales contracted infection abroad, and all persons going abroad are advised to be effectively vaccinated against typhoid and paratyphoid fevers. It will be seen in Table 2, compiled from figures published in the 1961 report of the World Health Organisation, that the incidence of these fevers is particularly high in Austria, Spain, Italy and Portugal.

Spread of typhoid fever

The reservoir of typhoid infection is invariably human, but outbreaks are usually associated with food or drink which has been contaminated by an infected person. Typhoid organisms can survive for several weeks in water. In communities with low standards of sanitation water supplies are particularly liable to contamination. Recognition of this fact has led to strict supervision of waterworks and employees in such undertakings. The Croydon outbreak of typhoid fever (1937) was the last example in this country of a major water-borne outbreak and it is a salutary reminder of the havoc which can be created by a contaminated drinking-water supply. There was strong evidence that a chronic typhoid carrier, working in an Addington well during the relevant period, was responsible for infecting the water supply. Untreated water from this well had been pumped into supply during the time work was in progress. Over 300 persons in the borough and about 30 persons residing in other districts were infected in Croydon. There were 43 deaths.

A more recent example of an outbreak, in which circumstantial evidence pointed to the contamination of supplies of drinking water, was that associated with Zermatt in March 1963. A total of 68 bacteriologically confirmed cases of typhoid fever in England and Wales occurred among persons who had recently returned from holiday in Zermatt. It is noteworthy that, in spite of this considerable

importation of infection, only one secondary case is known to have occurred in Britain. This illustrates the relatively unimportant role of person to person contact in the spread of this disease.

Food such as shellfish contaminated by infected water or sewage has also been the source of typhoid outbreaks. Contaminated milk and ice-cream have been associated with large outbreaks of typhoid fever. Milk may be contaminated directly by an excreter or indirectly e.g.. through contaminated water used for cleaning milking utensils: in the latter event the outbreak would in the strict sense be water-borne.

A notable example of milk-borne typhoid infection is the Bournemouth outbreak of 1936. In August and September of that year more than 500 cases were notified in Bournemouth, Poole and Christchurch and approximately 200 other patients who had been on holiday in these towns developed typhoid fever after returning home. It was established that all primary cases had consumed raw milk retailed by one firm which in turn was supplied by farms scattered throughout Dorset. Typhoid organisms were recovered from a stream which flowed through the grounds of two of these farms. Subsequent investigations brought to light a chronic typhoid carrier living in a large house from which sewage spilled into the stream.

Aberystwyth provides a good example of an outbreak in which ice cream proved to be the vehicle of infection. During the summer of 1946 over 90 cases of typhoid fever occurred in the borough, 30 more in the rural districts and about 75 in other parts of the country among holidaymakers who had been infected in Aberystwyth. The source of infection was speedily traced to an ice cream vendor who had suffered from typhoid fever in 1938. Tests showed that he was a chronic carrier.

More recently canned meats have been recognised as a potential vehicle of typhoid infection. Outbreaks in Harlow, South Shields and Bedford during 1963 and in Aberdeen during 1964 were all associated with corned beef in 6 lb. cans, opened and sliced before sale. An earlier outbreak at Pickering in 1955 was attributed to canned tongue.

Canned meats have previously been regarded as the safest of foods and spread of infection by this means has hitherto been thought to be due to contamination of the meat after removal from the can. In the four recent outbreaks there was strong circumstantial evidence that the corned beef was already contaminated before the can was

opened. No evidence of contamination by a pre-existing carrier working on the premises was obtained in any of these outbreaks after careful screening of the staff. Moreover, the same brand and pack of corned beef was implicated in each of the three English outbreaks. The factory producing this meat had been using untreated river water for cooling the cans in the autoclave. It was possible, therefore, that the meat in defective or perforated cans could have been contaminated with polluted river water. Though such contamination would normally result in blowing of the can with spoilage of the contents, it is now clear that pathogenic organisms may occasionally be present in cans which appear to be undamaged and the contents wholesome.

Spread of paratyphoid fever

Paratyphoid fever acquired in Britain is almost always due to paratyphoid B organisms. The principal reservoir of infection is human but paratyphoid B fever is usually spread by contaminated food, often imported food such as coconut or bulked Chinese egg. The source of an outbreak in Redditch in 1961 was traced to coconut biscuits. The coconut, which was imported from Ceylon, was found to be infected with paratyphoid B organisms. The Ceylon Government has since introduced Regulations designed to render this product free from contamination.

During 1963 there were several outbreaks of paratyphoid B infection in England associated with bakeries, all due to the same type (phage-type Taunton). The source was traced to imported bulked Chinese egg which had been used by all the bakeries concerned. Regulations were introduced early in 1964 requiring all imported whole egg to be pasteurised.

The Sporadic case

It is not always easy to detect the source of infection in the sporadic case, although a persistent excreter in the family or among other close contacts may be brought to light by the 'screening' which is done routinely by the medical officer of health whenever a case is notified. Screening implies repeated bacteriological tests of faeces and urine supplemented by the Widal test. The latter test detects antibodies in the patient's blood resulting from infection with typhoid or paratyphoid bacilli. These organisms possess somatic or '0' and flagellar or 'H' antigens and the typhoid bacillus possesses in addition a surface or Vi antigen believed to be associated with virulence. Specific antibodies in response to these antigens appear in the patient's blood

at some stage during the illness, but Vi antibodies are also present in the blood of a high proportion of chronic typhoid carriers; hence the value of the Widal test as a screening procedure.

Bacteriophage typing of typhoid and paratyphoid bacilli has proved a useful aid in identifying the source of infection. Phage-typing is a specialized procedure and is carried out in this country only at the Enteric Reference Laboratory at Colindale. Over 80 phage-types of the typhoid bacillus have now been identified.

The value of phage-typing in tracing the source of infection was well demonstrated in "The Tale of the Leavetaking Colonels" (Bradley 1949). During the preparations for D-Day several high ranking officers who had been staying at an hotel in Cornwall developed typhoid fever and one died. Investigations revealed that there had been typhoid incidents associated with this hotel in 1941, 1942 and 1943. A person living in the hotel during relevant periods was known to have had typhoid fever in South Africa during the Boer War and screening tests showed that he was still excreting the organism. Sewage from the hotel ran into a cesspit from which untreated effluent trickled down a drain passing within 20 yards of the well-head supplying water to the hotel. Links connecting carrier and patients were thus established but the point was conclusively proved when it was shown that organisms isolated from cases and carrier belonged to the same phage-type, one not hitherto encountered in this country. The carrier remembered the stream from which he had been infected during the Boer War and it was learned that cases were still occurring in the locality due to organisms of the same phage-type as had infected him 43 years previously.

Diagnosis

It is not usually difficult to diagnose the established case of typhoid fever but, from clinical and epidemiological viewpoints, early diagnosis is essential. Typhoid or paratyphoid fever should be considered as a possible diagnosis in any patient who has had unexplained pyrexia for three days or more. If the patient has recently been abroad, the diagnosis of typhoid or paratyphoid fever should be considered from the first day of illness. At this stage it is unlikely that there will be well established clinical signs to enable the physician to make a confident diagnosis, and laboratory aids must be sought. It is worthwhile remembering that the patient may be constipated in the early stages of the disease or may present with bronchitis.

The most useful test at this stage is blood culture. Specimens of faeces and urine should also be cultured, although they may not be positive until later in the illness. The Widal test should also be done at this stage because, even if it is negative, the reading will act as a standard to compare with subsequent tests. Sufficient serum should be drawn to permit titration in parallel with later specimens.

Collecting sets for blood specimens can be obtained from local Public Health Laboratories. These sets are equipped with a sterile syringe and needle, a bottle containing a blood culture medium, and a sterile test tube. Containers are also available for faeces and urine samples. Ten millilitres of blood should be withdrawn from the patient by venepuncture: half should be placed in the sterile test tube for serological analyses, and half in the blood culture bottle. Specimens of faeces and urine should be placed in the containers provided.

If a Public Health Laboratory is not locally available advice should be sought from the most convenient general hospital.

Organisms responsible for typhoid and paratyphoid fevers belong to the *Salmonella* group comprising some 800 different "serotypes". Most of these types do not give rise to systemic invasion and cause only local inflammation of the gastro-intestinal tract, which results in the 'food poisoning' type of clinical picture. *S. typhi*, *S. paratyphi A B* and *C*, and, rarely, other *Salmonella* species may, on the other hand, produce systemic infection with prolonged pyrexia, prostration and the characteristic clinical picture of 'enteric' fever.

Treatment

All patients suffering from typhoid or paratyphoid fever should be treated in a special unit for infectious diseases. It is generally recognised that chloramphenicol is the antibiotic of choice in treating typhoid and paratyphoid fever during the acute stage of illness. Many authorities advocate the additional use of steroids, e.g. prednisolone, in severely ill patients, particularly when response to antibiotic treatment is slow. Relapses are reported to be more frequent in chloramphenicol-treated patients, but there is no evidence that chloramphenicol affects the incidence of the carrier state.

It should be remembered that the polymorphonuclear leucocyte count of the peripheral blood is often depressed in patients suffering from typhoid and paratyphoid fevers. Chloramphenicol, itself a bone marrow depressant, may further reduce the leucocyte count to a

dangerously low level in these conditions; consequently frequent white blood counts are advisable while patients are having chloramphenicol treatment.

The Carrier

After an attack of typhoid or paratyphoid fever the patient often excretes organisms in the faeces or urine for varying periods. If organisms are still being excreted after a year it is unlikely that there will be spontaneous resolution and the patient is then regarded as a chronic carrier. Some will become permanent carriers (2–3 per cent of cases of typhoid fever and rather less of paratyphoid fever.)

Various factors determine the likelihood of a patient becoming a chronic carrier. The risk increases with age, particularly after 40. Patients with pre-existing gall-bladder disease are particularly prone and for this reason middle-aged women are more likely than men to become chronic carriers.

Organisms find their way with bile into the intestine and are then excreted in the faeces. Excretion may be continuous or intermittent although modern methods of examination have shown that intermittent excretion is rarer than was formerly believed.

Undoubtedly the most notorious carrier of all time was "Typhoid Mary" who, while employed as a cook in a private household in New York in 1901, contracted typhoid fever. She became a permanent, profuse excreter of typhoid organisms, infecting a member of the family for whom she worked. In her subsequent career as cook to many households and institutions she left in her wake a trail of typhoid victims until at last permanently detained in North Brother Island. Typhoid Mary is, of course, an extreme example of the potential menace of the chronic carrier but her record illustrates the need for such persons to be scrupulously careful in their personal hygiene and the need to prohibit them absolutely from handling food or drink for public consumption.

The urinary excreter is much less common but more dangerous. Typhoid organisms do not as a rule settle in the genito-urinary tract unless there is some abnormality.

There is still no reliable method of curing the chronic carrier. Where the gall-bladder is shown to be the seat of infection cholecystectomy is rational and in many instances effects a permanent cure. However, many people are understandably reluctant to subject them-

selves to this fairly major abdominal operation, and the patients' general physical condition may contra-indicate it.

Medical treatment has proved disappointing. Chloramphenicol, although effective in treating the acute case of typhoid and paratyphoid fever, is of little value in treating the carrier. Ampicillin given in high dosage over three months supplemented by probenecid, which inhibits excretion of penicillins and thus enhances serum levels of ampicillin, has yielded promising results (Christie 1964). More trials need to be done before this regime can be adequately assessed.

Control Measures

(*a*) *General*

It is important that general practitioners should inform the Medical Officer of Health immediately, preferably by telephone, whenever he suspects that a patient is suffering from typhoid or paratyphoid fever. He should not wait for confirmatory laboratory evidence. Early notification enables the Medical Officer of Health to set in motion machinery for screening contacts and for questioning persons involved at a stage when memory of relevant events is still relatively fresh. Early identification of the source of infection may be vital in limiting spread of the disease.

Basic understanding of the principles of sanitation and sound personal hygiene is probably still the surest barrier against infection. In highly developed countries such as the United Kingdom main water and milk supplies are usually safe, although a small amount of untreated milk is still supplied and this would, of course, be a source of danger if contaminated by a carrier. Recent experience has shown that contaminated food supplies can be a source of major outbreaks of typhoid and paratyphoid fevers. Modern trends in mass production of food with wide distribution render it particularly vulnerable as a vehicle of wide-spread infection. Canned meats, hitherto rightly regarded as the safest of meats, have been revealed as possible sources of typhoid infection in the light of the Harlow, South Shields and Bedford typhoid outbreaks in 1963, and of the Aberdeen outbreak in 1964. The lesson to be learned is that constant vigilance must be maintained both in preparation and distribution of food if future outbreaks are to be avoided. All persons engaged in

the handling of food need to pay scrupulous attention to personal hygiene and all canning factories should use pure and wholesome water for cooling purposes.

(*b*) *Specific*

In 1896 Almroth Wright showed that inoculation of killed typhoid organisms can protect against the disease. During the first World War a phenolised vaccine prepared from heat killed typhoid, paratyphoid A and B organisms was widely used in the Services and, it was claimed, reduced the incidence of typhoid fever. In 1941 Felix showed that the content of Vi antigen was much higher in a vaccine killed and preserved by alcohol than in the heat killed phenolised vaccine. A comprehensive trial of the two vaccines was undertaken by the World Health Organisation in Yugoslavia and it was found that alcoholised vaccine afforded no obvious protection while phenolised TAB has only 70 per cent protective value. (Yugoslav Typhoid Commission, 1957). For the time being, therefore, phenolised vaccine is regarded as the product of choice, but it must be stressed that it affords only limited protection against typhoid fever and may give rise to troublesome local or general reactions.

Administration of TAB vaccine

Dosage varies according to age. For primary immunisation two doses should be given at an interval of 4 to 6 weeks followed by a third dose 6–12 months after the second. Reinforcing doses at yearly intervals are advocated where the subject is at continued risk. All persons intending to travel abroad should be effectively vaccinated against typhoid and paratyphoid fevers. (Ministry of Health, 1962, 1964b). This will normally be done by the individual's own doctor.

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Table I

TYPHOID AND PARATYPHOID FEVERS

ENGLAND AND WALES 1941–1963

Year	TYPHOID FEVER			PARATYPHOID FEVER		
	Cases	Deaths	Fatality Ratio	Cases	Deaths	Fatality Ratio
1941*	1,058	82	7·8	3,705	66	1·8
1942*	468	69	14·7	390	20	5·1
1943*	385	57	14·8	328	15	4·6
1944*	284	45	15·8	258	10	3·9
1945*	301	29	9·6	234	15	6·4
1946	493	38	7·7	736	15	2·0
1947	290	25	8·6	416	16	3·8
1948	369	38	10·3	373	4	1·1
1949	311	19	6·1	582	13	2·2
1950	236	15	6·4	293	1	0·3
1951	206	12	5·8	1,095	9	0·8
1952	135	9	6·7	1,039	12	1·2
1953	101	3	3·0	353	2	0·6
1954	122	4	3·3	548	4	0·7
1955	193	7	3·6	876	8	0·9
1956	136	2	1·5	440	5	1·1
1957	125	8	6·4	310	2	0·6
1958	147	2	1·4	200	2	1·0
1959	123	3	2·4	379	2	0·5
1960	90	2	2·2	241	3	1·2
1961	97	1	1·0	254	1	0·4
1962	127	4	3·1	126	3	2·4
1963	247	4	1·6	342	1	0·3

*Excluding original notifications in Port Health Districts.

Table 2.

Typhoid and paratyphoid fevers reported during 1961

(W.H.O.)

Country	No. of Cases	Pop. in '000s.	Rate per 100,000 pop.
Austria	664	1,660	40·0
Belgium	392	9,184	4·3
Czechoslovakia	845	13,776	6·1
Denmark	32	4,617	0·7
Finland	372	4,467	8·3
France	2,102	45,983	4·6
Germany–E. Ger	1,125	16,061	7·0
,, Fed. Rep.	2,108	54,027	3·9
Greece	1,578	8,402	18·8
Hungary	697	10,028	7·0
Ireland	11	2,815	0·4
Italy	14,420	49,732	29·0
Luxembourg	11	317	3·5
Netherlands	105	11,637	0·9
Norway	14	3,611	0·4
Poland	3,316	29,965	11·1
Portugal	2,067	8,872	23·3
Spain	9,082	30,559	29·7
Sweden	572	7,520	7·6
Switzerland	239	5,496	4·3
U.K.–E. & W.	351	46,269	0·8
,, N. Ireland	16	1,430	1·1
,, Scotland	104	5,226	2·0
Yugoslavia	5,250	18,607	28·2

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