Memorandum on typhoid fever.

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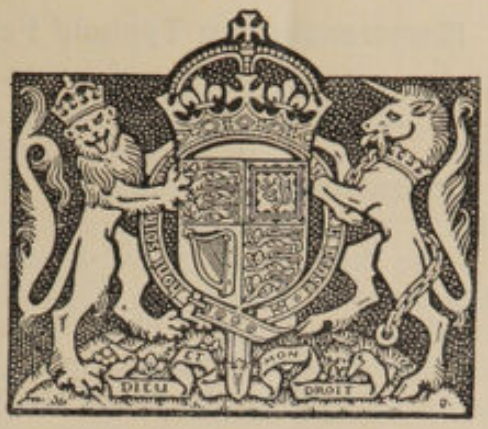

MINISTRY OF HEALTH

MEMORANDUM ON TYPHOID FEVER

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MINISTRY OF HEALTH

Memorandum on Typhoid Fever.

The typhoid (or enteric) group of fevers comprises typhoid fever proper and the three varieties of paratyphoid fever A, B and C. These fevers may be defined as general infections caused by certain organisms of which the *Bacterium typhosum* is responsible for typhoid fever and the *Bacterium paratyphosum A, B* and *C* for the three paratyphoid fevers respectively. The bacilli enter the body through the digestive tract and cause, besides a general toxaemia or " blood poisoning ", a characteristic group of intestinal symptoms by reason of a secondary invasion of the intestine from the blood stream.

Historical Note.

It was not until the middle of the nineteenth century that typhoid fever was formally differentiated from typhus fever. Long before this, however, some physicians, among the earliest of whom was Huxham of Plymouth, were accustomed to distinguish between " putrid malignant fever ", our typhus, and the " slow nervous fever " which corresponded to our typhoid. In 1820, Bretonneau of Tours distinguished " dothinentérie " (enteric fever) as a separate disease and pointed out its contagious nature. Louis of Paris in 1829 first applied the name " typhoid " to the fever. In England, Sir William Jenner, by papers written in 1849 and 1851, confirmed clearly and finally the distinction between " typhoid " and " typhus " which had previously been drawn by Hewett, Gerhard, Stewart and others. The discovery of the bacillus of typhoid fever is generally credited to Eberth in 1880 and it was isolated in pure culture by Gaffky in 1884. The distinction between typhoid and paratyphoid fevers was made by Achard and Bensaude in 1896, and in 1902 Buxton described the two varieties Paratyphoid A and B. Paratyphoid C was identified in 1919 by Hirszfeld; both it and paratyphoid A are rare in this country.

Etiology.

The sole cause of typhoid or paratyphoid fever is the typhoid or paratyphoid bacillus and the sources of these organisms are the faeces, urine and, less commonly, the sputum of persons who have the disease, or the faeces and/or the urine of persons who, while apparently in good health, harbour the organisms in the intestinal or urinary systems (" carriers "). The portal of infection is the digestive tract and the vehicles by which the infection is conveyed are food and drink contaminated by the excretions of a patient or carrier. This contamination may be brought about either by excremental infection of foodstuffs (including drink) in bulk, or by the soiling of the hands of a carrier

or of those in attendance upon a patient, and infection of food by subsequent handling. Infection by hands should not occur with reasonable precautions. Water, however, is the most widely consumed of all commodities and the biggest outbreaks of typhoid fever in this country *in which the source of infection has been ascertained* have been water-borne. In the event of a single person contaminating a water supply many thousands of persons may be at risk. Sporadic cases occurring weeks apart, but re-appearing year by year in a district and giving the appearance of endemicity, may be due to the repeated specific pollution of a water supply and the " endemicity " ceases with the discontinuance or purification of the supply. Moreover, even where large populations are concerned, water-borne infection does not always give rise to " explosive " outbreaks.

A study of the outbreaks which have occurred in recent years shows that, while gross sanitary defects are becoming less and less responsible for the persistence of typhoid fever, special danger lurks in the modern methods of wholesale and wide distribution of milk and other foodstuffs which often make it very difficult to trace the human originator of the infection. The great majority of milk outbreaks have been due, not to direct infection by a carrier but to the washing or rinsing of milk utensils in specifically polluted water; they were to this extent water-borne, as was the case with outbreaks due to the consumption of shellfish gathered from layings polluted by water containing sewage. Thus human dejecta, in one form or another, are responsible for the spread of the disease; their ordinary form is domestic sewage. It is important to note that specific organisms of the enteric group may sometimes be recovered from sewage in the absence of avowed clinical cases in the areas from which the sewage is derived.

Outbreaks of water-borne typhoid fever are sometimes associated with early attacks of nausea and vomiting, with or without diarrhoea, among the consumers. These attacks occur within a period of 12-72 hours after ingestion of the polluted water and, therefore, about three weeks before the notification of such cases of clinical typhoid fever as may have contracted the specific infection at that time. The attacks may be so transient as not to necessitate medical attention and, in outbreaks of typhoid fever suspected to be water-borne, inquiry into their occurrence should always be made. Commonly the subjects of them do not develop clinical typhoid fever but occasionally they do, becoming ill again at the same time as those who have incubated the disease without previous disturbance.

Prevalence.

Few facts are more striking in epidemiological history than the enormous decrease both in the incidence and in the mortality of the enteric fevers in this country since the later years of the nineteenth century. The long range trend is well illustrated by a comparison of the figures relating to the annual death rates per million living between 1871-75 and 1936. In the former period the rate averaged 371; in 1936 it was 6. Between 1871-75 and 1886-90 the rate fell from 371 to 181; in 1914 it was 47. Since then there has been an almost unbroken decline to 6 for 1936.

Typhoid fever proper is always more prevalent in the autumn; hence its former popular name of " autumnal fever ". It is stated to be most common among young adults, the greatest susceptibility being between the ages of 15-25, but it is probable that the incidence on children is greater than was formerly thought as their attacks are often atypical. There is little or no difference between the sexes in the attack rate. The mortality varies greatly in different epidemics; it may be as low as 5 or as high as 20 per cent. or even higher. The prognosis is more serious in elderly patients. Persons who have once contracted the disease and recovered are generally immune for life, though a second attack is not unknown. The immunity is specific; no protection is afforded by typhoid against the paratyphoid fevers and the converse is equally true. Paratyphoid fever is usually milder, runs a shorter course and is less fatal than typhoid fever.

Diagnosis.

In a typical case of typhoid fever the diagnosis presents little or no difficulty, especially after the first week, but suspicion should always be aroused by a *fever which has continued for a week with few or indefinite physical signs and without an eruption characteristic of another disease.* Confirmatory indications are a history of epistaxis, a dicrotic pulse, deafness, a rose-spot rash, a palpable spleen and some degree of bronchitis. Atypical cases in children may be overlooked by reason of their mildness. " Ambulant " cases and those in which pulmonary, nephritic or meningitic symptoms are prominent may prove difficult of diagnosis. The principal diseases which give rise to confusion are influenza, pneumonia, particularly the broncho-pneumonia of children, cerebrospinal fever, tuberculosis meningitis or peritonitis, acute miliary tuberculosis, undulant fever and appendicitis. The distinction from typhus fever has scarcely ever to be made in this country and the same is true of malaria and certain other exotic diseases; the use of the laboratory facilities which are now provided by most local authorities will usually suffice to confirm or correct the

diagnosis. In an appendix to this memorandum notes on the collection of specimens and on the principles of laboratory diagnosis have been added.

Prevention and Control.

The chief factors responsible for the large reduction in the incidence of enteric fever have been the improvement in the control and supervision of water, milk and food supplies, the more general introduction of the water-carriage system of sewage disposal, greater care in the collection and disposal of refuse and greater attention paid to cleanliness and personal hygiene.

Water.—The possibility of the pollution of a water supply which has been satisfactory for many years must not be overlooked. Special vigilance is required where a gathering ground is being built upon, or in the event of operations concerned with the maintenance, improvement, or extension of water works. The importance of the routine control of water supplies was emphasised in Circular 1684 of 1938, Memorandum 221 of 1939 and the Report on Public Health and Medical Subjects No. 71: " The Bacteriological Examination of Water Supplies " (revised edition of 1939), and attention is again drawn to these documents.

Food.—During the past fifteen years, in 40 outbreaks of typhoid and paratyphoid fever in which there were definite grounds for an opinion as to the vehicle of infection the numbers were—water 11, milk 12, other foods 17.

These fevers are not diseases of the cow and, in outbreaks in which milk is proved to be the vehicle of infection, the infection must have been introduced from without, at or after the time of milking. In this event subsequent pasteurisation would render the milk safe, although it is of course possible for milk to be infected after pasteurisation if sufficient care is not taken. It is noteworthy that none of the milks in the outbreaks in question was pasteurised.

These figures are given with reserve, but they indicate the need for greater care in the handling of food for human consumption. Individual cleanliness is essential; no person should prepare food without previously washing his hands, and hands should always be washed after the use of the toilet. In establishments dealing with food, adequate washing facilities should be provided and the personal routine of use should be strictly observed by the staffs to avoid the possible contamination of the food. The use of tongs when purveying unwrapped foodstuffs, the protection of food from flies and the destruction of flies are important measures.

Section 13 of the Food and Drugs Act, 1938, requires that persons employed in a room used for the sale, or the preparation for sale, of food intended for human consumption, other than milk, shall observe due cleanliness as regards themselves, the room, and all articles in it. It further requires that, except where the only food sold or stored in the room is in containers so that all risk of contamination is excluded, suitable washing basins with a sufficient supply of soap, clean towels and clean water, both hot and cold, shall be provided for the use of the persons employed in the room.

Milk.—In the case of milk, cleanliness in production, conveyance and distribution is dealt with in the Milk and Dairies Order, 1926, which includes special provisions relating to notifiable diseases, particularly in Articles 18 and 19, which enable a Medical Officer of Health, subject to specified conditions, to stop the supply of milk suspected to have caused or to be infected by such a disease, and to prohibit from taking part in the production, etc., of milk persons suspected to be suffering from or recently to have been in contact with persons suffering from such a disease.

The Sporadic Case.—The prevention of an outbreak lies in the early recognition and treatment of the sporadic patient. It has already been emphasised that every case of pyrexia which has lasted for a week or more without definite physical signs should arouse suspicion that the case may be one of the typhoid group, and appropriate precautions should be taken and means used to confirm the diagnosis. Both the typhoid and paratyphoid fevers, especially the latter, have been mistaken for influenza or pneumonia with disastrous spread of infection in households and institutions. Another danger, especially to patients in general hospitals, lies in the non-detection of the fever in persons admitted with "diarrhoea". Admission to hospitals, particularly those for children and infants, of persons suffering from diarrhoeal diseases is common and such patients ought to be treated as potentially infective until a definite diagnosis has been made.

Isolation of patients.—Unless the home circumstances are such as satisfy the Medical Officer of Health that a patient can, without danger to others, be nursed at home, he should be removed to hospital where adequate nursing facilities are available and where the measures necessary to prevent the spread of the disease are rigidly and habitually practised. The routine disinfection of the stools, urine and sputum of the patient, the treatment of soiled bed-linen, the setting apart of crockery and utensils for his sole use, the destruction of unconsumed food which may have been handled by the patient and the destruction of flies are some of the matters which have to be dealt with if there is to be no spread of the disease. It is obvious from these

considerations that there are relatively few houses invaded by typhoid fever in which it is practicable satisfactorily to nurse a patient.

The Carrier.—The problem of the " carrier " was dealt with at length in the Report of the Chief Medical Officer for the year 1932. It would hardly be practicable to secure the systematic identification, segregation and treatment of chronic carriers, and it is by no means certain that, even if it were practicable, such action would be effective. The principle adopted in this country has been, therefore, to require certain steps to be taken only if circumstantial evidence is obtained which results in the identification of a carrier who is employed in the preparation or handling of food or drink for human consumption. The Public Health (Infectious Diseases) Regulations, 1927 (S.R. & O. 1927, No. 1004) provide in Part III of the First Schedule that if a Medical Officer of Health has grounds for suspecting that any person in his district who is so employed is a carrier of enteric fever or dysentery, he shall report to the Local Authority. The Local Authority may then require a medical examination of the suspected person. If, from the result of such examination or from other evidence, the suspected person is found to be a carrier, the Medical Officer of Health must report to the Local Authority, who may give notice to the responsible manager of the business in which the carrier is employed and to the carrier himself, with a view to preventing for a specified time the employment of that person in any trade or business concerned with the preparation or handling of food or drink for human consumption. These steps are taken to prevent the carrier becoming a source of infection and should be combined with the instruction of the carrier in personal hygiene.

Immunisation.—Persons particularly exposed to the risks of infection, e.g., troops serving abroad and Europeans residing in countries where typhoid infections are common, generally receive subcutaneous injections of T.A.B. vaccine. This confers a high degree of protection, which lasts for at least a year. So far as exposure to infection is concerned, the most comparable circumstances in this country are those of nurses on duty in typhoid fever wards, and it is customary to immunise them before they are exposed to infection. In explosive outbreaks due to a single source of infection, prophylactic inoculation is of limited value because it is either too late to protect those who are incubating the disease or unnecessary for those who will escape through warning or through removal of the source. The protection of persons who live in the same district but have not been exposed to infection is a different matter and one for individual decision based on local circumstances. Administration of typhoid-paratyphoid vaccine by the mouth, though

obviously much more convenient than the subcutaneous method, confers uncertain protection and therefore it seems generally to be justified only when the orthodox method cannot be applied.

Ministry of Health,
London, S.W.1.

November, 1939.

APPENDIX.

Laboratory Diagnosis.

Culture and identification of the specific bacterium in the blood or excreta is the only method of diagnosis not open to doubt. Both are practicable, moreover, in the earliest stage of the symptoms and should be the first laboratory tests to be applied. Of importance, later, though less absolute in diagnostic accuracy, is the Widal test which depends on the development of specific agglutinin for the typhoid bacillus in the blood of the infected person; positive Widals may be obtained towards the end of the first week of illness but are rare and weak before that.

The following technical hints may be of service in the collection of specimens and their examination in the laboratory.

(1) *Blood culture.*—Blood should be drawn from a vein (with the usual aseptic precautions) as soon as the suspicion of typhoid fever arises. A convenient tool for the purpose is the Behring Venule but an ordinary 10 ml. all-glass syringe (dry, sterile) or a hypodermic needle (gauge S.W.G.19) attached to a piece of rubber tubing may be used. Whichever is employed, either an anticoagulant (citrate, oxalate, or liquoid) or fresh sterile ox-bile should be present in the recipient. McCartney bottles (with rubber diaphragm in the cap) are convenient when syringes are used. Plain screw-cap bottles can be employed for receiving blood from a piece of rubber tubing, though the necessity of removing the cap to insert it introduces the risk of contamination.

On arrival at the laboratory the blood is either incubated forthwith, if it is already mixed with sufficient bile, or is pipetted off aseptically into bile-broth (preferable) or ordinary nutrient broth in the proportion of 10 of medium to 1 of blood and then incubated. Subcultures from it on plates of MacConkey or other suitable medium should be done daily for at least 5 days before a negative result is recorded. A positive result is obtained when colonies of *B. typhosus* (identified as described below) have made their appearance. Should the blood specimen received at the laboratory be ordinary clotted blood, the serum should be pipetted off and the clot, broken up with a sterile glass rod, transferred to nutrient medium in similar fashion. The quantity of blood suggested (10 ml.) is preferable to less amounts but quite small quantities may give a positive culture and are better than none.

(2) *Culture from faeces.* (a) *Specimens.*—Freshly voided material should be taken, about half a teaspoonful being transferred to the outfit-tube provided. If delay of more than 18 hours is likely before the specimen can reach the laboratory, the faecal specimen should be put in sterile glycerine-saline (30 per cent. neutral glycerine in 0·6 per cent. saline) for transit. Should a fresh specimen not be available at the time of visit to the patient, a rectal swab may be taken instead; an ordinary throat swab may be used for this purpose.

(b) *Plating.*—At the laboratory the faeces (or the rectal swab) should be heavily inoculated on a plate of Wilson and Blair's medium [preferably prepared from the dry powder of the Difco brand (agents, Baird and Tatlock (London) Ltd.)], and/or on a plate of Jones's brilliant-green eosin agar, by means of a right-angled glass rod which is then used without recharging to spread lightly (single interrupted spread) on a second or third plate of the same media. In addition about 50 mg. of faeces (or the rectal swab) is emulsified in Kauffmann's differential liquid medium (20 ml.) or in ordinary peptone water (50 ml.) containing 1 in 150,000 brilliant green and incubated for 18 hours; loopfuls from the liquid medium are then plated on ordinary MacConkey agar or on litmus-lactose-agar or other differential medium.

(c) *Examination of Colonies.*—A dissecting microscope (a simple type with x6 lens) is almost indispensable for the examination of colonies and some experience of the appearance of typhoid and other Salmonella colonies is necessary. Portions of suspected colonies (black with reducing zone round in the case of Wilson and Blair medium) should be emulsified with a straight platinum needle in drops (loopfuls) of specific agglutinating sera,* diluted so that flocculation or granulation will take place with a homologous colony after stirring with the needle for a few seconds but not with heterologous colonies. Control drops of similarly diluted sera of other types should always be used simultaneously. Typical agglutination (as learnt by experience) is usually sufficient identification for routine purposes but it is well to plate out the colony identified on to MacConkey agar to ensure purity; the agglutinated drop may be used for this purpose. Pure cultures should then be subjected to fermentation tests and tests for motility, indol-formation, etc., and preserved for any further examination which may be later thought advisable such as agglutination and absorption of agglutinin tests.

(3) *Culture from Urine.*—Fresh specimens voided into sterile recipients should be transferred in 2 to 4 oz. quantity to sterile bottles for transmission. In the laboratory 10 ml. should be centrifuged at 4,000 r.p.m. for 15 minutes and the deposit, emulsified in a drop or two of the rejected supernatant, should be examined as described for faeces. In addition 10 ml. of urine (well shaken) should be added to the differential liquid media incubated and plated as described.

(4) *Agglutination tests with patient's serum* (*Widal Reaction*).—At least 1·0 ml. of blood should be provided for this purpose: it should be taken (as for a Wassermann specimen) with a dry syringe or needle into a dry sterile tube. Badly haemolysed blood is unsuitable for the test. The microscopic method in which a living broth culture of typhoid or paratyphoid bacilli is mixed with a series of dilutions of the serum in " hanging drop " and examined under the high power of the microscope is now seldom practised, though perfectly capable in experienced hands of giving correct information. The macroscopic method, in which mixtures of living or dead suspensions of the specific bacteria with serum dilutions are kept at 37°C or 50°C in a water bath, has many advantages. The most important point in the test is to ensure the proper quality of the bacterial suspensions, and it is strongly recommended that only those supplied by the Oxford Standards Laboratory of the Medical Research Council should be employed in routine tests. A pamphlet describing the technique of the test is supplied with these Standard Emulsions so that nothing more need be said here on that subject.

The agglutinins which may develop in persons infected by the typhoid or paratyphoid bacilli (or in subjects of typhoid-paratyphoid vaccination) are twofold in character, corresponding to the dual nature of the bacterial

* Obtainable from the Oxford Standards Laboratory.

antigens. The " flagellar " or " H " agglutinin, which is a response on the part of the infected (or inoculated) person to the antigenic action of the bacterial flagella, reveals itself in the test tube as a loose flocculation, developing rapidly (end-point within two hours), easily shaken up, often appearing up to high dilutions of the serum but absent or feeble in a variable but appreciable proportion of cases in different outbreaks of typhoid fever; in paratyphoid fever, on the other hand, it is almost invariably abundant.

The " somatic " or " O " agglutinin which is a response to the antigenic action of the bodies alone of the bacteria, reveals itself in the test tube as a granular clumping, developing slowly (end-point at 50°C = 24 hours), not readily broken up by shaking and reaching on the average less high titres in the serum: it is rarely absent in typhoid fever, though it may not be demonstrable till the third week of the illness or later. Titres of 1 in 30 for " H " agglutinin and 1 in 50 for " O " agglutinin in a macroscopic test with " Standard " suspensions would be strong presumptive evidence of the existence of a typhoid infection, provided the patient had never before had an attack nor received T.A.B. vaccine.

It is in cases with a history of either of these that difficulty arises in the interpretation of a Widal test. Repetition of the test with evidence of a progressive rise in titre in the course of the illness will strengthen the presumption of an existing typhoid infection, but even this may not be infallible since other infections may in such persons act as a non-specific stimulus and increase the production of the old typhoid agglutinin. Little reliance can be placed upon differing titres or irregularity in the rise of agglutinin for the typhoid bacillus as compared with paratyphoid A, B, or C in such persons as an aid to diagnosis between typhoid and paratyphoid fever.

Use of agglutination tests in the detection of " carriers ".—When large numbers of persons are under suspicion as possible typhoid carriers, it may take too long and be too expensive to make cultures of excreta from all of them. Hence it is common practice to do agglutination tests and to disregard those whose serum shows no trace of typhoid agglutinin. The others, i.e. all those showing either " H " or " O " agglutinin in titres of 1 in 15 or higher, are under suspicion (always provided that the test has been properly conducted and that the test emulsions are not sensitive to normal serum) and should have their faeces and urine examined on three or more occasions in the manner described. For this purpose it is often best for them to spend a night in a hospital ward so that the specimens can be collected without risk of substitution or other mode of falsification. They should be given half an ounce of magnesium sulphate early in the morning and the resulting stool taken for a specimen.

When inoculated subjects form a large proportion of those under suspicion, the ordinary agglutination tests are of little help in selection since the majority may give suspicious reactions. Whether the test of Vi-antibody, described by Felix as commonly to be found in " carriers ", will become a safe and certain guide remains to be proved; it cannot yet be performed under routine conditions.

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