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TYPHOID FEVER

With Special Reference to the Routes by which
the Bacilli enter and leave the body.

Being

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by

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TYPHOID FEVER

With Special Reference to the Routes by which the Typhoid Bacilli enter and leave the body.

Although the name Typhus (Typhos) dates back to the ancient Greeks, it is only within quite recent years that it has been applied to the disease at present known as Typhus Fever. Until the year 1837 when Gerhard & Pennock⁽¹⁾ shewed that Typhoid fever and Typhus fever were two distinct diseases, the name was applied to both; indeed, when the name first appears in Medical literature we find it used to express almost any condition attended with stupor and loss of consciousness.

All accurate and scientific knowledge of the Aetiology of Typhoid Fever dates, of necessity, from the year 1880 when Eberth discovered the Bacillus Typhosus. The bacillus once discovered and accepted as the causal agent, investigators were at once faced with two problems:-

The first - How does the bacillus gain access to the bodies of individuals affected ?

The second - By what routes do the bacilli leave the bodies of individuals affected?

(1) "On the Typhus Fever which occurred at Philadelphia in 1836, shewing the distinctions between it and Dothienteritis."

In view of their bearing upon the prophylaxis and treatment of the disease, both are questions fraught with immense importance not only to the scientist but to mankind in general.

As will be shewn later, thanks to the researches of a large number of observers, these questions have been, at least in part, answered. It is our intention to touch lightly upon such parts as have been already conclusively worked out and to throw some light, if possible, on the parts passed over by other observers.

The two most obvious possible routes by which the bacilli may enter the body are as follows:-

- (1) By way of the Alimentary Canal.
- (2) Through the Respiratory System.

I. THE ALIMENTARY CANAL.

Without doubt by far the most common route by which the typhoid bacilli gain access to the bodies of individuals affected is by way of the Alimentary Canal. This fact is now accepted by practically all physicians. The bacilli are taken into the mouth, swallowed, and from the mouth they pass through the Oesophagus and stomach to the small intestine.

Here they shew a special selective activity in

attacking the lymphatic apparatus, i.e. the Peyer's Patches and the Solitary Glands.

The bacilli then pass to the related lymphatic glands, and from them by the blood stream to various other parts of the body.

In addition to this, the usual and most common gate of entry, another portal which has only recently been considered a possible one is by way of the Tonsils. The fact that a large number of typhoid patients complain of "sore throat" in the first few days of the disease has long been known but very little significance appears to have been attached to the fact.

In a very interesting paper read before the British Medical Association at their Annual Meeting in July 1910, Professor Dr Otto Lentz calls attention to the frequency of tonsillitis in typhoid fever, (according to V. Drigalski in 40% of the cases). He states that both he himself and other observers have been able to demonstrate the presence of typhoid bacilli in the tonsillar scrapings, thus proving conclusively that the bacilli may gain access to the body through the tonsils. Still more recently, Dr Hamilton, the Medical Officer of Health for Eccles, in a special report issued on the extensive outbreak of enteric fever that occurred in Eccles during November

and December of last year, states that very many of the cases began with tonsillitis. This he regards as shewing that the bacilli may enter the body through the lymphatic apparatus of the upper digestive tract.

In regard to the frequency with which tonsillitis and "sore throat" occurs in typhoid fever, an analysis has been made of five hundred consecutive cases admitted to the Monsall Fever Hospital, Manchester, during the years 1908, 1909 and 1910. The cases taken are only those in which a positive Widal reaction was present and in which a definite and accurate history could be obtained. Of these five hundred cases, ninety-eight or 19.6% were suffering from definite tonsillitis on "infected throat" on admission.

The percentage is small, but this is explained when the fact that the majority of the patients were admitted late on in the disease is taken into consideration.

For the purpose of proving the theory of the possibility of the entrance of typhoid bacilli by the tonsils, it is evident that the only tonsillitis which can be of any importance is that which occurs during the first few days of the disease. Of the five hundred cases under consideration, 256 or 51.2% had a definite history of "sore throat" at some period of the disease.

Of these 256 cases of "sore throat", 76 or 29.6% occurred on the first day of the disease:

55 or 21% occurred on the 2nd day.

24 " 9.7% " " " 3rd "

12 " 4.6% " " " 4th "

9 " 3.5% " " " 5th "

16 " 6.2% " " " 6th "

14 " 5.4% " " " 7th "

206 or 80.4%, therefore, of these 256 cases, occurred during the first week and 155 or 60.5% during the first three days.

Of the remaining 50 cases:-

13 occurred on the 8th day.

6 " " " 9th "

6 " " " 10th "

3 " " " 11th "

3 " " " 12th "

2 " " " 13th "

5 " " " 14th "

1 " " " 15th "

2 " " " 17th "

4 " " " 18th "

2 " " " 19th "

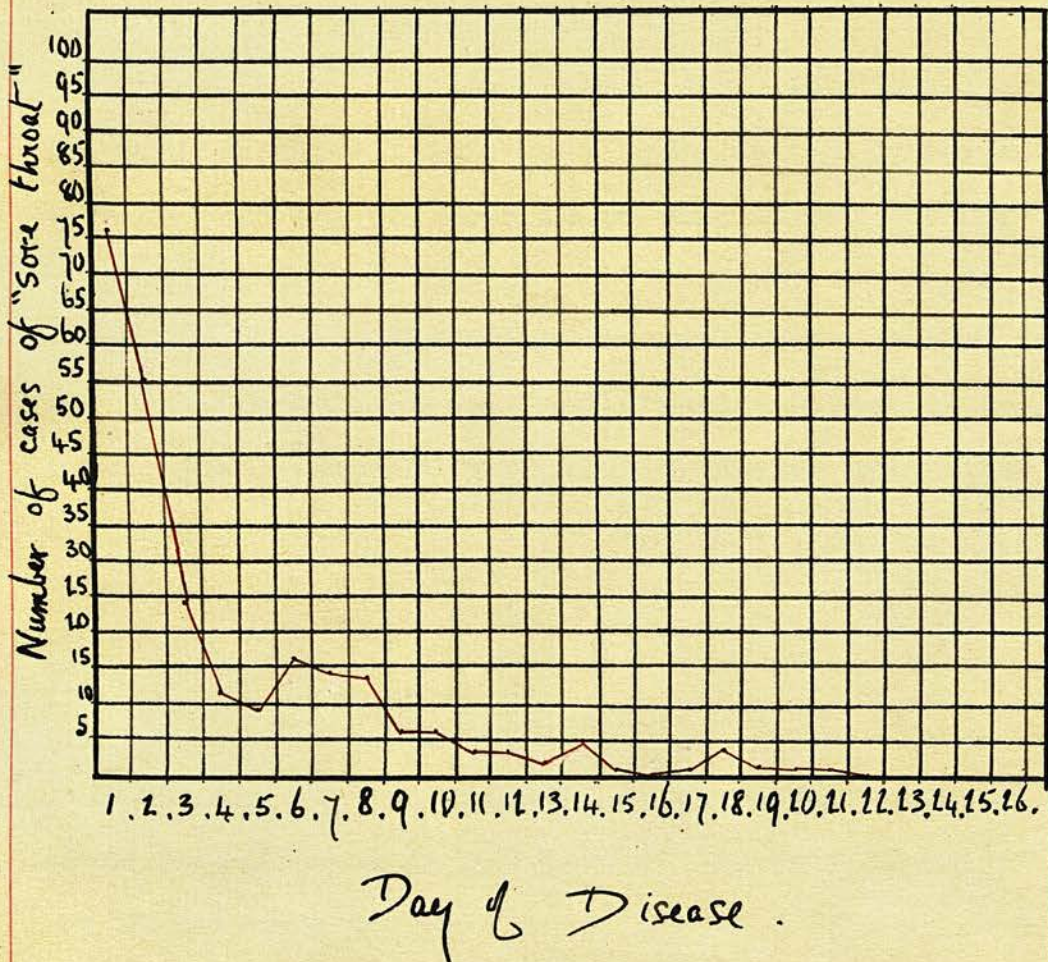
1 " " " 20th "

1 " " " 21st "

1 " " " 35th "

The time of maximum incidence of sore throat is well brought out by the accompanying chart in which the number of cases is represented by the height of the curve. A single glance at the chart shews the tremendous drop in the number of cases occurring after the first few days.

Analysis of 256 cases of "Sore throat" in Typhoid Fever.



Expressing these results as percentages of the total number of 500 cases of typhoid fever, we find that 41.2% of the 500 cases complained of "sore throat" during the first week of the disease and 31% during the first three days.

The conclusions arrived at from a survey of these 500 cases may be briefly summarised as follows:-

- (1) A very large number (51.2%) of typhoid patients complain of "sore throat" at some time during the disease.
- (2) A smaller, but still a remarkably large number (31%) of typhoid patients complain of "sore throat" during the first three days of the disease.

These facts, in conjunction with the finding of the typhoid bacilli in tonsillar scrapings by Lentz, already referred to, seem to be very strong presumptive evidence that in some, and possibly in all of these 31% of cases in which the sore throat occurs in the first three days of the disease, the bacilli do actually enter the body by the "Lymphatic apparatus of the upper Digestive Tract" (Lentz).

II. THE RESPIRATORY SYSTEM.

Opinion is still divided as to whether the typhoid bacilli ever gain access to the body by way of the Respiratory System.

Kerr⁽¹⁾ states that "it is indeed possible that in rare instances the primary nidus may be in the lung".

Goodall & Washbourn⁽²⁾ state definitely that infection always occurs through the Alimentary Canal.

Curschmann⁽³⁾ also takes this view. "If," he says, "infection through inhalation seems possible in rare cases, it will be found upon more careful investigation that here also the poison has gained entrance through the digestive tract".

The question turns largely on the study of certain cases of "pneumotyphoid". This term has been given to a class of case in which the attack is ushered in by pneumonia, usually lobar pneumonia, more rarely broncho-pneumonia. That these cases do occur is now recognised by most authorities, but the method of their causation is still debated.

The original idea was that they occurred as the direct result of the primary localisation of the typhoid bacilli in the lungs. Lépine, for example, writing in the "Revue de Medicin" in 1878, took this view. This theory, however, up to the present time has not been conclusively proved. It is true that

(1) Claude B. Kerr: "Infectious Diseases", page 241.

(2) Goodall & Washbourn: "A manual of Infectious Diseases", page 282.

(3) Curschmann: Nothnagel's "Encyclopedia of Practical Medicine", "Typhoid Fever & Typhus Fever", English edition, page 38.

in a certain number of cases of pneumonia occurring in typhoid fever, typhoid bacilli have been found alone, the sole apparent cause of the attack, but in these cases either the bacteriological report has been incomplete or else, as in cases reported by Bensaude⁽¹⁾ and Bordoni-Uffreduzzi⁽²⁾ the bacteriological examination has been made so late in the disease that even if the pneumococcus had been present earlier, it had had time to die out (Curschmann).

Even if it could be proved that cases of pneumonia occur with typhoid bacilli as the sole causative agent, it might still be contended that the bacilli gained entrance to the body by the usual intestinal route and were carried in the blood stream to the lungs.

ROUTES BY WHICH THE BACILLI LEAVE THE BODIES
OF INDIVIDUALS AFFECTED.

In recent years an enormous amount of work has been done to determine the routes by which the typhoid bacilli leave the body.

(1) Bensaude: Thèse, Paris, 1897.

(2) Bordoni-Uffreduzzi: Riforma Med. 1887, No.1.

In spite of this, the statement by Curschmann⁽¹⁾ that "in spite of numerous investigations we are still in the first stage of knowledge with respect to this question" probably still holds good.

At the present time the faecal discharges and the urine are, by universal consent, deemed the most important carriers of the infection, at the same time the possibility that the bacilli may leave the body by other routes must not be lost sight of.

The possible routes by which the typhoid bacilli may leave the body are:-

- (1) The Faecal Discharges.
- (2) The Urine.
- (3) The Expectoration.
- (4) The Expired Air.
- (5) The Sweat.

(1) The Faeces:

The fact that the faeces played an important part in the dissemination of the disease was recognised long before Eberth's discovery of the *Bacillus Typhosus* in the year 1880. As far back as 1856, Budd⁽²⁾ put forward the view that the typhoid poison came from the patient himself and that it was evacuated in the faecal discharges, and since the discovery

(1) Curschmann: Nothnagel's "Encyclopedia of Practical Medicine": "Typhoid and Typhus Fever", English Edition (1905) p.31.

(2) Budd: "On Intestinal Fever; Its mode of propagation". Lancet, 1856.

of the typhoid bacillus numerous observers have been able to isolate the organism from the stools of typhoid patients.

(2) The Urine:

The presence of typhoid bacilli in the urine has also been conclusively shewn in recent years.

In the year 1890 Neumann⁽¹⁾ first demonstrated the presence of typhoid bacilli in the urine in eleven out of forty-eight cases, and his observations have been confirmed by a large number of observers. At the present time it is recognised that typhoid bacilli can be isolated from the urine in about 30% of the cases.

(3) The Expectoration:

The possibility that typhoid bacilli may leave the body in the sputum appears to have been overlooked by the great majority of workers on typhoid fever. I am unable to find records of any work done to either prove or disprove their presence. The importance of some definite knowledge on the subject is at once apparent since if the bacilli are present in the sputum, this constitutes another possible means of direct infection. In this connection it is interesting to note that Sicard, writing in "Le Semaine

(1) Neumann: Berlin Klin. Woch. 1890, S.121.

"Medicale" in 1892 states that the bacilli are present "very probably also in the expectorations of typhoid patients suffering from bronchitis or infectious pneumonia".

The reasons for supposing that the bacilli are present are as follows:-

(i) The very frequent presence of ulcers on the mucous membrane of the mouth, of inflammation and swelling of the mucous membrane of the soft palate, the tonsils, and the posterior pharyngeal wall, and in some cases of ulcers in the tonsils and pillars of the fauces; also the fact that some observers (Duguet & Chantemesse) have been able to demonstrate the typhoid bacilli in the floor of these ulcers.

(ii) The frequency of ulceration of the larynx and the report of Schulz ⁽¹⁾ who found the bacilli both in sections and cultures from the lymphoid nodules.

(iii) The frequent occurrence of inflammation and swelling, sometimes of actual ulceration of the mucous membrane of the trachea. The formation of actual ulcers appears to be rare, but superficial erosions of the mucous membrane can almost invariably be found on post-mortem examination.

(iv) The almost constant presence of bronchitis

(1) Schulz: Berl. Klin. Woch. 1894, Bd. XXXV. No. 34.

which now, according to Goodall & Washbourn⁽¹⁾
 "should be considered a part of the disease rather
 than a complication".

In some cases this condition also appears to be
 caused by the typhoid bacillus, as in the cases cited
 by Polynère⁽²⁾, also in those published by Finkler.

(v) The occurrence of broncho-pneumonia, lobar
 pneumonia, pleurisy and empyema, in all of which in
 some cases some observers have been able to demon-
 strate the presence of the typhoid bacillus.

Particularly interesting in this connection are
 those cases previously referred to, termed "pneumo-
 typhoid" in which the pneumonia is the first symptom
 of the disease.

In these cases it is possible that the sputum
 may be a means of spreading the infection before the
 disease has been diagnosed as typhoid fever.

Granted the possibility that the Bacillus Typhos-
 us is present in the sputum, it is quite conceivable
 that it might be impossible to isolate the organism
 from that medium. The reasons for this may be numer-
 ous, but the most obvious are:-

- (a) The presence in the sputum of some substance
 which would inhibit the growth of the bac-
 illi on artificial media.

(1) Goodall & Washbourn: "A Manual of Infectious
 Diseases", page 189.

(2) Polynère: Thèse, Paris, 1889.

- (b) The presence of some organism, or number of organisms, which would either completely outgrow or inhibit the growth of the typhoid bacilli.

In order to settle this point, the following control experiments were carried out by the writer both in Professor Delépine's Laboratory (The Public Health Laboratory, Manchester) and in the clinical laboratory of the Monsall Fever Hospital, Manchester. Samples of two sputa (A and B) were taken:- Specimen A, a very purulent sputum containing a large number of organisms: Specimen B, a mucous sputum containing far fewer organisms.

An ordinary platinum loop needle was taken, and two loopfuls of a twenty-four hours old culture of *B. Typhosus* in broth put into 5 c.cs. of neutral broth, and well shaken up. $2\frac{1}{2}$ c.cs. of the broth were now poured into specimen A and $2\frac{1}{2}$ c.cs. into specimen B; in both cases the sputum being thoroughly mixed up with the broth.

Successive stroke cultures (made with a glass rod in the usual way) were now made on Litmus Lactose Agar plates and these incubated at 37°C . for twenty-four hours. Cultures in broth were also made from the specimens and both these and the specimens themselves incubated at 37°C . for twenty-four hours.

On the following day successive strokes were made on litmus lactose agar plates from the broth cultures

and from the specimens incubated for twenty-four hours.

Several typical typhoid colonies were found on the plates made from the specimens A and B directly.

No typhoid colonies, however, could be found on the plates made from the broth inoculated from the specimens, and none on the plates made from the specimens themselves incubated for twenty-four hours.

In order to establish the identity of the typhoid bacilli found on the plates they were submitted to the following tests:-

- (1) The organisms were examined under the microscope and found to be motile.
- (2) They had the appearance of typhoid bacilli on staining with the usual stains.
- (3) On staining for flagellae they were found to be flagellated.
- (4) Gram negative.
- (5) Typical growth on litmus lactose agar.
- (6) No acid or gas in McConkey's medium.
- (7) No clotting of milk.
- (8) No formation of gas in stab culture in glucose gelatin.
- (9) The organisms gave the Widal reaction with the serum of a typhoid patient.

On eighteen hours old sub-culture of the bacilli in neutral broth was completely clumped in ten minutes by dilutions of from 1 in 10 to 1 in 100.

There appears, therefore, to be no obvious reason why it should not be possible to isolate typhoid

bacilli from the sputum of typhoid patients, if they are present in the sputum in sufficient numbers.

In the following twenty cases in which the sputum has been examined for typhoid bacilli, the same procedure as that employed in the control experiments has been carried out.

Successive smears on litmus lactose agar plates were made and these plates incubated for twenty-four hours at 37°C.

Broth tubes were inoculated from the sputum; these were incubated for twenty-four hours at 37°C. and strokes made on litmus lactose agar plates which, as before, were incubated for twenty-four hours at 37°C.

In addition, the effect we tried of incubating the plates and broth tubes at temperatures of 40°C and 42°C.

Another method employed in each case after the broth tubes were inoculated, and strokes made on the litmus lactose agar, was as follows:-

Five c.cs. of neutral broth were added to the sputum. The sputum and broth were now well mixed, incubated at 37°C (in some cases also at 40°C and 42°C) for twenty-four hours and strokes made on litmus lactose agar from the scum floating on the top of the mixture.

Case 1. A. A. Male, aged 21.

Spleen enlarged. Bronchitis. Tonsillitis. Rose spots. Widal reaction positive. Mucous membrane of lower lip ulcerated. Sputum taken on 26th day of disease. No bacilli of any kind were found on plates. Large number of staphylococci and some streptococci.

N.B. The ulcers on the mucous membrane of the lower lip had been treated for several days previously by swabbing with pure Izal and were healing rapidly.

Case 2. E. B. Male, aged 24.

Spleen enlarged. Bronchitis with abundant sputum. Tonsillitis. Widal positive. Temperature 102.6. Sputum taken on 26th day of disease. No typhoid bacilli found, some non-motile diphtheroid bacilli found, several colonies of staphylococci.

Case 3. S.B. Male, aged 16.

Spleen enlarged. Bronchitis of lower lobe of left lung. Pneumonia of lower lobe of right lung. Scanty sputum. Temperature 103°F. Sputum taken on 26th day of disease. No bacilli of any kind found. Staphylococci and some pneumococci.

Case 4. A. C. Male, aged 9.

Spleen enlarged. Widal positive. Temperature 100.4°. Sputum taken on 11th day of disease. Some

motile spore-forming bacilli found, also large numbers of staphylococci and streptococci.

Case 5. D. B. Male, aged 48.

Spleen enlarged. Widal positive. Bronchitis with scanty sputum. Sputum taken on 14th day of disease. No bacilli. Staphylococci and streptococci in large numbers.

Case 6. J. F. Male, aged 12.

Spleen enlarged. Widal positive. Temperature 102.6°. Bronchitis (scanty sputum). Tonsillitis. Sputum taken on 20th day of disease. Some motile spore-forming bacilli found, also staphylococci and streptococci.

Case 7. P. F. Male, aged 9.

Spleen enlarged. Widal positive. Temperature 99.6°. Tonsillitis. Bronchitis with scanty sputum. Sputum taken on 16th day of disease. Bacilli having microscopic appearance and giving all cultural reactions of *Bacillus Coli Communis* found on plates inoculated directly from sputum. Staphylococci also present.

Case 8. R. S. Female, aged 28.

Spleen enlarged. Widal positive. Temperature 102°. Tonsillitis. Bronchitis with scanty sputum.

Sputum taken on 11th day of disease. No bacilli. Large numbers of staphylococci and streptococci, also some diplococci.

Case 9. E.R. Male, aged 26.

Spleen enlarged. Widal positive. Temperature 102.4. Bronchitis with abundant sputum. Sputum taken on 30th day of disease. Staphylococci and some diphtheroid bacilli.

Case 10. N.T. Female, aged 24.

Spleen enlarged. Widal positive. Temperature 103.6°. Bronchitis with scanty sputum. Ulceration of buccal mucous membrane. Sputum taken on 22nd day of disease. Streptococci and staphylococci.

Case 11. M.H. Female, aged 13.

Spleen enlarged. Widal positive. Temperature 103°. Tonsillitis. Sputum taken on 12th day. Some motile spore-forming bacilli, several colonies of staphylococci.

Case 12. F.P. Male, aged 26.

Spleen enlarged. Widal positive. Temperature 101°. Bronchitis with abundant sputum. Sputum taken on 23rd day. Some diphtheroid bacilli present, also staphylococci and streptococci.

Case 13. B. McC. Female, aged 25.

Spleen enlarged. Widal positive. Tonsillitis. Patient complaining of "sore throat". Bronchitis. Sputum taken on 22nd day. Bacilli having microscopic appearance and giving all cultural reactions of typhoid bacilli found. The bacilli, however, were not clumped by the serum of a typhoid patient. Staphylococci also present.

Case 14. H.R. Female, aged 22.

Spleen enlarged. Widal positive. Temperature 101.6°. Bronchitis. Sputum taken on 28th day. Staphylococci and streptococci.

Case 15. F.R. Female, aged 15.

Spleen enlarged. Widal positive. Temperature 103°. Patient was admitted to the Monsall Fever Hospital on August 11th, 1910. On September 7th patient had a relapse, with abundant crop of rose-spots, tonsillitis, and bronchitis with scanty sputum. On September 10th sputum taken. Bacilli having microscopic appearance and giving all cultural reactions of typhoid bacilli found. The bacilli were not clumped by the serum of a typhoid patient. Staphylococci also present.

Case 16. M.B. Female, aged 26.

Spleen enlarged. Widal positive. Temperature

101°. Sputum taken on 34th (?) day of disease. No bacilli present. Staphylococci and streptococci.

Case 17. E.T. Female, aged 21.

Spleen enlarged. Widal positive. Temperature 101°. Ulceration of mucous membrane of lower lip. Sputum taken, also scrapings from two ulcers on lower lip. Exact day of disease on which sputum taken unknown, probably about 20th. Diphtheroid bacilli and staphylococci from sputum, staphylococci and streptococci from ulcers.

Case 18. L.W. Female, aged 18.

Spleen enlarged. Widal positive. Temperature 103.4. Pneumonia. Consolidation of lower lobe of left lung. Tonsillitis. Sputum scanty. Sputum taken on 14th day. Some motile spore-forming bacilli also staphylococci.

Case 19. A.F. Female, aged 26.

Spleen enlarged. Widal positive. Temperature 102.8°. Bronchitis (scanty sputum). Tonsillitis. Sputum taken on 18th day. No bacilli. Some staphylococci and streptococci.

Case 20. J.W. Female, aged 22.

Spleen enlarged. Widal positive. Temperature 103°. Bronchitis. Sputum taken on 6th day of

disease. Bacilli having microscopic appearance, and giving all cultural reactions of typhoid bacilli found. The bacilli, however, were not clumped by the serum of a typhoid patient.

The temperature given in every case is the evening temperature on the day on which the sputum was collected.

With three doubtful exceptions, therefore, the result of the bacteriological examinations have been negative, as far as finding the typhoid bacillus is concerned.

The three cases referred to are Nos. 13, 15 and 20. In these three cases bacilli apparently identical with typhoid bacilli were found but these bacilli were not clumped by the serum of a typhoid patient. At the time when the bacteriological examinations were made, i. e. during the Summer and Autumn of last year, I was of opinion that this absence of clumping proved definitely that the bacilli could not be typhoid bacilli. Within the last few days, however, it has been brought to my notice that Dr Hutchinson, working in the Manchester Public Health Laboratory, has found that in several cases bacilli newly isolated from the stools of typhoid patients are not clumped by the serum of a typhoid patient.

After growing the bacilli through several generations the power of clumping is acquired.

On looking up the literature on the subject, I find that Major Gratton, writing in the "Journal of the Royal Army Medical Corps" in April, 1910, gives an account of two cases in which the bacilli when first isolated were not agglutinated by a typhoid serum.

In one case the bacilli were isolated from a suppurating joint and in another from the blood.

Scheller (1908) found that the agglutinability of typhoid colonies taken from the same plate varied enormously.

Ledingham (1910) also mentioned the fact that "it frequently happens that typhoid bacilli taken directly off the plate and tested with an antiserum give a very feeble and unconvincing reaction".

In view of these most interesting observations, it seems possible that the bacilli isolated from cases 13, 15 and 20 may after all have been typhoid bacilli. The method of procedure employed is open to criticism since one medium, litmus lactose agar, has been employed to the almost total exclusion of all others.

In some cases Conradi-Drigalski medium was used in addition to the litmus lactose agar.

It has been found at the Manchester Public Health Laboratories that litmus lactose agar is quite as useful as any medium of more complex composition. Also

it is highly probable that proficiency in the use of one medium is of far more importance than the unskilled use of a variety of media.

The importance of the fact that the worker should be familiar with one medium is insisted on by Dr Ledingham, writing on typhoid "carriers" in the Annual Report of the Medical Officer to the Local Government Board (1909-10) and this opinion is steadily gaining ground.

(4) The Expired Air:

At the present time the great majority of observers are of opinion that the expired air of typhoid patients does not act as a carrier of infection of typhoid fever. Curschmann⁽¹⁾, however, writing in Nothnegel's "Encyclopedia of Practical Medicine", mentions the fact that Sicard⁽²⁾ in the year 1892 published an article in the "Semaine Médicale", in which he stated that he had found typhoid bacilli to be almost constantly present in the expired air of typhoid patients.

(1) Curschmann: "Typhoid & Typhus Fever", page 32, Nothnegel's Encyclopedia of Practical Medicine, English Edition.

(2) Sicard: "De la part de l'air dans la transmission de la fièvre typhoïde", "Semaine Médicale", 1892, No.4.

The conclusions arrived at are most interesting and inasmuch as they are entirely at variance with the concensus of opinion at the present time, most remarkable.

As the writer has been unable to find records of any work either confirming these conclusions or casting doubt upon them, he thought it necessary to repeat Sicard's experiments.

The first part of the article in "La Semaine Médicale" is taken up by various arguments put forward by the author to prove the possibility of the presence of typhoid bacilli in the expired air of typhoid patients. It is interesting to find in the course of this discussion that he lays stress on the fact of the extreme dryness of the respiratory passages, a point later referred to in connection with the sputum of typhoid patients. The author's description of the method used to isolate the typhoid bacilli from the expired air is, translated into English, as follows:-

"We have used two slightly different pieces of apparatus in our researches on the expired air of typhoid patients. The first is simply a long test tube, holding a column of sterile water about three or four centimetres in height. In this a test tube is plunged communicating with the exterior by an

opening blocked with a plug of cotton-wool. The end in the water is drawn out to a fine point. A second test tube, drawn out at its outer end (which is also blocked by a plug of cotton-wool) barely projects through the cork into the interior of the test tube. The second tube is to allow the escape of air blown through the liquid. The patient blows gently through the first tube in such a manner that the air bubbles drop by drop through the water. The observer must be sure that the patient does not introduce any saliva or solid particles into the tube. After each experiment the outer opening of the tube through which the air is blown is blocked by a plug of sterilised wool.

The second piece of apparatus consists of a similar tube holding the same quantity of sterile water. To avoid, as far as possible, the introduction of liquid or solid particles into the tube it is bent into the form of a U tube, and it has a considerable enlargement at the base of the U in which these particles will be caught if any of them have entered.

We have used the latter apparatus constantly except on two occasions. It goes without saying that before each experiment the apparatus was thoroughly sterilised. We have, for the most part, confined our researches to patients who showed all the clinical and bacteriological symptoms and who were at the

height of the disease. In a single case we experimented on a typhoid patient at the beginning of convalescence. Each of the patients breathed into the tube for five minutes five times at different times during the day. As soon as the experiment was finished the apparatus was placed in the incubator for forty-eight hours at 37°C. At the end of this time, after rolling the tube for a few minutes between the fingers, ten drops of the water, through which the expired air had bubbled, were drawn off by means of a sterilised pipette. Successive cultures in liquid and solid media were made from these drops, and also preparations stained with Bismarck brown, intended to be photographed under the microscope. We have obtained, by means of these last preparations and of portions of the cultures, micro-photographs of typhoid bacilli which have been affixed to the original memoir sent to the Academy. Our experiments were carried out on ten patients at the height of the disease and on one convalescent. In one single case we were not able to demonstrate clearly the presence of typhoid bacilli in the water of the apparatus."

The author then proceeds to state the conclusions arrived at, which, to quote once more, are as follows:-

"These experiments shew, to recapitulate, that the air which leaves the mouth of typhoid patients, collected carefully in such a manner that it does

not contain any liquid or solid particles, is a vehicle for typhoid bacilli. We think, ourselves, that the method of bubbling the air through the water is most important in view of the subsequent inoculations. The incubation of the water at 37°C for a certain length of time also plays a part in the subsequent production of cultures in the nutrient media. Let us insist once more that even admitting that the air blown in, in spite of all the precautions taken, may contain a certain amount of liquid or solid particles, these experiments still prove that a typhoid patient spreads around him typhoid bacilli and undoubtedly causes the air around him to be contagious."

In testing the expired air of the following twelve cases for typhoid bacilli, an apparatus identical with that described by Sicard has been used. Instead of using "ten drops" of the water to make cultures, the whole of the water has been mixed up with litmus lactose agar and plates made. The effect of allowing the patients to breathe directly on to litmus lactose agar plates has also been tried. All the twelve patients were suffering from a typical attack of typhoid fever, with enlarged spleen, positive Widal reaction, etc.

The writer has been unable to find typhoid bacilli, or even bacilli closely resembling typhoid bacilli,

in any of the twelve cases. As Lepine "demonstrated the presence of typhoid bacillu" in nine out of the ten cases examined it seems probable that the bacilli observed by him were not typhoid bacilli, more especially as no detailed account is given of the tests used to prove that the bacilli found were typhoid bacilli.

The twelve cases in which the expired air has been tested for typhoid bacilli are:-

(1) W.H. Male, aged 40. Temperature 102°F.
Expired air examined on 33rd day of disease.

(2) W.H. Male, aged 23. Temperature 102°.
Expired air examined on 16th day of disease.

(3) M.N. Female, aged 45. Temperature 102.2.
Expired air examined on 20th (?) day of disease.

(4) H.M. Female, aged 18. Temperature 103.8.
Expired air examined on 25th day of disease.

(5) L.O. Female, aged 23. Temperature 103.2.
Expired air examined on 10th day of disease.

(6) E.B. Female, aged 11. Temperature 100.
Expired air examined on 14th day of disease.

(7) A.S. Female, aged 20. Temperature 103.6.
Expired air examined on 17th day of disease.

(8) P.B. Male, aged 27. Temperature 100.4°. Expired air examined on 16th day of disease.

(9) J.B. Male, aged 24. Temperature 101°. Expired air examined on 23rd day of disease.

(10) T.B. Male, aged 18. Temperature 102.8°. Expired air examined on 20th day of disease.

(11) A.A. Male, aged 8. Temperature 99.2°. Expired air examined on 12th day of disease.

(12) E.J. Female, aged 6. Temperature 99.8°. Expired air examined on 13th day of disease.

The temperature given in every case is the evening temperature on the day on which the expired air was tested.

The number of cases examined is so small that it is impossible to arrive at any very definite conclusion but the experiments, as far as they go, appear to indicate that the expired air of typhoid patients can be neglected as a factor in the spread of the disease.

(5) The Sweat:

The writer has been unable to find any records of work done to prove or disprove the presence of typhoid bacilli in the sweat of typhoid patients.

In the few cases in which the sweat has been examined bacteriologically, he has been unable to find typhoid bacilli.

S U M M A R Y .

(1) Routes by which the typhoid bacilli enter the body:

The most common route is by the lymphatic apparatus of the lower part of the small intestine.

An additional and probably also very common route is by way of the tonsils and the "lymphatic apparatus of the upper digestive tract".

It is very doubtful whether the bacilli ever enter the body by the Respiratory System.

(2) Routes by which the typhoid bacilli leave the body:

The most common routes are by the faecal discharge and the urine.

The bacilli also very probably leave the body in the expectoration. It has, however, not been found possible to demonstrate conclusively the presence of typhoid bacilli in the sputum of typhoid patients.

On account of the extreme dryness of the air passages and the consequent scantiness of the sputum in typhoid fever, it is probably only in very rare cases, if ever, that the sputum can act as a means of infection.

It has not been found possible to demonstrate the presence of typhoid bacilli in either the expired air or the sweat of typhoid patients and there is no evidence to shew that the bacilli leave the body by these two routes.

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