THE "EFFECTIVE PERIODS" OF TYPHOID
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In a previous communication¹ we intimated our intention to continue observations upon the typhoid "carrier" whose case we described. Since then we have traced another outbreak to a typhoid carrier and have prosecuted inquiries from several standpoints in order to determine certain factors associated with the transmission of the organism. One of these is connected with the "effective" periods of the carrier, and although the facts already ascertained are limited to few cases we consider that their publication may call further attention to the whole question of typhoid carriers and so indirectly furnish additional material for investigation.

It may be remembered that Mrs. H., the subject of our earlier paper, was found to be the cause of three outbreaks of enteric fever in institutions where she was acting as cook. In November, 1907, she was proved to be a typhoid carrier, and her removal from any contact with food resulted in the disappearance of enteric fever from the institution where she was working. From that time we have had her under strict control, her fæces have been examined frequently, and her clinical condition has been duly noted. In addition to the bacteriological examination of the fæces attention has been paid to the character of the stools, and in Chart 1 these are described as formed, disturbed, diarrhoeic. There appears to be some relationship between the unformed stools and the presence of bacillus typhosus in the fæces.

On Dec. 20th, 1907, typhoid bacilli were obtained from the fæces. Negative results were then the rule until the following April 14th, when a luxuriant growth of bacillus typhosus appeared on the plates. Further daily examinations showed the organisms to be present on May 11th, 21st, and 29th, and on June 10th. The urine did not contain the bacillus typhosus. About May 21st Mrs. H. fell ill. The pulse-rate was 120, the temperature was 100° F., and she presented a "typhoid" appearance. Chart 1 gives the temperature and pulse curves. Differential blood counts showed an increase of mononuclear cells—35 to 50 per cent. Unfortunately, at the time it was impossible to arrange for a count of the total number of white cells. Her blood gave a good and prompt agglutination, 1 in 25, but was negative in higher dilutions. With a view to the consideration of other causes the blood was examined bacteriologically. No organisms were present. Her opsonic index was then determined for staphylococci, streptococci, bacillus coli communis, and bacillus typhosus. This was carried out by the opsonic assistant at the Bristol Royal Infirmary, Dr. J. M. H. Munro, to whom we are much indebted. The result was as follows: staphylococci, 0.99; streptococci, 1.07; bacillus coli communis, 1.2; and bacillus typhosus, 1.7. Minute examinations of the fæces failed to reveal any gall-stone, and there were no clinical signs of biliary obstruction.³ We concluded that the patient was probably suffering from a self-inflicted attack of enteric fever, although we recognise that the attack may have been a cholecystitis, or some form of enteritis. The associated presence of bacillus typhosus in the stools led us to regard it as probably a typhoid enteritis. The duration of the illness was about three weeks.

Since this "carrier" was removed from her position in the dairy in November last she has lived in a separate block with some typhoid convalescents. In July, 1908, a woman with whom she had been daily closely associated for some months was attacked with typhoid fever. It was found that after the carrier had eaten as much as she could of her lunch she handed the remainder to her companion. This suggested a probable means of infection and an endeavour was made to find bacilli on the hands of the carrier after defæcation and before ablution. The investigation is still in progress. Up to the present only cocci, moulds, and motile bacilli have

been isolated. No bacillus coli communis or typhoid bacilli have been found. The carrier, however, now endeavours to prevent any soiling of the skin after defæcation, &c. It may be possible to obtain positive results from other carriers before they alter their usual habits.

Second carrier case.—Before considering the question of "periodicity" and "effective periods" we may perhaps mention the details of another case we have met with. In September, 1907, J. H—n had enteric fever and died. His wife, who had nursed him prior to his removal to hospital, had a slight attack of enteric fever in October–November, 1907. After recovery she continued her household duties. All went well until June 6th when her four children were simultaneously attacked with enteric fever. In the absence of any other cause the woman herself fell under suspicion, and it was found that her blood agglutinated bacillus typhosus 1 in 200. On several subsequent occasions the Widal reaction has been obtained in similar dilutions. The fæces are being repeatedly examined from the standpoint of "periodicity."

The May period of infectivity.—We have already pointed out that Mrs. H. was responsible for three outbreaks. In May, 1904, she was at a home for girls, Brislington, where 25 cases of typhoid fever and two deaths occurred. In May, 1905, she was at a girls' home in Clifton, where typhoid fever broke out. In May, 1907, the second and larger group of Brentry cases commenced. At all these places she was present for some time before any typhoid fever appeared. January, February, and March were the months during which she was "ineffective." This year (1908) her isolation has prevented any wide transmission of the organisms, but, curiously enough, she appears to have infected herself about the same time of the year—viz., May—and a single fellow inmate in July. The fæces examined in January, February, and March did not contain typhoid bacilli. In Chart 2 we show these periods. The time during which she was in a position to infect food is shown by a thin line and it will be seen that it was not until May that she became "effective," while, under favourable circumstances, her effectiveness then continued to the end of the year. In the second case, Mrs. H—n, it is again the food preparer who acts as the typhoid carrier. After recovery from her November attack she continued her household duties and everything went well until the end of May or June, when the whole family, except herself and one son, were infected with the typhoid bacillus.

We may now summarise shortly some of the carrier cases already reported.

Kayser's and Klinger's carrier cases.—

CASE 1.—Mrs. E., a confectioner, had enteric fever in 1894. Nearly all her assistants suffered from indigestion and diarrhoea shortly after entering her service. On May 20th, 1904, her assistant, L. R., had enteric fever. On May 24th typhoid bacilli were found in the stools of Mrs. E. On August 8th, 1904, her lodger, J. W., was attacked with enteric fever.

CASE 2.—Mrs. M., a secondhand clothes dealer, had enteric fever in 1874. In 1899 she had an attack of severe biliary colic. On Nov. 24th, 1904, she was found to be a carrier. On May 20th, 1904, her son-in-law, who lived with her, fell ill with enteric fever. On Nov. 17th, 1904, her lodger, A. B., was similarly attacked.

CASE 3.—Mrs. Z., a tailor's wife. In January, 1905, a new servant came into the house. Three weeks later the maid developed enteric fever.

CASE 4.—Mrs. L. Her servant was attacked with enteric fever in April, 1905.

CASE 5.—Miss N. had enteric fever in 1881. Her servant showed signs of enteric fever on June 28th, 1905.

CASE 6.—Mrs. S. had enteric fever in 1877. In August, 1900, she had an attack of biliary colic. In September her children developed typhoid fever.

Soper's case.—The details of this case have been so carefully and fully worked out by Dr. Soper that we may safely assume that during the intervals of the dates mentioned the carrier was "ineffective." In June, 1902, the carrier, who was a cook, joined a family three weeks before the summer exodus. At the end of this time enteric fever appeared. In October, 1903, she entered the service of another family. Nine months later—viz., June, 1904—the family went for the summer holiday, taking the cook with

* The superior figures refer to the bibliography at the end.

CHART 1.—Observations on Carrier Mrs. H.

CHART 2.—Periodicity.

CHART 3. —Periodicity.

CHART 4.—Typhoid Bacilli in Fæces.

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
<u>H.</u>	00	000	000	+	++	0+					+	+
<u>KAYSER.</u>		0 0	0						+			
<u>KLINGER. I.</u>	0	++0	0	+ 0	0 +	+	+	0 0	0	0 +	++	+
... 2.		0 +	+	+	+							

The + signifies presence of typhoid bacilli and the O signifies their absence.

them. Arrived at their summer residence the household visited had an outbreak of enteric fever. Either the carrier had been "ineffective" during these nine months or the members of the family had been immunised. The cook found a new situation, and in September, 1906, she caused another outbreak of enteric fever shortly after she arrived, while in January, 1907, another family owed its attack of enteric fever to her entry into the house.

When these outbreaks due to typhoid carriers are mapped out, as in Chart 3, several interesting points appear. It has been already pointed out that the faeces of the typhoid carrier do not always contain typhoid bacilli. Chart 3 shows that the "effectiveness" of the carrier is also intermittent. The thin line on the chart covers the periods when the carrier was in such relation with other persons—generally as a food preparer—as to make infection possible. The shaded areas indicate the times when the potential became an actual infection. For every carrier, therefore, there appear to be periods of maximum and minimum danger, and a knowledge of these times should be of great value in prophylaxis.

Another point which arises during a consideration of Chart 3 is the almost uniform absence of "effectiveness" of the carrier during the early months of the year. The evidence already gained goes to prove that the typhoid bacillus may live for considerable periods in the gall-bladder and hepatic bile-passages, and there is little doubt but that the carrier harbours the typhoid bacillus continuously.

What is the meaning of this period in which the carrier fails to be "effective"? Is it simply coincidence, or shall we find it appearing uniformly when a larger number of cases are available for reference? Has it anything to do with periodicity in the virulence of the bacillus? Does the organism live a "hibernant" existence in the intra- and extra-hepatic biliary passages during these months, and become actively parasitic on re-awakening for the remaining months of the year? Has this "period of effectiveness" anything to do with the type of food taken, or with the general tissue metabolism, or with the heat regulation apparatus? Does this "seasonal effectivity" offer any explanation of the "waves" of endemic enteric fever, the May revival starting the supply of fresh infections which subsequently develop by extension into the autumnal burst? These are questions which call for further observations, and we do not propose to anticipate the replies.

The seasonal waves of typhoid fever are quite characteristic, and the variations in the virulence of epidemics often exhibit "local" features; sometimes, however, the local virulence may assume national characters. We do not know the causes which are responsible for the intensifications of the virus, but evidence is accumulating to show that the human tissues play a definite part. Direct transmission of human faeces at a period of bacterial virulence to water, milk, shell-fish, or other media in which the organism can proliferate is responsible for widespread outbreaks. Human excreta when spread over the surface of soil may prove effective through the agencies of flies or strong wind currents, but it has to be remembered that typhoid bacilli do not proliferate actively in surface soil and cease to be viable after a few weeks (*vide* Mair²), so that soil infection probably accounts for a small proportion of cases only. Climatic influences are conjectural; it is possible so to arrange the evidence from Britain, Europe, India, and the tropics that rain, drought, heat, and moisture may be severally indicted. Cold alone occupies an isolated position.

When sporadic outbreaks are contrasted with epidemic human transmission again assumes importance. There is every hope that an intelligent appreciation of this fact by the typhoid convalescent may minimise the occurrence of scattered cases of enteric fever, but it is the obvious duty of the physician to frame rules for the guidance of the patient and to see that they are carried out (*vide* Appendix). Similarly, it behoves the community to protect itself from possibilities of infection by the provision of adequate control over typhoid convalescents. There are certain indications which might be followed until more knowledge points to other pathways.

1. *Systematic examination of the faeces of convalescents or suspected carriers*—These examinations must be made day by day and extend over long periods. Chart 4 shows that it is impossible to accept any statement as to the periods of infectiveness or freedom from infection unless records of

daily examinations are available. Anyone who undertakes this class of work knows that the demands on time, technique, and labour are so great that the community will no doubt adopt the plan of precautionary measures for those convalescents who have contact with foods either in the homes or in the distribution of meat, milk, vegetables, &c., or during the manufacture of cocoa and other eatables, reserving bacteriological measures for the cases whose periodicity does not follow the usual course.

2. *Urine*.—The marked excretion of the typhoid bacilli during the later weeks of the acute attack does not appear to have its parallel in the carrier. We have made a number of examinations of the urine, but they have so far yielded negative results.

3. *Blood*.—The agglutinating properties of the blood may afford evidence of the "effectiveness" of the carrier, but during the attack of Mrs. H. in June her Widal reaction did not vary from the 1 in 25 found on previous occasions. The differential counts we have made in the cases examined yielded an increase of mononuclear cells and this has suggested the need for further observations of a similar nature upon carriers and convalescents. It is quite possible that the extended inquiry may show this to be a valuable adjunct in the determination of "effective" periods.

4. *Temperature and pulse*.

5. *Hands*.—It may be worth while to make bacteriological examination of the nails and fingers. Positive results will exert marked mental effect on those who are requested to take antiseptic precautions after the toilet.

6. *Immunity*.—Determinations of immunity can only be carried out in bacteriological laboratories, but it may be necessary to resort to them in some instances. Speaking generally, the immunity of the typhoid carrier must vary considerably from time to time. It lies near to hand to think of raising the immunity of the carrier by injections of vaccines. Such a procedure will probably minimise the chances of re-infection, so that the carrier becomes less liable to recurrent attacks, but whether the raised immunity will comprise increased bactericidal powers and subsequent destruction of the bacilli is a question which can be answered only when investigations now in progress are more advanced and when our results of treatment with tar derivatives, &c., are available. We do not consider that a typhoid carrier should be considered as "cured" until daily examinations of the faeces have determined the absence of the bacilli during a period extending at least from April to November. This fact is brought out in Chart 4.

We do not attempt to generalise from these necessarily incomplete and preliminary observations, and we venture to hope that the profession, while using prophylactic measures to their full, will not rush into anti-typhoid-carrier therapy until the details have been adequately determined by laboratory investigations.

We are much indebted to Dr. D. Fleck and Dr. R. A. Beaver for their unwearied help in the collection of material and clinical observations and to Mr. J. C. Heaven for collaboration in the preparation of charts.

APPENDIX.

SUGGESTED INSTRUCTIONS TO TYPHOID CONVALESCENTS.

(To be handed to Patients when discharged from Hospital.)

Typhoid fever is caused by a germ (the typhoid bacillus) which enter the body in food or drink or swallowed dust. When the convalescent stage is reached, the germ may remain in the intestines, and cause relapses of the disease. Sometimes the germ remains permanently in the intestines, and may cause a return of the disease many years after the first attack. The germ may also induce the formation of gall-stones. Thus it is evident that the contents of the intestine of the typhoid convalescent are infective, and that the convalescent may be the unconscious means of transmitting the disease to his, or her, own family or friends. Cooks, male or female, dairymen or dairymen, milk-vendors, greengrocers, butchers, fishmongers, provision dealers, workers in cocoa, chocolate, or confectionery, waiters and waitresses, and the mother who prepares food for the family, form a class of convalescents in which the opportunities of transmission of the disease are very frequent. The following provisional rules are suggested with a view to diminish the risk of infection:—

1. The hands and nails should be thoroughly washed, first in disinfectant solution, then in soap and water, and well rinsed before touching any foodstuffs, especially milk.
2. After the bowels are opened or the bladder is emptied the hands and nails should be at once disinfected and washed.
3. Strong disinfecting solution should be poured over the stools, &c., before the plug of the water-closet is used or the lid of the dry closet is shut down.
4. When the motions are loose the risk of infection is increased and additional care should be taken.
5. The convalescent should periodically visit the medical attendant, so that the blood, &c., may be tested, and measures may be taken to

control the action of the germs. As there is generally no need to deal with the drains, or to disinfect rooms or houses for these special cases, no upset of the domestic arrangements is necessary.

6. In the household where a patient is convalescing from typhoid fever the additional precautions of boiling all the milk or water used for drinking or in the preparation of food should be undertaken, and uncooked foods should be avoided.

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THE COMMON COLD: ITS PATHOLOGY AND TREATMENT,

WITH ESPECIAL REFERENCE TO VACCINE THERAPY.¹

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I.—INTRODUCTION.

In a recent publication on catarrhal fevers by Dr. R. Prosser White we find the following: "I venture to submit that our zeal and interest in a disease should be proportional not to its rarity but to its frequency; and to call trifling, a disease which incapacitates members of every class of society oftener and more commonly than any other, and has the reputation of initiating so diverse and numerous ailments, is a travesty of facts. This condition, the bane of the household and the scourge of the community is allowed to run riot, practically ignored by our leaders, our medical schools and our text-books." A feeling exactly in accord with that expressed by these very true words was the cause of my undertaking the present research into this common affection, which, again to quote Dr. Prosser White, "is a source of inconvenience, if not danger, to the strong, and is often followed by severest consequences in the old and the young, the feeble and the debilitated—which may be the active factor in overburdening an already embarrassed heart, setting up the final catarrh in the later stages of phthisis or multiplying the difficulties and distresses of the chronic invalid suffering from bronchitis and emphysema." The work conducted during two years' tenure of the Gull studentship has been completed in my private practice, with the result that I think I can fairly claim to have placed the bacteriology upon a sounder footing, indicated means whereby a differential diagnosis of the causal organism or organisms may be made in any given case from a consideration of the clinical features, and to have demonstrated the utility of vaccine therapy not only in shortening acute attacks and thereby preventing secondary complications, but also in curing chronic cases and in securing immunity, more or less complete, from further attacks, acute or chronic, in those who are especially susceptible to this very troublesome and common complaint.

II.—DEFINITION OF A COLD.

For the purposes of this research a cold may be defined as a local inflammation of any portion of the respiratory tract, from the mouth and external nasal meatus to the bifurcation of the bronchi, together with the sinuses annexed thereto; such as the frontal and ethmoidal sinuses, the maxillary antrum, and the Eustachian tube; inflammations due to the ordinary pyogenic cocci are, however, excluded. The conditions thus included are the so-called colds in the head, sore throats, and tracheal coughs. The word "fever" has been avoided, inasmuch as any rise of temperature is, more often than not, local and not general; indeed, the true body temperature, obtained either per rectum or by means of the urine, is more often than not subnormal. Colds are always acute at the onset but may go on to a chronic stage, persisting for even 20 years, punctuated at intervals by acute exacerbations. The acute cold exhibits the following stages. 1. Local anæmia of the mucous membrane. This probably precedes infection, so ought perhaps to be called a pre-catarrhal condition. This is succeeded by local hyperæmia,

the natural response of the body to the preceding anæmia. 2. After infection there is a period of incubation, during which the hyperæmia increases to a greater or less extent. Few opportunities of measuring this have presented themselves, but in one case it could be fixed at only two hours; the usual period, however, seems to be about 12 hours, but varies according as to whether the infection is a fresh one from without or due to a lighting up into activity of organisms already resident in these parts. During this period there may be dryness and tickling of the palate and fauces and a few sneezes may be given, soon to be followed by a general feeling of malaise and chilliness, which marks the completion of the incubation period and the onset of the third stage—viz., the period which may be called the "catarrhal plateau." This is characterised by greatly increased mucous secretion, the attempt of the body to rid itself of the invaders. If the fauces be involved there is a definite sore-throat, if the trachea a resultant cough. The feeling of general malaise continues, often accompanied by headache, constipation, and distaste for food; there may be some pyrexia; the secretion of sweat and urine is diminished and the latter may be loaded with urates. After from 18 to 48 hours the mucous secretion diminishes and the fourth or subacute stage is entered upon. The mucous discharges become thick and contain leucocytes and lymphoid cells which cause the discharges to become yellow in colour. This lasts for a period varying from two or three days to as many weeks, when it either ceases and cure is established, or it persists for months or even years and enters upon the fifth stage, which is that of true chronicity, marked by continuous excessive secretion of thick mucus and the feeling aptly described as "stiffness of the nose." Such a chronic condition is punctuated at intervals by periods of exacerbation or by acute attacks due to a second organism.

III.—BACTERIOLOGY.

A.—Technique Employed.

Before any attempt can be made at the determination of the bacterial agents in the production of pathological conditions it is obviously necessary to determine what are the normal bacterial inhabitants of the part or parts. Accordingly healthy noses and throats were examined as well as catarrhal. The technique employed was as follows.

1. *For the trachea.*—The mouth having been thoroughly gargled several times with sterile water, by means of a violent cough some mucus was expectorated and received in sterilised water; a small compact piece was washed two or three times and then inseminated upon one or more of the following—agar, blood agar, nutrose ascitic agar or so-called "nasagar," blood serum. After 24 hours' incubation at 37° C. films were prepared as well as some from the original mucus, stained with methylene blue and by Gram's method, and examined microscopically. The organisms were then isolated when necessary.

2. *For the throat.*—Swabs were taken from the hyperæmic areas, soft palate, posterior pharyngeal wall, fauces or tonsils, and treated as in the case of the tracheal mucus.

3. *For the nose.*—In order to avoid contamination with the organisms infecting the vibrissæ and vestibule the following procedures were adopted: (a) A piece of sterilised glass tubing about three inches long and of ample bore so as to admit the passage of a platinum loop was inserted up the nostril; along this tube a sterile loop was pushed and the protruded end rubbed over the surface of the nasal mucosa; it was then withdrawn through the glass tubing and a smear made upon agar, blood agar, blood serum, or nasagar, two or three such smears being usually made upon different media. (b) As an alternative method a sterilised nasal speculum was used to separate the nasal orifice and by means of a sterile swab cultures taken as high up the septum and turbinals as it was possible to get. (c) Experiment, however, showed that these precautions were hardly necessary in the case of nasal catarrh where organisms are always plentiful and that certain advantages were to be obtained by using the following procedure. The orifice of the nose having been well washed with warm soap and water and dried upon sterile lint, one nostril was closed and the nasal secretion forcibly expelled from the other upon sterilised cotton-wool. Ample material is thus obtained to inseminate numerous tubes and plates and to prepare films. In several cases cultures were made by two of these methods and identical results obtained.

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