ance, but such confession is an evidence of sincere concern for the welfare of the patient.

Let it be remembered that there may be more than one point of obstruction or strangulation, especially in cases secondary to former attacks of peritonitis. Do not forget that visible intestinal peristalsis with paroxysmal rigidity and stiffening of definite loops of intestine, after percussion of the abdominal wall, are absent in volvulus (axial rotation) and internal hernia with strangulation, unless these conditions are engrafted on chronic obstruction. This symptom may be of diagnostic value, however, to establish the presence of intestinal obstruction in chronic forms of occlusion, where the muscular coat has become hypertrophied.

Recollect the absence of peristalsis and the possible occurrence of adynamic obstruction in appendicitis, renal and biliary colic, and peritonitis, which are due to inhibition of power in the musculature of the intestine. In these instances pain and sensitiveness may prevent the passage of feces along the intestinal canal and simulate obstruction. There is perhaps a sort of neurotic constipation here, such as may occur in healthy persons who have not access to decent toilet facilities.

When the surgeon has concluded that strangulated intestine is causing the symptoms, he should endeavor to make up his mind as to the location of the trouble and the character of the strangulating process.

The most common site of strangulating lesions, not associated with internal hernia, is the right lower quadrant of the abdomen. The lower portion of the ileum and the cecal region, therefore, should be inspected first. Volvulus, however, is most apt to occur in the sigmoid colon, especially in the aged. Intussusception is not particularly common in the ileocecal region, but it is perhaps most frequently found in some portion of the colon. It is the more frequent disease of the young. Strangulative lesions, being usually acute, are more difficult of differentiation than those other obstructive lesions which are chronic.

The change in contour of the belly, due to tympany, will sometimes aid in settling the site, as has already been stated. In obese patients this determination becomes a matter of increased difficulty. It must be recollected that the sigmoid colon twisted on its axis may fill from distension the abdominal cavity in an astonishing way and extend even to the right hypochondrium. In such cases, however, the left flank also is apt to be convex from distension. The upper lumbar region, on both sides behind, will give on percussion, it is said, a long deep note instead of the normal high and flat note, when the obstruction is in the sigmoid or descending colon. This change in percussion note in the back will be found only on the right side, when the occluding lesion is in the transverse colon or at the splenic flexure. This sign seems to have some value.

The pain is less severe in volvulus than in strangulation by omphalo-mesenteric remains, or bands; and sometimes the pain of volvulus may be referred to the back. In volvulus high up in the small bowel there may occur frequent evacuations from the bowels. This is unlike internal hernia-form strangulation and strangulation from bands, which are accompanied by absolute constipation. Occasionally a little blood may be passed with the feces in cases of volvulus, especially of the sigmoid flexure. Rectal tenesmus is an indication of volvulus being the cause of the obstruction, rather than strangulation from other causes. Fecal vomiting is not common in volvulus, but it is common in strangulation

from entanglement under bands and in openings. Volvulus is more apt to be preceded by habitual constipation, and causes less intense collapse than strangulation from bands.

A previous history of peritonitis would point rather to strangulation by bands, or kinks or knots, than to strangulation from volvulus, were it not a fact that peritonitis may cause narrowing of the mesentery from infiltration and cicatricial changes which tend to make axial rotation (volvulus) occur more readily.

The differential diagnosis is farther obscured at times by the circumstance that volvulus of the small intestines and strangulation by bands and cords may be coexistent.

My final word is: If the diagnosis can not be established with a fair degree of certainty within twenty-four hours, or at most forty-eight hours, open the abdomen aseptically and inspect its contents.

313 South Seventeenth Street.

[THIS SYMPOSIUM ON ILEUS TO BE CONTINUED. THE DISCUSSION WILL FOLLOW THE LAST PAPER.]

THE OCCURRENCE OF TYPHOID BACILLI IN THE STOOLS OF TYPHOID PATIENTS,

WITH A DISCUSSION OF THE PATHOGENESIS OF TYPHOID FEVER.*

DRS. J. H. PRATT, F. W. PEABODY AND A. D. LONG.

BOSTON.

The view is generally held that the intestinal contents in typhoid fever are swarming with typhoid bacilli. The fact that many investigators have often had difficulty in isolating *Bacillus typhosus* from the stools of undoubted cases of typhoid fever has been attributed to imperfect technical methods. Some observations made by one of us seemed to indicate that the reason typhoid bacilli were not obtained from the stools during the height of the disease might be due, not to faulty bacteriologic methods, but to the fact that the typhoid micro-organisms were either absent from the feces or present in extremely small numbers.

The studies here presented extend over two years. About 75 per cent. of the patients had fever at the time of the examination. All were clinically typhoid fever. In only one instance was the agglutination test persistently negative. It is probable that this was a case of infection with *Bacillus faecalis alkalingenes*. Each day the sickest patients to be found in the wards were selected for the examination. For the opportunity of making this study we are indebted to the visiting physicians of the Massachusetts General Hospital.

When Gaffky¹ reported, in 1881, that he had cultivated on artificial media the specific micro-organism of typhoid fever, he made no claim that he could isolate it from the intestinal contents. In 13 cases he obtained the typhoid bacillus from the spleen and in one case from the liver. Pfeiffer,² in 1885, was the first to assert that typhoid bacilli were present in the stools. As he knew nothing about *Bacillus coli* and did not fully

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* From the Laboratory of Clinical Pathology, Harvard University (Director, Prof. R. H. Fitz). This investigation was begun in the Laboratory of Bacteriology. The facilities of the bacteriologic department were available through the courtesy of Prof. H. C. Ernst.

1. Mitt. a. d. Kaiserl. Ges. Gesundheitsl., 1884, II, 372.

2. Deutsche med. Wochschr., 1885, p. 500.

identify the bacilli he isolated, his results can not be accepted. Merkel and Goldschmidt,³ Karlinski⁴ and Wilt-schaur⁵ claimed they could demonstrate typhoid bacilli in the stools without difficulty. Karlinski,⁴ in 1889, stated that he obtained positive results in all of the 21 cases he examined. As none of these investigators differentiated the micro-organisms they obtained from *Bacillus coli*, their observations are of no value. It is interesting to note that Wilt-schaur⁵ was the first to state that the number of typhoid bacilli in the stools is very small. Wäthelet⁶ showed that the methods of the earlier investigators were inadequate. He made a bacteriologic examination in 12 cases of typhoid fever, and reported that he was able to isolate the typhoid bacillus in only 4 of them. He studied about six stools from each patient. He examined in all 600 colonies that developed on ordinary gelatin and only 10 of these were typhoid colonies. Even his results can not be accepted, as he did not state how he identified the micro-organisms he isolated as typhoid bacilli. G. Roux, writing in Bouchard's *Traité de Pathologie* as late as 1896, stated that it was impossible to isolate *Bacillus typhosus* from the intestinal contents owing to the constant presence of large numbers of colon bacilli. The first trustworthy work dates from the introduction of the glucose fermentation tests and the use of litmus-milk for differentiating colon and typhoid bacilli. Since 1897 the agglutination test has been generally employed.

The first practical medium for separating typhoid from colon bacilli was the iodine-potato-gelatine of Elsner.⁷ The publication of his paper, in which he stated that by this new method he had isolated *Bacillus typhosus* from the stools in 15 out of 17 cases attracted much attention. His method was used and indorsed by Brieger,⁸ Grawitz,⁹ Lazarus¹⁰ and Sterling¹¹ in Germany, by Pollak¹² in Austria, Jemma¹³ in Italy, Chantemesse¹⁴ in France, Horton-Smith¹⁵ in England and Mark Richardson¹⁶ in America. Pollak,¹² Brieger⁸ and Lazarus¹⁰ obtained positive results in all the cases they studied. The published reports of these investigators seemed to demonstrate the truth of the old theory that typhoid bacilli developed in enormous numbers in the intestinal contents of typhoid patients. The theory advanced by Metchnikoff and Sanarelli¹⁷ in 1894 seems to have attracted little or no attention. They held that the typhoid bacilli only occasionally wandered from the spleen and mesenteric lymph nodes into the intestines. The work of Brieger,⁸ Chantemesse,¹⁴ Lazarus¹⁰ and Sterling¹¹ must be rejected, however, as these investigators did not clearly differentiate between typhoid and colon bacilli.

Although the method of Elsner⁷ in the hands of some investigators yielded excellent results, other bacteriologists found it unsatisfactory and failed to cultivate the typhoid bacillus in many undoubted cases of typhoid fever.

The paper of Hiss,¹⁸ in this country, and the monograph of v. Drigalski and Conradi,¹⁹ in Germany, seem to indicate that the failures of many earlier investigators to isolate typhoid bacilli from the stools were due to the lack of satisfactory methods. Of 19 febrile cases at the New York Hospital, the typhoid bacillus was isolated by Hiss from the stools in 17, that is, 89.5 per cent., by his method. Often the bacilli were present in large number. Higley²⁰ obtained positive results in 20 out of 21 cases by the use of Hiss's medium. v. Drigalski and Conradi¹⁹ cultivated the typhoid bacillus from the feces by their litmus-lactose-agar method in every one of the 50 cases of typhoid fever they examined. The results of these bacteriologists must be accepted, as they fully identified the micro-organisms they isolated as typhoid bacilli. v. Drigalski,²¹ in a later paper, stated that he subsequently examined cases in which he could not demonstrate typhoid bacilli in the stools even at the height of the disease. Klinger²² was able to isolate *Bacillus typhosus* from typhoid stools in only 25 out of 75 febrile cases (33.3 per cent.) by the v. Drigalski-Conradi method. Krause and Stertz²³ in 33 out of 44 cases, Lipschütz²⁴ in but 1 out of 17 cases, and C. Cole²⁵ in 2 among 21. All used the v. Drigalski-Conradi method.

Malachite green media check the growth of colon bacilli, while they allow the development of most strains of typhoid bacilli. Klinger,²² using malachite green agar as an enriching medium, isolated *Bacillus typhosus* in 26 out of 43 cases. He examined 35 stools during the febrile period by four methods: the v. Drigalski-Conradi, the Endo, the caffein with biologic precipitation, and the enriching malachite green agar. He succeeded by the simultaneous employment of all four methods in cultivating *Bacillus typhosus* 28 times from 35 stools, or in 80 per cent. of the cases.

Before attempting to reconcile the good results that early investigators obtained with imperfect methods and the comparatively poor results of Klinger, Krause and Stertz, Lipschütz and others with improved methods, a summary of our own work will be presented.

METHODS.

We have used for isolating *Bacillus typhosus* from the stools the v. Drigalski-Conradi litmus-lactose plates, Hiss's media and malachite green enriching methods. The medium of v. Drigalski and Conradi permitted a sharp differentiation of typhoid and colon colonies. The typhoid colonies were always bluish and usually small and translucent, looking like drops of dew. Sometimes, however, the first generation of typhoid colonies grown from the feces were large (3 to 4 mm. in size) and opaque. Colon bacilli formed large, opaque, red colonies. We have prepared the v. Drigalski-Conradi medium many times, and the different lots have presented a uniform appearance, and typhoid and colon colonies have always grown in a typical manner.

The failure of many bacteriologists to obtain a satisfactory medium depends on the fact that they did not use the right litmus. We have employed only Kahlbaum's litmus solution, which is made according to the formula of Kubel and Tiemann from specially treated

3. Centrbl. f. klin. Med., 1887, p. 393.

4. Centrbl. f. Bakt., 1889, vi, 65.

5. Centrbl. f. Bakt., 1890, vii, 279.

6. Ann. de l'Institut Pasteur, 1895, ix, 253.

7. Ztschr. f. Hygiene, 1896, xxi, 25.

8. Deutsche med. Wochschr., 1895, xxi, 835.

9. Centrbl. f. Bakt., 1892, xii, 729.

10. Berliner klin. Wochschr., 1895, xlix, 1068.

11. Centrbl. f. Bakt., 1897, xxii, 334.

12. Centrbl. f. innere Med., 1896, p. 785.

13. Münch. med. Wochschr., 1897, xxxiii, 911.

14. Comp. rend. de la Soc. de Biol., 1896, p. 215.

15. Lancet, 1899, p. 1346.

16. Boston Med. and Surg. Jour., 1903, cxlviii, 152.

17. Ann. de l'Institut Pasteur, 1894, viii, 193.

18. Med. News, 1901, lxxviii, 728.

19. Ztschr. f. Hygiene, 1902, xxxix, 283.

20. Med. News, 1902, lxxx, 585.

21. Centrbl. f. Bakt., 1904, xxxv, No. 6.

22. Inaug. Disser., Strassburg, 1904; republished in Arb. a. d. Kaiserlich. Gesundheit., 1906, xxiv, 35.

23. Ztschr. f. Hygiene, 1903, xlv, 469.

24. Centrbl. f. Bakt., 1904, xxv, 798.

25. Amer. Med., 1906, xi, 480.

litmus stock. This was the preparation of litmus that v. Drigalski and Conradi employed. With no other, according to Bassenge,²⁶ is there such a sharp differentiation of the color between typhoid and colon colonies. During the early part of this investigation Petri plates of ordinary size were used, later the large plates (15 to 20 cm. in diameter) as recommended by v. Drigalski and Conradi, Hiss's method in our hands was far less satisfactory than that of v. Drigalski and Conradi.

Klinger²² was able to isolate *Bacillus typhosus* from the stools in a much larger percentage of cases when he used the enriching malachite green method of Lentz and Tietz²⁷ than when he employed the blue agar of v. Drigalski and Conradi. Our attention was not drawn to the work of Klinger and Lentz and Tietz until the research as originally planned had been completed. It was then decided to make another series of observations, employing malachite green media in addition to the v. Drigalski-Conradi method. Lentz and Tietz's agar was tried and also a new enriching method devised by Peabody and Pratt. The malachite green methods failed to yield as good results as that of v. Drigalski and Conradi. This was probably due to the fact that the strains of the typhoid bacillus present in the intestinal contents of most of our cases were more susceptible to the inhibitory action of malachite green than our stock culture and the typhoid bacilli present in the cases studied by Klinger.

For example, a large v. Drigalski-Conradi plate inoculated November 27 from the feces of the patient Regan showed about 450 typhoid colonies. This particular strain of *Bacillus typhosus*, although present in the feces in large number, failed to develop on the malachite green agar or in the malachite green bouillon. There were nevertheless many bacteria in this specimen of feces that developed luxuriantly on the malachite green agar. On the Lentz and Tietz agar plate at the end of twenty hours were about 250 discrete colonies of nearly uniform size, averaging about 2 mm. in diameter, and a great multitude of minute colonies. A v. Drigalski-Conradi plate made from this green plate failed to show a single typhoid colony. It is possible that the negative result in this case was due less to the inhibitory action of malachite green on the typhoid bacilli than to the presence of an unusually large number of fecal bacteria capable of developing on malachite green media. Their growth may have choked the typhoid bacilli.

When typhoid bacilli are found in the stools the possibility that they came from urine voided during defecation must be borne in mind. Precautions should always be taken to avoid this source of error.

RESULTS.

1. Pratt in 1905 isolated *Bacillus typhosus* in 6 out of 43 cases—14 per cent.
 2. Pratt and Peabody in 1906 isolated *Bacillus typhosus* in 4 out of 31 cases—12 per cent.
 3. Pratt and Long in 1906 isolated *Bacillus typhosus* in 7 out of 26 cases—27 per cent.
- Total *Bacillus typhosus* isolated in 17 out of 100 cases—17 per cent.

Twenty-one of the cases were examined during convalescence only. All of them were negative. If the febrile cases alone are considered, then the percentage of positive results is increased from 17 to 21 per cent. The results in the first two series of examinations given above were obtained by the v. Drigalski-Conradi method. Pratt and Long used, in addition, the malachite green method. Employing the same medium with which v.

Drigalski and Conradi obtained positive results in 100 per cent. of the 50 cases they examined, we succeeded in isolating the typhoid bacillus in only 17 out of 79 febrile cases. Failure to isolate *Bacillus typhosus* from the stools is usually attributed to a faulty method or to poor technic. Our personal experience has convinced us that our low percentage of positive cases is due to the fact that in a great majority of the cases of typhoid fever that we studied the typhoid bacilli were either entirely absent from the stools or present in small number.

In 51 cases 1 stool examined.	In 3 cases 5 stools examined.
In 23 cases 2 stools examined.	In 2 cases 6 stools examined.
In 12 cases 3 stools examined.	In 1 case 12 stools examined.
In 8 cases 4 stools examined.	

Total number of stools examined, 206. The typhoid colonies were rarely present on the plates in large number. In the case in which twelve stools were examined the first six were negative. The following is a summary of the bacteriologic tests made in this case:

Sadie F.—November 7. (Sixth week of disease.) v. Drigalski-Conradi plates negative.

November 10. v. Drigalski-Conradi negative.

November 14. v. Drigalski-Conradi negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 16. Malachite green bouillon negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 17. Malachite green bouillon negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 19. Malachite green bouillon negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 20. Temperature 98.8. Malachite green bouillon negative. Lentz and Tietz positive; only three or four blue colonies: *Bacillus typhosus*. v. Drigalski-Conradi negative.

November 22. Malachite green bouillon negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 23. Malachite green bouillon negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 24. Malachite green bouillon negative. Malachite green agar negative. v. Drigalski-Conradi negative.

November 27. Temperature 103.6. Lentz and Tietz negative. v. Drigalski-Conradi positive; seven blue colonies: *Bacillus typhosus*.

In all, 34 examinations were made by the three methods. Only two of these were positive, once the Lentz and Tietz method and once the v. Drigalski-Conradi. Although thousands of colonies grew on the blue plates inoculated from these twelve stools, not over ten or eleven were typhoid colonies. The examinations were made from fresh stools except in a few instances when the specimens were passed twelve to twenty-four hours previously. In only one of our cases did typhoid bacilli persist in the stools in considerable number. At the first examination made November 12, all three methods were negative. The four subsequent examinations were all positive. The detailed report is as follows:

Banks.—November 12. (End of second week.) Malachite green broth negative. Lentz and Tietz negative. v. Drigalski-Conradi negative.

November 15. Temperature 102.8. v. Drigalski-Conradi positive. About twenty-seven blue colonies: *Bacillus typhosus*. Malachite green broth negative for typhoid.

November 16. Temperature 102. Malachite green broth negative. Lentz and Tietz negative. v. Drigalski-Conradi plate shows fifty blue colonies; positive: *Bacillus typhosus*.

November 25. Temperature 100.2. Malachite green broth typhoid. Lentz and Tietz negative. v. Drigalski-Conradi positive; two hundred red colonies to seventy-five large blue colonies: *Bacillus typhosus*.

November 27. Temperature 101. Lentz and Tietz negative. v. Drigalski-Conradi positive; about thirty blue colonies: *Bacillus typhosus*.

26. Deutsche med. Wochschr., 1903, xxix, 675.

27. Münch. med. Wochschr., 1903, xlix, 2139; Kln. Jahrb., 1905, xiv, 495.

Typhoid bacilli may be present in large number in one stool and absent in another stool passed a few hours later. This was well shown in one instance after intestinal hemorrhage. A black formed stool which was shown by the guaiac test to contain blood was examined. Typhoid colonies made up from 70 to 90 per cent. of the total number that developed on three v. Drigalski-Conradi plates. We have never seen such a preponderance of typhoid bacilli in any other stool. The next movement of the bowels consisted of formed masses which were brownish-black externally and yellow internally. Four v. Drigalski-Conradi plates were made. Not a single blue colony developed. Observations made in this case show how quickly typhoid bacilli can disappear from the intestinal contents and also that they develop readily when a favorable culture medium, such as blood, is present.

All but one of our positive cases were still febrile at the time the typhoid bacillus was recovered from the stools. It was found in all stages of the disease from the second to the thirteenth week. Only one case was examined during the first week, as the patients almost invariably enter the hospital later in the disease. Singularly enough, contrary to the theory expressed by Lipschütz²⁴ and others, no connection could be traced between diarrhea and the presence of typhoid bacilli. It should be stated, however, that typhoid bacilli are present as often in normal solid movements as in unformed feces. Some cases with marked enteritis, as indicated by the passage of fluid stools containing considerable mucus, occurring in small masses intimately mixed throughout the specimen, were examined with negative result.²⁸

We have demonstrated repeatedly that the number of typhoid bacilli in some stools must be very small if the micro-organism be present at all. For this purpose fresh stools were taken from cases at the height of the disease and an unusually large number of plates inoculated. In one case twenty v. Drigalski-Conradi plates were made from a thick fluid movement containing much mucus obtained from a patient with high fever. Not a single blue colony developed on any of the plates. Eleven plates containing Hiss's medium were also negative. Eighteen blue plates from a single stool of another undoubted case of typhoid were likewise negative. Dr. Orton at the Boston City Hospital examined fifteen stools from one typhoid patient by Hiss's method without finding *Bacillus typhosus*.

The fact that typhoid bacilli grew abundantly in the stools of one of our cases while they were absent in the majority of the cases may have been due to differences in the strains of the typhoid bacilli. It is now known that different races of typhoid bacilli vary considerably one from another. Our patients came not only from Boston, but from many towns in this part of the state and a few from distant places. The patient in whose stools the greatest number of typhoid bacilli was found lived in Boston, but, of course, he may have been infected with a different strain of typhoid bacilli than any of the other patients.

Through the kindness of Dr. J. Homer Wright we

have been able to study the intestinal contents after death in one case. Four days before death the stools were examined by the v. Drigalski-Conradi method and no typhoid bacilli found. At autopsy a blue plate was inoculated with a drop of bile and several hundred typhoid colonies developed, while two large plates inoculated with material from the first part of the jejunum did not yield a single typhoid colony. Material from near the ileocecal valve as well as from the ileum 60 cm. above the cecum was likewise negative. Typhoid bacilli were obtained from the spleen, but not from the heart's blood.

PATHOGENESIS.

Typhoid fever must be regarded as a primary septicemia. Schottmüller²⁹ pointed this out in 1902. The bacillus has been found in the blood repeatedly by the fourth day of the disease. Kayser³⁰ cultivated the micro-organisms from the blood with his bile medium in 100 per cent. of the 21 cases he examined during the first week. Working with the Strassburg typhoid commission, Brion and Kayser had the opportunity to make several examinations during the incubation stage, and in no instance recovered *Bacillus typhosus* from the stools. The typhoid bacilli quickly pass from the blood into the bile. When the typhoid bacilli were injected into the ear vein of a rabbit we recovered the micro-organism the following day from the gall bladder. Dörr³¹ obtained *Bacillus typhosus* from the bile in less than eight hours after it had been introduced into the circulation. Pratt³² reported, in 1901, that the typhoid bacillus was cultivated from the gall bladder in 21 out of 30 cases of typhoid fever that came to autopsy at the Boston City Hospital.

The micro-organism becomes widely disseminated throughout the body. In one case Pratt recovered it from the heart's blood, the spleen, the liver, the kidney, a mesenteric lymph node, the gall bladder, the urinary bladder, the right middle ear, and the bone marrow. It has been isolated from the urine in about 25 per cent. of all cases examined (Jacobi,³³ Munch³⁴). Petruschky³⁵ calculated that in one of his cases each c.c. of urine contained 172,000,000 typhoid bacilli, and Gwynn³⁶ estimated that 500,000,000 per c.c. were present in a case he reported. A number of recent investigators have found typhoid bacilli more often in the urine than in the stools. Among 98 convalescents studied by Herbert,³⁷ only three showed typhoid bacilli in their stools, while they were present in the urine of eighteen. He found they occurred in the urine in large number, in the stools only in small number. The presence of the typhoid bacilli in rose spots is well known. It has been found repeatedly in the sputum when bronchitis was associated with the typhoid infection (v. Stühler,³⁸ Richardson,³⁹ Dieudonné,⁴⁰ v. Drigalski,⁴¹ Jehle⁴² and Rau⁴³). Dieudonné recovered typhoid bacilli from the sputum seven weeks after fever had disappeared. Undoubted cases of typhoid fever without intestinal lesions have been reported (Opie and Bassett⁴³).

29. Münch. med. Wochschr., 1902, xlix, 1561.

30. Münch. med. Wochschr., 1906, lili, 823.

31. Wien. klin. Wochschr., 1905, xviii, 884.

32. Amer. Jour. Med. Sci., 1901, cxxii, 584.

33. Deutsch. Arch. f. klin. Med., 1902, xxii, 442.

34. Semaine Méd., 1904, xxiv, 121.

35. Centrbl. f. Bakt., 1898, xxlii, 577.

36. Johns Hopkins Hosp. Bull., 1899, x, 109.

37. Münch. med. Wochschr., 1904, xi, 472.

38. Centrbl. f. Bakt., 1900, xxvii, 354.

39. Boston Med. and Surg. Jour., 1897, cxxxvii, 433.

40. Centrbl. f. Bakt., 1901, xxx, 481.

41. Wien. klin. Wochschr., 1902, xv, 232.

42. Ztschr. f. Heilkund., 1904, xxv (Inn. Med.), 385.

43. Johns Hopkins Hosp. Bull., 1901, xii, 198.

28. To answer the inquiry of Dr. W. H. Park made when this paper was presented (see discussion at end of the paper), the effect of diet has been studied and found to have little influence on the occurrence of typhoid bacilli in the feces. There are two medical services in the Massachusetts General Hospital. Patients in the wards of the "East" service are allowed a liberal diet, while on the "West" side the ordinary milk diet is given. Nearly an equal number of positive cases were obtained from the two services, nine from the "East" side and eight from the "West."

Jehle⁴¹ observed a case in which there were no characteristic changes in the intestine, and yet the sputum contained typhoid bacilli. Rau isolated *Bacillus typhosus* from the sputum when cultures from the stools were negative.

Baumgarten years ago stated that the typhoid ulcers in the intestines should be regarded as metastases rather than as primary lesions. This theory was revived in 1902 by Schottmüller.²⁹ If the intestinal lesions were due to the action of typhoid bacilli in the intestine it is difficult to explain the absence of intestinal changes in cases of so-called primary typhoid cholecystitis.⁴⁴ In these cases, in spite of the discharge of enormous numbers of typhoid bacilli into the intestine with the bile, there are no intestinal manifestations. Not only are there no intestinal symptoms, but in a fatal case reported by Burlew⁴⁵ there were no typhoid ulcers in the intestine, although bile containing typhoid bacilli entered the duodenum freely. In chronic typhoid bacillus carriers, although the typhoid bacillus may be the predominating micro-organism in the intestinal contents, no intestinal disturbances are produced and health is maintained.

It is interesting to note in this connection that in a study by Wennagel⁴⁶ in Krehl's clinic, infiltration of the lymphatic tissue of the intestine was found not only in the second, but also in the third, fourth and even fifth week. Necrosis and sloughing of the swollen Peyer's patches were observed as early as the second and as late as the seventh week. He concluded that the characteristic typhoid symptoms are not the result of the intestinal lesions, but the two are co-ordinate. Typhoid fever is thus a general infection in which intestinal alterations can occur. Not only are there cases of typhoid fever without intestinal lesions, but Velich⁴⁷ has observed severe typhoid ulceration of the intestine without any disturbance of the health; in other words, without typhoid fever.

In cases of infection during intrauterine life the portal of entry for the typhoid bacilli must have been the umbilical vein. Yet in a case studied by Blumer⁴⁸ typhoid bacilli were found in the intestines.

It is probable that the typhoid bacilli in the intestinal contents come chiefly from the bile. There is no evidence that they are thrown off in large numbers from the ulcers as was formerly taught. If so, one would expect to find an increased number in the lower part of the ileum, but Forster and Kayser,⁴⁹ as well as v. Drigalski,²¹ showed they were less abundant in the lower than in the upper portion of the small intestines. Furthermore, v. Drigalski was often unable to cultivate typhoid bacilli from the surface of the ulcers when they were present on the surrounding mucosa. Councilman⁵⁰ says that he has not infrequently been unable to demonstrate bacilli in sections through the base of typhoid ulcers. Mallory⁵¹ found that histologically the lesions were diffuse and bore no intimate relation to the typhoid bacilli.

Typhoid bacilli may be present in the intestinal contents in the usual number when the ulcers have entirely healed, as in a case reported by Jürgens.⁵²

The mesenteric and other lymph nodes exhibit hyperplasia and necrosis. Curschmann⁵³ states that the bronchial lymph nodes are not infrequently markedly swollen in typhoid fever. Even when intestinal lesions were absent the mesenteric lymph nodes, in some cases at least, have been enlarged. Ulceration of the lymph nodules of the intestine is probably due simply to the exposure of the necrotic tissue to the action of the intestinal bacteria. The lesions in the lymph apparatus of the intestine result, as do the lesions in lymphatic structures elsewhere, from the action of the bacteria or their toxins entering these tissues from the circulating blood and not to the invasion of the intestinal wall from its mucous surface.

The sporadic occurrence of chronic typhoid bacilli carriers indicates that the harboring of typhoid bacilli within the intestinal tract for a long period of time depends on the host, not on a particular variety of the parasite. In the study of typhoid fever in Strassburg, Brion and Kayser⁵⁴ found only three typhoid bacillus carriers among 200 typhoid patients. The interesting case reported by Soper⁵⁵ of the New York cook who infected twenty-six or more individuals illustrates the same point. If the ability to develop in the intestines depended on a peculiar property of the typhoid bacillus, then the individuals she infected would, in turn, have become typhoid bacillus carriers.

The view that the persistence of typhoid bacilli in the stools is due solely to their retention in the gall bladder can not be accepted for the typical cases studied by v. Drigalski,²¹ Friedel⁵⁶ and others in which the typhoid bacillus are present in almost pure culture in the feces. Typhoid bacilli, as has been pointed out, are present in the bile in practically every case of typhoid fever, and yet, as we have shown in many cases, they are not demonstrable in the stools. In these typhoid bacilli carriers it would seem that either the normal bactericidal power of the intestinal wall is diminished or there is some other change that enables the typhoid bacillus to develop in the intestinal contents. In some cases the typhoid bacillus has largely replaced the colon bacillus (Friedel).

Attention should be called to the fact that in a hemorrhagic stool we examined typhoid bacilli were present in enormous number. It is evident that the blood shed into the intestine furnished favorable conditions for the growth of the typhoid bacillus. The fact that in the next stool passed the same day no typhoid bacilli could be found supports our conclusion that ordinarily the typhoid bacillus does not develop in the intestinal contents. In this opinion we are not alone. Brion and Kayser's⁵⁴ observations have convinced them that the intestine is "*nicht der Vegetationsort*" of the typhoid bacilli. It would seem that the number of typhoid bacilli in the intestinal contents must vary greatly in different epidemics of the disease. This is a reasonable explanation for the divergent results obtained by different investigators who have studied the stools by approved methods. Otherwise it is difficult to understand how Elsner,⁷ Higley,²⁰ Pollak¹² and others were able to obtain positive results in a large proportion of their cases by the use of poor methods, while recent investigators working with superior methods have been able to obtain positive results in only a relatively small percentage of cases. Hayashikawa⁵⁷ studied the occurrence of typhoid bacilli in the stools in Halle and in Prague.

44. This is probably not a primary condition at all, but secondary to a typhoid septicemia, and represents an instance of typhoid infection in which the chief local lesion is in the gall bladder and not in the intestine.

45. *Medicine*, 1903, ix, 734.

46. *Deutsch. Arch. f. klin. Med.*, 1906, lxxxvii, 551.

47. *Arch. f. Hygiene*, 1904, xlix, 113.

48. *THE JOURNAL A. M. A.*, 1901, xxxv, 1674.

49. *Münch. med. Wochschr.*, 1905, p. 1475.

50. Personal communication.

51. *Jour. Exper. Med.*, 1898, iii, 611.

52. *Ztschr. f. klin. Med.*, 1904, lii, 40.

53. Nothnagel's spec. Path. u. Therap., 1898, 227.

54. *Deutsch. Arch. f. klin. Med.*, 1906, lxxxv, 552.

55. *THE JOURNAL A. M. A.*, 1907, xlviii, 2019.

56. *Ztschr. f. Med. Beamte*, 1905, xviii, 61.

57. *Ztschr. f. Heilkunde*, 1903, xxiv (Inn. Med.), 19.

He concluded that in the type of typhoid fever present in Germany more typhoid bacilli are present in the stools than in the cases that occur in Bohemia.

In our fatal case v. Drigalski-Conradi plates made from different portions of the intestine showed that the great number of typhoid bacilli that entered the duodenum with the bile were destroyed so speedily that none could be demonstrated in the upper part of the jejunum. Forster and Kayser⁴⁹ noted that there were more typhoid bacilli in the duodenum than in the ileum. A table published with their paper shows that in one case they found typhoid bacilli absent in the jejunum, although present in the duodenum. They made no comment on this remarkable observation. v. Drigalski²¹ found in all his cases that the typhoid bacillus occurred in pure culture in the duodenum. Cushing and Livingston⁵⁸ demonstrated several years ago that the normal bacterial flora of the human stomach and duodenum was very meager. Rolly and Liebermeister⁵⁹ recently showed that the wall of the duodenum in the rabbit has marked bactericidal power.

Although v. Drigalski found typhoid bacilli present on the inner surface of the stomach in every case he examined at autopsy, it is difficult, in view of the bactericidal power of the gastric mucosa, to believe that the portal of entry of the typhoid bacillus is through the wall of the stomach. Curschmann,⁵³ however, endorses the view of Stern and Hamburger that the typhoid bacilli are so resistant to weak acids that they are probably able to live in the stomach.⁶⁰

It will be seen that these observations harmonize with one another. In the light of this new knowledge, it can readily be seen that the old theory that the intestine is the portal of entry of the typhoid bacilli can no longer be accepted unless additional evidence can be produced in its favor. If the duodenum is able to destroy the great number of typhoid bacilli that enter with the bile, how is it possible that the relatively few micro-organisms contained in the infected food are able to pass through the duodenum alive and gain an entrance into the body through the solitary lymph nodules and Peyer's patches of the lower part of the ileum? In regard to the place and mode of entry of the typhoid bacilli nothing definite is known aside from the fact that some part of the alimentary tract is infected. Forster has suggested that typhoid bacilli may enter the body through the tonsils. Brion and Kayser found paratyphoid bacilli, and v. Drigalski typhoid bacilli, in the tonsils. These observations aid but little in the solution of this problem, inasmuch as typhoid bacilli have been found in many organs of the body. In the instances cited, entrance to the tonsils from the blood can not be excluded.

CONCLUSIONS.

Typhoid fever is a general infection. The typhoid bacillus is an invasive micro-organism. It is able to develop in the blood and the tissue-juices of the body. It does not develop in the intestinal contents except under unusual conditions. It more frequently occurs in large number in the urine than in the feces. The gall bladder is a favorite habitat of the typhoid bacillus and it develops luxuriantly in the bile. The typhoid bacilli in the intestine come in large part from the bile. They are rapidly destroyed in the duodenum and jejunum,

and it has recently been shown that the wall of this portion of the intestine has marked bactericidal power. It is probable that destruction of all the typhoid bacilli that enter with the bile rarely occurs in the lumen of the bowels. The number, however, becomes so greatly diminished that their presence can not be demonstrated in the stools of many patients with typhoid fever. Employing the most approved methods for isolating *Bacillus typhosus* from feces we were able to recover this micro-organism in only 21 per cent. of the febrile cases. Usually when present they occurred only in small number. They were found in greatest number in a stool containing much blood. It is not improbable that if there was a method that permitted the bacteriologic examination of the entire stool for typhoid bacilli as has been devised for detecting the presence of cholera bacilli, a few micro-organisms might be found in every stool. This, however, would not affect our conclusion, that the typhoid bacillus does not find conditions favorable for its growth in the intestinal contents. It is demonstrable in the feces in such a considerable proportion of cases because it is eliminated in great number by the bile. It is also not infrequently excreted in the urine and sputum, and it may be found in these secretions when absent from the stools. The portal of entry of the typhoid bacillus is not known. There is no more evidence in favor of entrance through the intestine than through the tonsils or the gastric mucosa.

STATISTICS COLLECTED FROM THE LITERATURE* IN REGARD TO THE OCCURRENCE OF TYPHOID BACILLI IN THE STOOLS OF TYPHOID PATIENTS.

Investigator.	No. of cases examined	Method Employed	No. of cases in which <i>B. typhosus</i> was isolated.
Birt	5	Caffeln.	0
Clauditz	8	v. Drigalski-Conradi's.	2
Cole, C	21	v. Drigalski-Conradi's.	2
Courmont and Lacomme	8	Caffeln.	0
v. Drigalski and Conradi	50	v. Drigalski-Conradi's.	50
Elsner	17	Elsner's.	15
Picker and Hoffmann	11	Caffeln.	11
Gabriltschewsky	2	Gabriltschewsky's.	1
Gebauer	16	Piorkowski's.	12
Grawitz	3	Elsner's.	2
Hayashikawa	20	Piorkowski's.	12
Higley	20	Hiss's.	20
Hiss	108	Hiss's.	45
Horton-Smith	16	Elsner's.	4
Jemma	33	Elsner's.	30
Klinger	75	v. Drigalski-Conradi's.	25
Klinger	75	Endo's.	38
Klinger	43	Lentz and Tietz's malachite green.	26
Krause and Stertz	44	v. Drigalski-Conradi's.	23
Lentz and Tietz	205	Lentz and Tietz's malachite green.	150
Lipschütz	17	v. Drigalski-Conradi's.	1
Mackenna	3	Piorkowski's.	3
Piorkowski	4	Piorkowski's.	4
Pollak	20	Elsner's.	20
Richardson	13	Elsner's.	10
Schütze	5	Piorkowski's.	5

DISCUSSION.

DR. W. H. PARK, New York, said that it is a very simple thing and yet a very important one to have proper materials for the medium. Dr. Park and his co-workers started with malachite

* In addition to the references cited elsewhere, the following may be consulted:

Birt: Brit. Med. Jour., Oct. 28, 1905, p. 1111.

Clauditz: Hyg. Rund., 1904, xiv, 718.

Courmont et Lacomme: Jour. de physiol. et de pathol. générale, 1904, xvi, 287.

Picker und Hoffmann: Arch. f. Hygiene, 1904, xlix, 257.

Gabriltschewsky: Ztschr. f. Hygiene, 1900, xxxv, 104.

Gebauer: Fortschr. d. Med., 1900, ii, 21.

Mackenna: Edinburgh Med. Jour., 1899, vi, 399.

Piorkowski: Berliner klin. Wochschr., 1899, p. 145.

Schütze: Ztschr. f. klin. Med., 1899, xxxviii, 39.

† Febrile.

58. Contributions to the Science of Medicine, dedicated by his pupils to W. H. Welch, Baltimore, 1900, p. 543.

59. Deutsch. Arch. f. klin. Med., 1905, lxxxi, 413.

60. For literature on this subject see Krehl: Pathologische Physiologie, vierte Auflage, Leipzig, 1906, p. 302.

green and added all sorts of green and then came back to the malachite until they got their methods right. He does not feel that the old media would fail to give the typhoid bacillus when the Rogalsky media will. When a man knows his medium, he can work with that better than with any other. In his laboratory they work a dozen different cases with different media and come out the same because each one knows the medium he is working with. Dr. Park said that in the first place the laboratory man must get the feces early. If six hours elapse one will not get the bacilli. It shows how the feces in a short time destroy the bacilli. Milk makes the bowel contents more suitable for the preservation of the typhoid bacilli until passed externally. He said that different results are often obtained in different epidemics. Dr. Park's theory has been that the bacilli are in the mesenteric glands and Peyer's patches, from which they passed through into the blood and remained in the blood a certain time before dying, because very few of them are found in any cubic centimeter of blood. He thinks that it is rare to find five or six or ten in that quantity. In attempting to make the diagnosis from the feces he and his confrères had results not quite so discouraging as Dr. Pratt. One sample was mislaid and turned up in ten days. It had fermented and run out of the bottle into the paper covering it. Dr. Park examined it and found it almost a pure culture of typhoid bacilli. The feces in that person had been a suitable medium.

DR. A. L. BENEDICT, Buffalo, said that in some experiments with typhoid on the theory that the patient should be fed liberally with cereals as well as milk, and also using treatment along the line suggested by Bouchard, giving animal charcoal and antiseptics. The favorable results have made him consider that clinical typhoid is typhoid plus colon bacillus infection of the intestine, and that from a purely clinical standpoint a typhoid patient who is well fed, who is not milk poisoned, so to speak, and whose toxins are absorbed from the canal by charcoal or restrained by an antiseptic, presents a course of about two weeks and a half, is practically never delirious, shows no marked dangerous symptoms at any time and shows no tendency to hemorrhage or lung involvement. Dr. Benedict has not had a large experience with this treatment, but what he has had is sufficient to suggest that it might really be worth while to go over these cases jointly with pathologists and see how much of clinical typhoid is really typhoid and how much of it is color bacillus infection. The fact that cases that appear clinically like typhoid and abort, or proceed through a course typical of typhoid, are shown to be due to bacilli intermediate between the colon and the typhoid bacillus, is significant in this connection.

DR. H. G. BECK, Baltimore, said that the result of Dr. Pratt's studies naturally suggests the influence that dietetic treatment may have on the development of typhoid organisms in the intestines. In pointing out the relative frequency of typhoid bacilli in the urine as compared to their occurrence in the stools it strikes one that the administration of urinary antiseptics is vastly more important than the administration of intestinal antiseptics. And, furthermore, on account of their more frequent and persistent presence in the urine, it emphasizes the urgent necessity of safeguarding the public by careful instruction to typhoid convalescents, warning them of the danger of spreading typhoid, if they are promiscuous in their habits of voiding urine, or fail to use proper urinary antiseptics.

DR. J. H. PRATT, Boston, said that the point Dr. Park brings up in regard to the possible relation of diet to the occurrence of typhoid bacilli in the stools is important. It is possible that a strict milk diet may influence the growth of *B. typhosus* considerably. As some patients have been on a strict milk diet and others under the care of physicians who employed Dr. Shattuck's liberal diet, Dr. Pratt thinks that there is a sufficient number of cases to throw some light on this problem. In answer to Dr. Benedict's question, he stated that this study has a direct bearing on the use of intestinal antiseptics in the treatment of typhoid fever. The typhoid bacilli multiply in the tissues of the body, not in the intestines. In only one of their hundred cases were

the bacilli found persistently in the feces in considerable number. Through the natural defenses of the body the myriads of typhoid bacilli eliminated with the bile are quickly destroyed in the intestines. In the case of typhoid "bacillus carriers," the attempt to free the stools of this micro-organism by the administration of the so-called intestinal antiseptics has failed utterly. Few undoubted cases of infection of the blood with the colon bacillus in typhoid fever have been reported. Blood cultures which have been employed so extensively in the diagnosis of typhoid fever have shown the rarity of colon septicemia.

Special Article

THE LITERARY SIDE OF A PHYSICIAN'S LIFE —RONALD ROSS AS A POET.

S. WEIR MITCHELL, M.D.

PHILADELPHIA.

"In Exile, by R. R., 1906, Privately Printed," is the wording on the title page of a little book, whose anonymous author says: "These verses were written in India between the years 1891 and 1899, as a means of relief after the daily labors of a long, scientific research."

I am at liberty to say that the author is Ronald Ross, sometime an English army surgeon, and now professor of tropical diseases in the Liverpool University. The story of the years which step by step led to his final and convincing proof of the causal relation of the mosquito to malarial disease, is to be found in his Nobel lecture given at Stockholm. It is a sad account of labor in the terrible heats of India when the sweat from his forehead rusted the screws of his microscope, or when for days the congested eyes of overuse forbade all study.

His lecture tells modestly of the difficulties this amazing research encountered. In any climate and under the most indulgent conditions, what he did would have been remarkable. In India the lack of sympathy on the part of his military superiors, abrupt army orders, limited means and absence of help seemed ever ready at his happiest approach to success to mock him with delays. He must have felt as if, at times, some malign fate stood ready with obstacles over which no energy, no self-assurance of ultimate victory could prevail. I know of no medical story more interesting, no research which so surely found what it exacted, that heroism back of which lay energizing sense of duty.

The story of this adventurous research has yet to be fully told, as Ross will never tell it. In his lecture and essays he does justice to all concerned, but his was the final victory, the convincing proof. I allude to it here only to present Ronald Ross under another point of view. The weary physician, the exhausted laboratory worker has had a variety of ways of resting or relieving his mind. Physical exercise, some fad of collecting this or that may suffice, but it is an almost unnoticed truth that merely to change the mode of use of the mind competently rests and refreshes. The subject is a tempting one. An apt illustration is the fact that Ronald Ross, when half blind or exhausted with work, turned to verse and sought in a difficult field for the relief that change of mental occupation affords, for the making of good verse is not an easy occupation, as several of the greatest poets have confessed.¹

This little book is an interesting record of moods of mind, of hope, despair, sorrow and final triumph. It gives one a vivid conception of the effects of exile, personal losses and the torment of tropical conditions on a man with an imagination of high order, somewhat lacking for use in verse that which only much technical training can supply.

There are many verses in this book which exacting self-criticism might have altered or left out. There are some easily amended defects of rhythm—verses which are needlessly obscure; but these concern me little. There are many quatrains of virile power, descriptions of eloquent force or notable passages of insight and deep feeling.

1. Byron, Matthew Arnold and others.