those isolated in Case I, and were mainly straight rods 1.5 to 2.0 μ in length, a few being longer. A suspension inoculated into the ear veins of two rabbits proved this strain to have a low virulence.

SUMMARY. A review of cases of primary mesenteric gland tuberculosis in which the type of bacillus has been differentiated shows that over 60 per cent. have been caused by the bovine type of bacillus. Among children the bovine infections greatly prevailed, whereas in adults infections with the human variety were in the majority. No pathological or clinical differentiation of the two forms of tuberculosis is as yet possible. In children, as well as in adults, bovine or human tuberculosis may become limited and healed and the bacilli may die. In striking contrast to the cases summarized above, it is interesting to note that those reported in this paper, two in children and one in a young adult, were due to the human variety of bacillus, as shown by the morphology, cultural characteristics, and virulence of the isolated strains.

BLOOD CULTURES IN TYPHOID FEVER.¹

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THE principles established by Castellani and Schottmüller concerning the bacteriology of the blood in typhoid fever and the knowledge that we have in positive blood cultures a means of determining early and with certainty the presence of this disease, have induced many investigators to search for methods of facilitating the work. The recent advances have, therefore, been mainly in the line of demonstrating the ease with which the work may be done; but as the literature indicates, the frequency of positive findings is not greater with the new than with some of the old methods.

Much of the difficulty hitherto experienced in cultivating the bacilli has been attributed to the bactericidal power of the blood. To overcome this hindrance Castellani² used large quantities of bouillon, and obtained positive results in 78 per cent. of the cases. Schottmüller,³ however, used agar, the blood being present in the proportion of 1 to 3 of the medium. He was successful in finding the bacillus in 81 per cent. of the cases.⁴ Numerous other methods

¹ Preliminary studies were presented before the New York Pathological Society, in October, 1906.

² *Settimana Medica*, 1899.

³ *Mösch. med. Woch.*, 1902, Nr. 38.

⁴ If we were to adhere to the theory that the blood of a typhoid fever patient exerts marked inhibitory influence upon the development of the typhoid bacillus, Schottmüller's success in the work must be explained on the hypothesis of Eppenstein and Korte, that agar in solidifying destroys or diminishes the bactericidal properties of the blood.

have been employed for cultivating the bacillus. Lemiere⁵ was successful with cultures made from defibrinated blood. Eppenstein and Korte⁶ grew the bacilli in oxalated blood. Müller and Graef⁷ observed the growth of the bacilli in the fibrin net-work of clotted blood. Klodnitzky⁸ succeeded in growing the bacilli from blood laked in ordinary sterile water. In twenty-five cultures made in our laboratory, we found multiplication of the bacilli in oxalated blood twenty-three times (without the addition of any nutrient material).

From these data it will at once be seen that the unfavorable influence of the blood upon the growth of the bacilli has been considerably overrated. We cannot escape from the fact that with a variety of methods the results obtained by nearly all investigators have been uniform. It seems that in working with one or another method many of the real conditions underlying the success or the failure of the work have been overlooked.

Thanks to the coöperation of the attending staff of the Mt. Sinai Hospital, I am able to report 158 blood cultures taken in 131 cases of typhoid fever at different stages of the disease (this series includes 2 cases of paratyphoid, 1 of mixed infection with a streptococcus, and 1 case in which secondary infection by the pneumococcus occurred). The subject matter will be taken up in the following order: (1) A description of the technique of obtaining the blood and of the media used. (2) The results; a comparison of the advantages of the various media; a note on the characteristic appearance of the colony of the typhoid bacillus in glucose agar; and a note on 2 cases of mixed infection. (3) The results in relapses. (4) The relationship of the positive findings to the presence of the Widal reaction. (5) The relation of the bacteremia to the stage, course, and severity of the disease. (6) The significance of negative cultures. (7) A note on the possible significance of the bacteremia in relation to the prognosis. (8) Conclusions.

TECHNIQUE. The method used in obtaining the blood is that introduced into the laboratory by Dr. Libman.⁹ The blood is usually withdrawn from one of the veins in the bend of the elbow. In stout patients and in children, in whom these veins are often invisible or too small, a vein on the back of the hand or the dorsum of the foot has occasionally been used. It is wise to inspect these different parts first, and see where one can best find a vein of sufficient size. After the constriction bandage has been applied above the part selected and the field has been scrubbed with soap and water, it is rubbed with ether, alcohol, and finally with 1 to 500 solution

⁵ Münch. med. Woch., 1900, Nr. 32.

⁶ Ibid., Nr. 24.

⁷ Centralbl. f. Bakt., 1907, vol. xliii, Heft 8.

⁸ Russki Vrach, vol. vi, Nos. 27, 28, and 29.

⁹ Johns Hopkins Hosp. Bull., July, 1906.

of mercuric bichloride. Because a large number of media was used for each blood culture, it was necessary to withdraw a moderately large quantity of blood, 10 c.c. or more. It will be shown later that although the use of so large an amount of blood increases the chances of obtaining a positive result, a smaller amount is usually sufficient. When the work was first taken up bouillon media were mainly used; later the series of eight media used as routine in the laboratory were employed. In the course of most of the recent work the following eleven media were employed:

1. Plain nutrient bouillon (from meat infusion, 0.9 per cent. acid to phenolphthalein¹⁰) in flasks containing 120 c.c.
2. 2 per cent. glucose bouillon (titre and quantity like medium 1).
3. Plain nutrient agar (0.9 per cent. acid to phenolphthalein).
4. Plain nutrient agar to which $\frac{1}{4}$ to $\frac{1}{2}$ volume of ascitic serum has been added.
5. 2 per cent. glucose agar (titre same as that of the plain agar).
6. 2 per cent. glucose agar with $\frac{1}{4}$ to $\frac{1}{2}$ volume of ascitic serum.
7. Plain agar (neutral in reaction to phenolphthalein).
8. 5 per cent. glycerin agar (0.9 per cent. acid).
9. 10 c.c. of Conradi's bile medium.
10. 5 c.c. of Kayser's bile medium.
11. 10 c.c. of a 0.2 per cent. solution of ammonium oxalate.

The work was more or less developmental in character, and was carried on without any preconceived notions concerning the possible merits of one or another medium. The eight media referred to above, as belonging to our routine series, were numbers 1 to 8 of the above list. The latest studies were made with media 1, 2, 5, 9, 10, and 11. The oxalated solution was used for two reasons: first to test the growth of bacilli in oxalated blood without the addition of any nutrient material, and second, to test the efficiency of this solution as an intermediate measure in blood culture work between the bedside and the laboratory.¹¹ In the use of the bile media, the directions given by Conradi¹² and Kayser¹³ were closely followed. In each series after the blood was withdrawn it was rapidly distributed into the media and incubated at 37.5° C. The cultures were observed from three to seven days, and careful records were made both as to the time of appearance and the features of the growths. The following summaries give the results obtained with the different media:

¹⁰ The titre of 0.9 per cent. acid was chosen because it was found to give a better growth of typhoid bacilli than more acid media. It is part of our routine to make frequent sub-inoculations from each of the fluid media upon glucose serum agar and plain nutrient agar as well as plain nutrient bouillon and glucose bouillon.

¹¹ Epstein, *AMER. JOUR. MEN. SCI.*, September, 1907.

¹² *Munch. med. Woch.*, 1906, Nr. 34.

¹³ *Ibid.*, Nr. 17.

SUMMARY I.

Medium.	No. of cultures.	Amount of blood, C.c.	Positive results.	Negative results.	Positive results in per centage.	Time in hours.
1. Plain bouillon	61	2	61	20	75	48
2. 2 per cent. glucose bouillon	88	2	70	16	61.4	38
3. Plain agar	31	2	12	19	38.7	50
4. Plain agar and serum	26	1.5	6	16	31	68
5. 2 per cent. glucose agar	83	2	67	16	80	31
6. 2 per cent. glucose agar and serum	20	1.5	6	12	40	58
7. Neutral plain agar	16	1.5	1	15	6.6	
8. 5 per cent. glycerin agar	32	2	12	20	37.5	68
9. Conradi (10 c.c.)	28	1.5	16	12	57.5	26
10. Kayser (5 c.c.)	29	2	17	12	58.6	31
11. Ammonium oxalate solution (16 c.c.)	25	3.5	23	2	92	29

SUMMARY II. THE TWO BOUILLONS COMPARED.

Both bouillons were used simultaneously in 80 positive cultures.

Both bouillons were positive in 51 cultures, 63.7 per cent.

Both bouillons were negative in 8 cultures, 16 per cent.

Plain bouillon was positive
2 per cent. glucose bouillon was negative } in 7 cultures, 8.7 per cent.

Plain bouillon was negative
2 per cent. glucose bouillon was positive } in 14 cultures, 17.4 per cent.

So that in all, plain bouillon was positive in 58 of the 80 cultures, 72.5 per cent., and

2 per cent. glucose bouillon was positive in 65 of the cultures, 81.25 per cent.

Total positive results for both bouillons, 90 per cent.

The average total amount of blood used for the bouillon media was 4 c.c. per culture.

SUMMARY III. AGAR MEDIA COMPARED.

A. Plain agar
2 per cent. glucose agar } used together in 26 cultures.

Both were positive in 10 cultures, 38.4 per cent.

Both were negative in 3 cultures, 11.5 per cent.

Glucose agar was positive alone in 13 cultures, 50 per cent.

Plain agar was positive alone in 0 cultures, 6 per cent.

B. 5 per cent. glycerin agar
2 per cent. glucose agar } used together in 31 cultures.

Both were positive in 10 cultures, 30.1 per cent.

Glycerin agar was positive
Glucose agar was negative } in 2 cultures, 6.3 per cent.

Glycerin agar was negative
Glucose agar was positive } in 14 cultures, 45.1 per cent.

Of the total 31 cultures, 2 per cent. glucose agar was positive in 24 cultures, 77.4 per cent.; whereas glycerin agar was positive in 12 cultures, 38.4 per cent.

SUMMARY IV. BILE MEDIA COMPARED.

Both media were used in 27 cultures.

Both media were positive in 11 cultures, 41.8 per cent.

Both media were negative in 6 cultures, 22.2 per cent.

Conradi medium was positive
Kayser medium was negative } in 4 cultures, 14.8 per cent.

Kayser medium was positive
Conradi medium was negative } in 6 cultures, 22.2 per cent.

In the 27 cultures in which both bile media were used, the total positive results obtained were 21 cultures, 77.8 per cent.

The average total amount of blood used for the bile media was 3.5 c.c. per culture.

SUMMARY V. AMMONIUM OXALATE SOLUTION COMPARED WITH THE OTHER MEDIA.

Used in 25 cultures, positive in 23.

A. Ammonium oxalate solution } used together in 19 cultures.
Plain bouillon

Growth appeared in the oxalate blood in 17 cultures, and in plain bouillon in 13 cultures

B. Ammonium oxalate solution } used together in 20 cultures.
2 per cent. glucose bouillon

Growth in oxalate blood in 18 cultures.

Growth in glucose bouillon in 17 cultures.

C. Ammonium oxalate solution } used together in 23 cultures.
2 per cent. glucose agar

Growth in oxalated blood in 21 cultures.

Growth in glucose agar in 20 cultures.

D. Ammonium oxalate solution } used together in 13 cultures.
Conradi medium
Kaysers medium

Growth in oxalated blood in 11 cultures.

Growth in Conradi's medium in 8 cultures.

Growth in Kaysers' medium in 7 cultures.

Average amount of blood used in this medium was 3.5 c.c.

In studying these results we can readily see which media appear to be best suited for the work. We find that the media can be arranged in two groups, one of which is distinctly favorable to the growth of the bacilli and another which is unfavorable. It is evident, of course, that the word "unfavorable" must be used cautiously, because in any one blood culture the organisms may be few in number and, therefore, may appear on some of the media and not on others. In such instances it is greatly a matter of chance which medium gives positive results. The bacterial invasion of the blood in typhoid fever appears to be more uneven than it is in infections by other bacteria, for even in some cases in which the bacteria are comparatively numerous, we find that the given amount of blood divided equally into like portions of the same medium gives an unequal number of colonies in each portion. This difference is at times very striking. Müller and Graef, in their cultures from clotted blood, had the same experience. I am not able to say what the cause of the uneven distribution is; possibly clumping of the organisms plays some part. I have at times found that fully developed colonies of typhoid bacilli (of the type to be later described) would appear on 2 per cent. glucose agar within the first sixteen hours of incubation, and then thirty-six to forty-eight hours might elapse before any more colonies appeared on the same plate. We must assume from this fact that, as a result of a conglomeration or actual clumping, the respective colonies arise from different numbers of bacilli.

In this connection it may be stated that in the entire series of 158 cultures I have at no time seen so large a number of bacteria in the blood as that observed by Schottmüller and by Schueffner.¹⁴ Whether this difference is due to difference in the type of the cases

¹⁴ Münch. med. Woch., 1907, Nr. 35. !..

studied or not, I cannot determine; possibly differences in technique may account for the discrepancy.

From the study of the variations which occur in the number and growth on the different media and different portions of the same medium, I am inclined to the belief that up to a certain degree the media exert but little influence on the result of the culture. The bacilli will grow on any medium provided such a medium is not actually antagonistic. It appears that bacilli fail to grow well in neutral media and in media the titre of which is above 0.9 per cent. acid. The experiments of Müller and Graef with clotted blood as well as those of Eppenstein and Korte with oxalated blood, and those of Meyerstein¹⁵ with bile salts led to the belief that the fluidity of the blood was essential to the development of the bacilli. The later work of Müller and Graef showed that the fluid state of the blood for growth is not necessary, as they had observed the growth in the fibrin net-work of clotted blood.

It is likely that a number of bacilli which reach a culture medium are impaired in their vitality in consequence of the detrimental influence to which they are exposed in the body; so that the blood withdrawn for the culture may contain bacilli, few of which, if any, are viable. But the claim so frequently made that the failure of the bacteria to grow is wholly due to the continuation of the bactericidal action of the blood (*in vitro*) is not supported by experience. The work of Eppenstein and Korte bears evidence to the contrary. They conclude from their experiments that the bacillus develops an immunity against the bactericidal action of the blood of the host. This view gains support from the fact that the bacteria multiply in defibrinated, oxalated, laked, and clotted blood without the addition of any nutrient medium.

What has been said of the cultures on ordinary media applies also to the bile media of Conradi and Kayser. The results with these methods show no advantages over the ordinary methods. My own results indicate a distinct disadvantage. I found no evidence that bile uniformly augments the growth of the bacilli. The experiments which Meyerstein recently performed proved that the bile salts do not possess any "anreicherung" influence upon the growth of the typhoid bacilli. His observations, as well as those of Nicolle and Adil-Bey,¹⁶ and those of Levy,¹⁷ show, moreover, that these salts exert a detrimental influence upon the growth of other organisms. In conditions, therefore, which simulate typhoid fever and in which organisms other than the typhoid bacillus may be present in the blood, our knowledge of the inhibitory influence of bile on certain bacteria (for instance the pneumococcus) makes it evident that a negative result might be obtained, whereas the use of the ordinary media may result in a positive finding. And, as we have seen, the

¹⁵ *Centralbl. f. Bakt.*, 1907, vol. xliv, Heft 5.

¹⁶ *Annales de l'Inst. Pasteur*, 1907, No. 1.

¹⁷ *Virch. Arch.*, February, 1907, Heft 2.

ordinary media will also not interfere with the development of the typhoid bacillus.

I wish to draw particular attention to the use of 2 per cent. glucose agar.¹⁸ This medium not only permits good growth of the typhoid bacillus and other organisms,¹⁹ but the colonies of the typhoid bacillus develop in it in a characteristic way. The features of the colonies on the medium are as follows: They usually appear in the first twenty-four to thirty-six hours of incubation and are pinpoint in size, with a disproportionately wide area of green coloration around them. This areola is well defined at the circumference, and may be limited by a ring of darkened blood. The colonies show little tendency to increase in size for the first two or three days, whereas the surrounding green areola widens very rapidly. This description applies only to colonies of typhoid bacilli in the depths of the medium. The surface colonies also develop a green color, but they are much larger than the deep colonies and present nothing that may be considered characteristic.

The development of a green coloration about the colonies in the glucose blood medium is a feature that is not restricted to the typhoid bacillus itself; other bacteria may give rise to the same phenomenon. Ruediger²⁰ studied the question of the production of this pigmentation, and found that the pneumococcus, the streptococcus, *Staphylococcus aureus*, and the typhoid bacillus produce it; whereas, *Bacterium coli* does not, producing instead a rapid and diffuse hemolysis. From our experience, however, the only colonies that need to be considered from a differential standpoint are those of *Staphylococcus aureus*, *Bacterium coli*, and the para-colon group. *Staphylococcus aureus* grows usually in much larger and more disk-like colonies; and in addition to the green color which it produces, there develops within twenty-four to thirty-six hours a clear area (complete hemolysis) immediately around the colonies between the colony and the area of green coloration. The hemolytic ring may be very narrow and in the early stages of incubation may be entirely absent.

In one case of general infection by the colon bacillus, which we had the opportunity of studying, the colonies in the glucose medium developed to a much larger size within the given period than do colonies of the typhoid bacillus. They showed, moreover, a greater tendency to break through and spread out upon the surface of the medium, and produce gas. Gas bubbles were also produced by the paracolon bacillus, but the colonies otherwise resembled very closely those of the typhoid bacillus.

When, therefore, we find that stained smears from the colonies of

¹⁸ Libman, loc. cit.

¹⁹ Although this medium is better than the bile media for routine work, in connection with bacteria other than the typhoid bacillus, it is sometimes not as good as agar unless serum be added.

²⁰ Jour. Infect. Dis., September, 1907.

the type described as characteristic for the typhoid bacillus show the presence of a Gram-negative bacillus, we can safely place the organism in the typhoid-colon group.²¹ Moreover, when colonies are present on this medium which do not correspond to the type described the presence of the typhoid bacillus may be excluded. The character of the colony which the typhoid bacillus produces on 2 per cent. glucose blood agar affords us then a great help in identifying the organism early. Most of our positive results on the glucose agar were obtained within twenty-four hours after taking the culture. In some instances the typical typhoid colony developed within sixteen hours. Delay in development of the colonies may at times be accounted for by errors in the titre of the medium.

Of the 154 cultures taken promiscuously, some for diagnosis and others for research, 110 gave growths of the typhoid bacillus and 2 of paracolon (so-called paratyphoid) bacilli. In 1 case of typhoid fever, complicated by pneumonia and otitis media, a streptococcus was obtained from the blood. The typhoid bacillus was no longer present (the Widal reaction was positive). In another case studied through the kindness of Dr. Eli Moschkowitz, both the typhoid bacillus and a streptococcus were found in the same culture. The results obtained with 2 per cent. glucose bouillon, 2 per cent. glucose agar, and ammonium oxalate solution were the most encouraging; so that our experience leads us to suggest the use of these three media for diagnostic work. As for the quantity of blood, it may be said that 2 c.c. is sufficient to give positive results in 80 to 85 per cent. of positive cases; but when a larger amount of blood can be withdrawn without inconvenience, it is desirable to obtain it, especially in the later weeks of the disease when the organisms are apt to be very few in number. It is necessary to draw attention to the fact that while the total percentage of our positive results is about the same as that given by other authors, more of our cases were studied during the third and fourth week, and as the results are generally considered to be better in the first and second week, the methods which we have decided to adopt for routine work seem to promise better results than the methods generally used.

SUMMARY VI.

Week of disease.	No. of cultures.	Cultures positive.	Widal positive.
1	8	7 (88.5 per cent.)	2 (28.5 per cent.)
2	44	39 (88.6 ")	28 (63.5 ")
3	42	25 (60 ")	36 (86 ")
4	15	8 (53.3 ")	12 (80 ")
5	7	5 (71.5 ")	5 (71.5 ")
6	3	1 (33.3 ")	3 (100 ")
7	3	1 (33.3 ")	2 (66.6 ")
Total	122	86 (70.5 ")	88 (72.1 ")

²¹ All the bacilli isolated in our cases were, of course, further identified by the study of their cultural features and by the presence of agglutination with immune typhoid serum.

SUMMARY VII. RELAPSES

Intercurrent relapses, 5—all positive.

Day of relapse.	No. of cases.	Result of culture positive.
2	5	3
3	5	4
4	2	1
5	4	4
6	2	2
7	2	1
11	1	1
12	1	0
14	1	0

The last two summaries permit us to draw certain deductions concerning the efficiency of the blood culture as a diagnostic means in that stage of the disease when other means are unavailing. They also draw our attention to the investigation of the relationship of the bacteremia to the course of the disease. As shown in Summary VI, and as already mentioned above, the results obtained agree in general with those of other investigators. The relationship of the positive blood culture and the positive Widal reaction has been studied by a number of authors. The statistics of Coleman and Buxton²² show that many of the positive cultures antedate the presence of the Widal reaction. Ghaetghens²³ studies showed that of 917 Widal tests made, in the first week of the disease, 25 per cent. were negative, in the second, 10 per cent., and in the third, 4.7 per cent. He also found that in 140 cases in which the Widal reactions remained negative, 34 were diagnosed by positive blood cultures, an experience previously shared by a number of other observers. Our own results confirm the previous observations.

The lack of relationship between the result of the culture and the type and severity of the disease has also been noted by nearly all the writers who have reported on large series of cases. Although some fever is usually present at the time when the blood culture is positive, there is no direct dependence of the result upon the height of the temperature. A positive result may be obtained with the temperature at 100° F. as likely as at 105° or 106°, provided such a temperature occurs in the course of the active stage of the disease. A number of our cases yielded positive results shortly before defervescence; that is, within one, two, or three days, but in no cases was a positive result obtained after defervescence was established. Conradi's results in afebrile cases of the disease are certainly exceptional. Coleman and Buxton state that in cases with a long duration, the bacillus is in the blood as long as the temperature persists. My own results support this view in part only. We must distinguish in prolonged cases between those in which the prolongation is due to the fever alone, and those in which prolongation of the tempera-

²² AMER. JOUR. MED. SCI., June, 1907.²³ Arbeiten aus dem k. Gesundheitsamte, 1907, Heft 1.

ture is due to some complication (such as phlebitis or bronchopneumonia, etc.). In the former group of prolonged cases positive results can be expected. The cases with intercurrent relapses may be regarded in the same group as the last mentioned. The five cultures of our series which were taken in such cases were all positive (Summary VII).

We have had the opportunity of studying 23 relapses; 16 of these gave positive results, approximately 70 per cent., a figure which is nearly the same as that given by a study of the primary attacks. Our experience with negative cultures during the afebrile period warrants the conclusion that in the relapse we are dealing not with the continuation of the original bacteremia, but a new bacteremia. In the intercurrent relapse it is possible that the bacteremia is continuous with the original bacteremia. In 4 of the 16 cases of relapse with positive results, negative results were obtained in the primary attack. An analysis of the results obtained on different days of relapse shows (although the series is too small as yet to be conclusive) that the results are better when the fever nears the fastigium than they are in the earlier days. In 1 case we had the opportunity of making cultures on the third, seventh, and eleventh days of a relapse. The first two cultures were negative, and the third positive. This observation also confirms the view expressed by Schottmüller, that in the true relapse there is a new invasion of the blood.

From a consideration of the results obtained by most investigators it appears to be certain that the bacteremia is concerned in the production of at least some of the clinical aspects of the disease. As Coleman and Buxton state, the number of positive cultures is such that one must conclude that the typhoid bacillus is present in the blood in every case of typhoid fever at some time or other. My own studies with the different media indicate that negative results in the early stages of the disease are accidental. These observations are important not only from the standpoint of etiological and pathological studies, but also from the standpoint of diagnosis, for they show that a continued fever (and this conclusion was drawn by Schottmüller and later by Libman²⁴) which lasts for several days after the cultures have shown the blood to be free from typhoid bacilli is in all probability not that of typhoid fever.

To sum up, all the results hitherto obtained show that in typhoid fever there is a bacteremia which becomes progressively less marked as the disease goes on. Whether the cases which extend beyond the third, fourth, and fifth week and in which positive results are obtained are due to repeated invasions of the blood current or not, is a question which cannot at present be decided. From the present state of our knowledge it is difficult to formulate a definite view of the

²⁴ Trans New York Academy Medicine, March 7, 1907.

significance of the bacteremia in typhoid fever. The case recently published by Conradi²⁵ in which bacilli were present in the blood before the onset of the fever, and the case described by Widal, in which a positive blood culture was obtained on the second day of disease, would appear to lend strength to the view of Schottmüller concerning the close relation of the bacillemia to the fever. Certain facts presented by our own studies make us hesitant concerning the occurrence of bacillemia from the very inception of the disease, for in one case the culture taken on the fifth day was negative, and another culture taken a few days later was positive. In the second case, two cultures taken during a relapse were negative, and the third positive. We are in need of some studies of cases in which the blood cultures were made on the first or second day of the disease (or of the relapse).

Our studies do not warrant us in drawing any conclusions concerning the relation of the number of bacilli present to the prognosis of a given case. Schottmüller and Schueffner are of the belief that there is a relationship. Further studies in this direction are also desirable. It is not at all unlikely that the study of the biological differences of the organisms from the blood of different patients will throw some light on prognosis and therapy.

Our studies permit the following conclusions:

1. The bactericidal influence of the blood in typhoid fever in relation to the obtaining of positive results in the blood cultures has been overestimated. Great dilutions of the blood are not essential; a number of media will give good results.

2. The best results in our experience were obtained with the use of 2 per cent. glucose bouillon, 2 per cent. glucose agar, and ammonium oxalate solution.

3. On 2 per cent. glucose agar the typhoid bacillus grows in such a characteristic way that the presence of a certain type of colony on it is quite diagnostic, and the absence of such a colony points very strongly against the presence of the typhoid bacillus.

4. The bile media were not found to be as reliable as the media mentioned above.

5. The results presented are in agreement with those obtained by others. The total positive results obtained by us are in agreement with the results obtained by others, notwithstanding the fact that more of our cases were studied later in the course of the disease.

6. Although the maximum results are obtained in the first and second week, there is not sufficient proof as yet that the bacilli are present in the blood from the very inception of the fever.

7. Protracted cases yield positive results if the continuation of the fever is not due to complications (or starvation).

8. A continued fever lasting several days after the blood has been

²⁵ Münch. med. Woch., 1907, Nr. 41.

shown to be free from typhoid bacilli will nearly always prove not to be a case of typhoid fever.

9. The results in relapses are the same as those in the primary attacks. The bacillemia in the relapses is due to a new invasion.

10. We cannot draw any definite conclusion, as yet, concerning the value of the blood cultures in determining the prognosis.

It is with a deep sense of gratitude that I wish to acknowledge my indebtedness to Dr. E. Libman for his advice and constant guidance in this work. To Drs. Hertz, Ryttenberg, and Fried, I wish to express my thanks for their kind assistance.

THE UNCERTAIN RESULTS OF SUTURING NERVES.

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WHEN one reads the reports of the numerous cases of nerve suture and observes the small percentage of successful results, he is forced to conclude either that the repair of nerves is uncertain and erratic, or that the technique of such operations is far from satisfactory. There certainly seems to be a difference in the ability of different nerves to regenerate. Contrast, for example, the perverse persistence of the trifacial in reproducing itself after the removal of segments as much as one inch in length with the obstinate resistance to reunion or regeneration of the median or ulnar nerve after it has been carefully sutured together and apparently placed in the most favorable condition for repair.

Whether regeneration of nerves occurs as an outgrowth from the neuron or central nerve cell, according to Waller, Ranvier, His, Waldeyer, and others, or whether, according to Bethe, Nissl, Dohm, Ballance and Stewart, and Tizzoni and Cattani, the regeneration is the result of proliferation of the cells in the sheath of Schwann, is a matter which has not been decided, but the latter theory seems to be gaining ground.

It is generally thought that immediate suture of a divided nerve is more likely to be successful than secondary suture, but this seems to be a matter of no importance, according to Bowlby.¹ Thus, in 81 cases of primary nerve suture there were 32 successful results, 34 partially successful, and 14 failures, while in 73 cases of secondary nerve suture there were 32 successful results, 26 partially successful, and 15 failures—the primary suture giving 39 per cent. of successes and the secondary 43 per cent. of successes. Powers² reviews 22 cases of nerve grafting in which a segment of a nerve from a dog or

¹ An American Text-book of Surgery.

² Trans. Amer. Surg. Assoc., 1904.