Original Communications.

BACILLUS DYSENTERIÆ, SCHMITZ.

(WITH A BRIEF NOTE ON CERTAIN OTHER NON-MANNITE FERMENTING BACILLI.

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PART I.—B. DYSENTERIÆ SCHMITZ, AS REPORTED FROM COUNTRIES OTHER THAN INDIA.

Although references to this organism appear in earlier literature, the first complete description of the bacillus which now bears his name was given by Schmitz in 1917.

As the original article is not at present accessible to the writer, the following quotation taken from an article by Murray published in this Journal in 1918 is given.

"Schmitz investigated an epidemic of dysentery among Roumanian prisoners of war. It was typically a contact epidemic occurring during the months of January and February (1916).

"The unfavourable conditions of food, the extremely insanitary condition of the prisoners, insufficient heating arrangements or other protection from climatic conditions during a very severe winter enabled the epidemic to spread at this unusual time of year. There were 815 cases, of which 104 showed typical dysenteric stools, while the remainder had more or less severe diarrhoea with or without traces of blood and mucus. The duration of the attack was ten to fourteen days, and it required six weeks before recovery was complete. Of 104 cases, 5 died of dysentery, and 58 others
Bacillus Dysenteriae Schmitz

out of the original 815 cases died of pneumonia. From the earliest part and throughout the epidemic, bacilli of the dysentery group were recovered from the stools of the patients. It was only possible to investigate 79 patients, but they were examined very thoroughly. As many colonies as possible were picked off from each plate. Bacilli which could be pronounced dysentery bacilli were found in 22 patients, and these were only found in the typical blood and mucus stools. Stools which were merely watery were negative. Twelve plates gave 138 colonies, of which 61 proved to be dysentery bacilli, and out of 38 subcultures from 9 plates 22 were dysentery bacilli (57.89 per cent). Out of another 39 cases the bacillus was found in 19; the stools of the rest were faecal.

A description of the organism is then given to which reference will be made at a later point, and the author continues:

"In only one case was any other type of dysentery bacillus found; this proved to be a 'Y'.

"That this organism (i.e. Schmitz' bacillus) is to be regarded as the causal agent of the epidemic is evidenced by the fact that it was only found in the sanguino-purulent portions of the faeces, where it alone occurred, and further that the sera of a series of patients agglutinated this bacillus in high dilutions."

The occurrence during the war and post-war periods of cases of dysentery apparently caused by B. dysenteriae Schmitz was by no means limited to the outbreak described above.

Thus Murray in his collection of dysentery bacilli identified six strains of this type, four of which came from France or Flanders, and two were of unknown origin. He concluded that B. dysenteriae Schmitz is a clearly defined and homogeneous species.

Thomson and Mackie (1917) isolated from cases of dysentery in Egypt an organism biochemically similar to the Schmitz bacillus.

Andrewes (1918) described as B. ambiguus an organism which was probably B. dysenteriae Schmitz. This occurred among strains which had been collected from one or other of the war theatres.

Among the various types of dysentery bacilli isolated from cases in the Salonika Army, Dudgeon describes under the name of B. para-Shiga + an organism which corresponds biochemically with B. dysenteriae Schmitz, and which he believes to be identical with this organism. This bacillus was frequently isolated, and Dudgeon in the Central Laboratory investigated thirty strains. In one case the patient's serum agglutinated the organism isolated from the stools.

Hirschbruch and Theim (1918), in examining 214 cases of dysentery, isolated bacilli of the Schmitz type in 52 (24 per cent). In one fatal case with a typical history of dysentery there was found post mortem severe purulent colitis with catarrhal enteritis in the lower part of the ileum and swelling of individual follicles. B. dysenteriae Schmitz was readily
cultivated from the intestine, but not from the bile, liver or spleen. A laboratory assistant working with this material was seized with slimy diarrhoea which lasted a fortnight, and *B. dysenteriae* Schmitz was isolated from cultures of the stools. The authors consider the Schmitz bacillus a definite cause of dysentery.

Kirschner and Segall (1920) record the isolation of *B. dysenteriae* Schmitz during the 1920 epidemic of dysentery in Vienna.

Tanaka (1923) records from Japan an organism resembling Schmitz bacillus recovered from two patients with dysentery and three with mild diarrhoea.

Ornstein (1920-21) made an exhaustive research into the characters and morphology of Schmitz bacillus, and concludes that it is a distinct and characteristic species which produces a well-marked and specific antigen. Mention is made of somewhat similar species which can, however, be differentiated biochemically and serologically. This one organism which he names *B. fallax* can be differentiated by its power of producing acid from saccharose after prolonged incubation, while another, *B. inconstans*, may occasionally produce gas in dextrose. This worker found that true *B. dysenteriae* Schmitz (as opposed to these similar strains) is not clumped in Michaelis' acid media. A high titre serum was readily produced, living organisms being more easily agglutinated than dead cultures.

Stutzer (1923) isolated, from an outbreak of dysentery in East Prussia in 1917, an organism which he named *B. paradysenteriae* X, which is apparently identical with Schmitz bacillus.

Kruse entertained no doubt as to the claims of this organism and it has been adopted as strain J in his classification. Sartorius (1929 and 1930) confirms that *B. dysenteriae* Schmitz and Kruse J. are one and the same organism.

Perry and Bensted (1929) report the occurrence of this organism in cases of dysentery in Egypt, having isolated it nine times from adult cases (6·9 per cent of the total) and five times from children (1 per cent).

Riding (1930) describes two cases of acute bacillary dysentery caused by *B. para-Shiga* (indol +) which occurred in Sudanese natives.

The rôle of *B. dysenteriae* Schmitz in the aetiology of dysentery has not, however, been universally accepted. Thus Andrewes, having described *B. ambiguus*¹ concludes that the organism can be rejected as having no connection with dysentery. This conclusion is reached largely because of the fact that the bacillus clumps when subjected to the Michaelis "acid agglutination" test. It is interesting to note that Murray applies this argument the other way round, and concludes that as *B. dysenteriae* Schmitz is agglutinated by Michaelis' acid agglutination, the latter test is of no value in distinguishing pathogenic from non-pathogenic dysentery bacilli. It may be remarked that in working with the "Flexner" type of

¹ There is, however, no serological evidence that *B. ambiguus* and *B. dysenteriae* Schmitz are identical.
dysentery bacilli, the writer has on two occasions made use of Michaelis' test and has reached the same conclusion as Murray.

Manson-Bahr (1920) is of the opinion that organisms of this type are of doubtful aetiological significance. "Organisms giving similar biochemical reactions to these (i.e. Schmitz bacillus, B. ambiguus, &c.), may be isolated from true Shiga stools which have been allowed to decompose for a few hours: . . . . they may be either concomitants, the products of a stale dysentery stool, or . . . . are derived from the necrotic mucosa." It is not quite clear what the author implies by this suggestion—whether he thinks the organisms are born of this material, or—whether they are present throughout in the mucosa and do not multiply until certain favourable conditions, the outcome of staleness, arise, or whether products of this necrotic material lead to fundamental mutations (as later suggested by Calalb) of normal organisms. He further gives it as his opinion that intensive investigation in cases where such organisms are found would lead to the recovery of the true (sic) dysentery bacillus from every case.

Calalb (1925) isolated in Roumania a number of strains which gave the biochemical reactions of B. dysenteriae Schmitz, but which did not agglutinate with a serum prepared from a stock culture of that organism. Sera prepared from these strains contained, in addition to homologous agglutinins, heterologous agglutinins of relatively high titre for "Shiga," "Flexner" and "Y." It is not stated if the serum was tested against the stock strain of Schmitz. The author states that these "para-dysentery" organisms were never isolated when cultures were made in the first days of the illness; that these organisms appeared only after the disappearance of true dysentery organisms; that their antigenic properties were related to those of standard Shiga and Flexner; that the latter organism after years of artificial culture tended to produce "paradysentery" forms; and in consequence the hypothesis is advanced that paradysentery organisms are none other than modified forms of the standard types.

A review of the references which have been given can, however, leave no reasonable doubt that B. dysenteriae Schmitz is an entity and is capable of causing dysentery. It has been the sole dysentery-like organism to be discovered in certain extensive outbreaks of this disease. It has been isolated by numerous skilled and reliable observers from fresh specimens in the early stages of the disease, unassociated with any pathogenic organisms, and in circumstances identical to those in which accepted dysentery bacilli are found. It has given rise to the production of homologous agglutinins in the patient's serum. It has been isolated from dysenteric lesions in a fatal case, and it has apparently given rise to a case of laboratory infection.

The case in favour of its pathogenicity is, in fact, singularly complete. Andrewes' criticism—that B. ambiguus (assuming this to be identical with Schmitz bacillus) is agglutinated by Michaelis' test—carries no real weight, while of the observations of Manson-Bahr and Calalb it can only
be said that they do not accord with those of other workers, including, as will be seen later, military pathologists throughout India.

**CHARACTERS OF B. DYSENTERIE SCHMITZ.**

*B. dysenteriae* Schmitz is a typical coliform organism, Gram-negative, non-motile, and measuring about 0.5µ by 1.0-3.0µ.

It grows readily on all ordinary media.

Table I shows its biochemical reactions contrasted with those of *B. dysenteriae* Shiga and *B. dysenteriae* Flexner (Andrewes' types.)

<table>
<thead>
<tr>
<th></th>
<th>Schmitz</th>
<th>Shiga</th>
<th>Flexner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Glucose</td>
<td>Acid</td>
<td>Acid</td>
<td>Acid</td>
</tr>
<tr>
<td>Mannite</td>
<td>-</td>
<td>-</td>
<td>Acid</td>
</tr>
<tr>
<td>Dulcite</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Saccharose</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Indol</td>
<td>+</td>
<td>-</td>
<td>+ or -</td>
</tr>
</tbody>
</table>

It will be seen that Schmitz and Shiga differ from Flexner in being non-mannite fermenters, while Schmitz is to be distinguished from Shiga by the fact that it produces indol.

As determined by the agglutination test, Schmitz possesses an antigen peculiar to itself. It is not agglutinated by a high titre serum specific for any of the other dysentery organisms, neither is a serum prepared from Schmitz capable of agglutinating any of these organisms.

The agglutininogenetic properties of Schmitz are limited. Thus Dudgeon mentions that he found difficulty in preparing a high titre serum; Murray succeeded in preparing a serum of 1:1000 titre only, while Hirschbruch and Theim did not get a titre beyond 1:1600. This point is of interest in relation to Indian experiences. On the other hand Schmitz and Ornstein claim to have had no difficulty in producing a high titre serum, although they do not state the titre which was reached.

No convincing results have been obtained from animal feeding or intestinal inoculation (Dudgeon), but it has been clearly shown that the rabbit is more resistant to this organism than to *B. dysenteriae* Shiga.

**PART II—B. DYSENTERIE SCHMITZ IN INDIA.**

A search of the files of the *Indian Medical Gazette*, the *Indian Journal of Medical Research*, the *Journal of the Royal Army Medical Corps*, and the Reports of the Public Health Commissioner with the Government
of India from 1918 onwards fail to reveal any reference to this organism, with the possible exception of two strains recorded in a paper on jail dysentery by Cunningham and King, 1917, until it was isolated by Manifold in Poona in 1925-26.

On several occasions Manifold isolated from cases of clinical and microscopical bacillary dysentery an organism which had the morphological and biochemical reactions of \( B. \) \( dysenteriae \) Schmitz, but which was not agglutinated to full titre by high titre serum specific for this organism. In spite of this, it was found that the serum of patients who had suffered from dysentery, and from whose stools this organism had been isolated, agglutinated suspensions of \( B. \) \( dysenteriae \) Schmitz, but not the homologous organism.

Owing to a change of appointments the work was at this stage handed on to the writer of this article who was able to investigate the question first at Bangalore and later at Poona during the years 1929, 1930 and 1931. He was further aided by receiving cultures of organisms of this type from various military laboratories in India.

Manifold's findings were repeatedly confirmed. From time to time organisms were isolated under the most suggestive conditions from cases of clinical and microscopical bacillary dysentery which gave all the biochemical reactions of \( B. \) \( dysenteriae \) Schmitz, but which failed to agglutinate, or at best agglutinated only to a small fraction of the titre, with serum prepared from that organism.

<table>
<thead>
<tr>
<th>Sera</th>
<th>Suspensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmitz</td>
<td>214</td>
</tr>
<tr>
<td>Schmitz 1,000</td>
<td>Nil</td>
</tr>
<tr>
<td>214</td>
<td>5,000</td>
</tr>
</tbody>
</table>

In confirmation two further cultures of \( B. \) \( dysenteriae \) Schmitz were obtained through Major H. J. Bensted, M.C., R.A.M.C. One (\( B. \) \( dysenteriae \) Schmitz-Hawkins strain) was from the National Collection of Type Cultures, the other being the strain maintained at the Royal Army Medical College. Both proved to be identical with the strain of \( B. \) \( dysenteriae \) Schmitz maintained by the Enteric Laboratory, Kasauli, from which high titre serum for India was prepared.

To continue the investigation a strain of the Indian Schmitz-like organism isolated during the early stages of a typical case of dysentery was selected. This strain will hereafter be called by its laboratory index number "214." A rabbit was inoculated intravenously with a killed suspension of "214" and in due course a serum was produced which, when tested, gave the results shown in Table II.
The results obtained with stock high titre Schmitz serum are shown as a control.

Many different sera have now been prepared from “214” and allied strains and on every occasion results of a similar nature have been obtained, i.e. “214” serum has agglutinated a suspension of B. dysenteriae Schmitz to a titre from four to ten times higher than that to which it agglutinated its homologous organism.

Table III shows the results of four cross absorption tests, carried out at different times and with different sera.

<table>
<thead>
<tr>
<th>Sera</th>
<th>Suspensions</th>
<th>1st test</th>
<th>2nd test</th>
<th>3rd test</th>
<th>4th test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmitz control</td>
<td>Schmitz 214</td>
<td>500</td>
<td>25</td>
<td>5,000</td>
<td>Nil</td>
</tr>
<tr>
<td>Schmitz abs. Schmitz</td>
<td>Schmitz 214</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
<td>Nil</td>
</tr>
<tr>
<td>Schmitz abs. 214</td>
<td>Schmitz 214</td>
<td>195</td>
<td>Nil</td>
<td>25</td>
<td>Nil</td>
</tr>
<tr>
<td>214 control</td>
<td>Schmitz 214</td>
<td>1,000</td>
<td>125</td>
<td>500</td>
<td>125</td>
</tr>
<tr>
<td>214 abs. Schmitz</td>
<td>Schmitz 214</td>
<td>25</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>214 abs. 214</td>
<td>Schmitz 214</td>
<td>125</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

1 Carried out by Major C. D. M. Buckley, M.C., R.A.M.C., at the Enteric Laboratory, Kasauli, in November, 1932.

Carried out by Jemadar Jaswant Rai, under the direction of Lieutenant-Colonel R. F. Bridges at the Enteric Laboratory, Kasauli, in October and November, 1934.

When it is recalled that at the time this investigation was started B. dysenteriae Schmitz had been maintained in artificial culture for over thirteen years, and that “214” was freshly isolated, a very likely explanation of these results suggests itself.

It is well known that B. dysenteriae Sonne begins, in many cases almost as soon as it is isolated, to produce “rough” variants. A serum prepared from a recently isolated, unselected culture will agglutinate both smooth and rough forms, while a serum from a selected rough colony will agglutinate only a suspension of rough organisms. The explanation of this appears to be that the smooth and rough forms have different antigens; both are present in the unselected culture, whereas in the selected rough culture only the rough antigen is present. The agglutinogenic properties of the smooth variant are feeble in comparison with those of the rough.

The position of “214” and Schmitz, although not identical, is probably
analogous. "214" over a period of four years, has shown no tendency to form "rough" variants, but it seems, nevertheless, highly probable that the strain now known as B. dysenteriae Schmitz (and maintained by the National Collection of Type Cultures) is a variant which has developed from the strain originally isolated.

Assuming this hypothesis to be correct, "214" would appear to contain two antigens, one of which (probably corresponding to the smooth antigen of Sonne) is of poor agglutinogenetic properties, and may be called "A"; the other of powerful agglutinogenetic properties, and presumably analogous to the rough antigen of Sonne, may be called "B"; "A" probably predominates and "B" is present to a much lesser extent.

As regards Schmitz (stock strain) the position is not quite clear. It will be noted that there is a striking difference between the first three and the fourth absorption tests in the results of "214" serum absorbed by Schmitz. In the first three tests all agglutinins for "214" were removed, while in the fourth test 50 per cent remained. This would suggest that at the time the first three tests were carried out, Schmitz contained a certain proportion of "A" antigen and a preponderance of "B", whereas when the fourth test was carried out it had lost most of its "A" antigen and contained only "B". This point requires further investigation, which the writer is not at present in a position to carry out.

An apparent anomaly is the failure of "214" to absorb completely from its homologous serum all agglutinins for Schmitz, despite the exhibition of very massive doses of the organism. Nevertheless it appears most probable that inadequate absorption is the explanation.

An alternative, but on the whole less likely explanation is that no such change as is suggested has taken place in B. dysenteriae Schmitz (Hawkin's strain), but that this organism is represented in India by an allied strain with a different antigenic composition. Had even one strain with the antigenic characters of B. dysenteriae Schmitz (Hawkin's strain) been isolated in India, this possibility would gain enormously in weight. On the other hand, the fact that, so far as can be ascertained, no such strain has been found renders the hypothesis unlikely.

With "214" serum as a starting point, an investigation was made of all strains of Schmitz-like bacilli which came to hand until the writer left Poona. In all, 55 strains were tested. Of these, 3 were discarded on the ground that they produced acid in saccharose (vide B. fallax of Ornstein). Of the remaining 52, 41 agglutinated to titre with "214" serum, while 11 were inagglutinable either with "214" or any other serum. Of the 41 agglutinatable strains, 5 showed agglutination to about 5 per cent of titre with a serum prepared from B. dysenteriae Schmitz; the remainder were inagglutinable with this serum.

Twenty-seven of the forty-one strains (all of the "214" type) were isolated by the writer in Bangalore and Poona. All twenty-seven were recovered from the stools of cases of clinical bacillary dysentery under the
same circumstances as are the accepted dysentery bacilli. In certain of the cases in which specimens were received at an early stage, the organism was found in approximately pure culture in plates made from washed exudate. It became more difficult to isolate as the cases advanced and was not recovered when the stools became free from obvious mucus. No other pathogenic organism capable of explaining the symptoms was found in the stools of these cases. On no occasion in Bangalore or Poona was the organism isolated except from cases presenting clinical symptoms of bacillary dysentery, despite the fact that in this period some 3,000 platings from apparently normal stools were examined. Two strains of the organism said to have been isolated from normal stools, were, however, forwarded for investigation by another laboratory.

It was possible to carry out agglutination tests with the serum of only five of these cases. None agglutinated the homologous organism. As suggested by Manifold these sera were also tested against suspensions of \emph{B. dysenteriae} Schmitz. Two agglutinated this organism in dilutions of \(1:250\), one in \(1:125\), one in \(1:50\), and one was negative. These results (higher agglutination of Schmitz than of "214") are analogous to those produced in the immunization of a rabbit with this organism.

The type of case from which "214" was isolated varied from mild to moderate. One severe case was reported.

**Practical Application of These Observations.**

As it is clear from these observations that high titre serum prepared from the stock strain of \emph{B. dysenteriae} Schmitz is of little assistance in identifying the strain which occurs in India, a serum prepared from "214" is being issued in lieu thereof. This allows the strain, believed to represent \emph{B. dysenteriae} Schmitz, to be definitely identified by serological as well as by biochemical methods, and permits of the ready recognition of other strains, similar biochemically but of different antigenic composition, which are being made the subject of special investigation.

Organisms having the biochemical reactions of \emph{B. dysenteriae} Schmitz and presumably chiefly "214" are widely distributed throughout India: 206 cases of dysentery were attributed to organisms of this type in 1932-33, while in the same period the number from which Shiga was recovered was 637.

**Part III—Other Non-mannite-fermenting Bacilli (Exclusive of \emph{B. Dysenteriae} Shiga).**

In order to show clearly the present position as far as India is concerned, it is thought advisable to make brief reference to other non-mannite fermenting dysentery-like bacilli (other than Shiga) which are being found. For fuller details reference should be made to a recent paper by Large (1934), who is carrying out an investigation of these organisms.

Three non-indol producing strains are occasionally found. Two have
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the exact biochemical reaction of B. dysenteriae Shiga, but are not agglutinated by a Shiga high titre serum, nor do they show cross-agglutination against each other. These have the morphological and biochemical reactions of the organism named B. para-Shiga by Dudgeon.

The other differs from Shiga in that it produces acid in dulcite. It was first described by Archer (1933) from Wellington, and has since been found in Quetta.

One other indol producing strain is of not uncommon occurrence. It is biochemically identical with Schmitz and "214," but has a completely different antigen. It has been described by Large (1934), and probably accounts for some at least of the eleven inagglutinable strains mentioned above.

These four strains have occurred in association with cases which are clinically dysentery. The question of their pathogenicity is under further investigation, but is difficult to decide owing to their scarcity.

Saccharose-fermenting, indol-positive strains (probably identical with Ornstein’s B. falax) are occasionally found in normal stools unassociated with symptoms of dysentery.

SUMMARY AND CONCLUSIONS.

(1) B. dysenteriae Schmitz is believed to be capable of causing typical acute bacillary dysentery.

(2) An organism closely allied to B. dysenteriae Schmitz (Hawkins strain) is commonly associated with bacillary dysentery in India.

(3) It is considered possible that this organism represents the original phase of B. dysenteriae Schmitz, and that the stock strains [B. dysenteriae Schmitz (Hawkins strain) and the strains maintained at the Royal Army Medical College and the Enteric Laboratory, Kasauli] have, in the course of prolonged artificial life, undergone mutation.

(4) The substitution for B. dysenteriae Schmitz high titre serum of a serum prepared from strain "214" has facilitated the identification of the organism, which is widespread throughout India.

(5) In addition to B. dysenteriae Shiga and B. dysenteriae Schmitz "214," other non-mannite fermenting dysentery-like bacilli have been identified in India. The pathogenicity of these strains is still under investigation.

ACKNOWLEDGMENTS.

My thanks are due to the staffs of the District Laboratory, Bangalore, and the Southern Command Laboratory, Poona—particularly to Assistant Surgeon L. C. Smith, the late Jemadar J. Michael, Jemadar Narain Singh, and Corporal G. T. Williams, R.A.M.C.; to Major C. D. M. Buckley, M.C., R.A.M.C.; and to Lieutenant-Colonel R. F. Bridges, R.A.M.C.; and Jemadar Jaswant Rai for much assistance in the later stages of this investigation; also to the many Army pathologists who have assisted by sending strains for investigation.
REFERENCES.


Articles marked * have not been consulted in original but in review form in the Tropical Diseases Bulletin.