PARATYPHOID C, AN ENDEMIC DISEASE IN BRITISH GUIANA.

By GEORGE GIGLIOLI, M.D. (Pisa), D.T.M. and H. (Lond.).
(*C.M.O. Demerara Bauxite Co., Ltd.*)

Statistical data and literature referring to enteric and parenteric fevers in British Guiana are very scanty and incomplete. In this Colony, as in many others, the disease has been masked under the diagnosis of typho-malaria. It was not until 1890 that Ferguson (1890) furnished definite clinical and pathological evidence, proving the existence of typhoid and its frequency in the Colony, and in the city of Georgetown in particular. Since then Rowland (1910, 1912), Kennard (1905, 1908), Wise (1911), Minett (1912) and Rose have reported on the disease, as seen in the Georgetown Public Hospital.

Haemoculture is still far from having been adopted as a routine diagnostic procedure in the Colony, consequently no reliable data are available as to the existence and relative frequency of enteric and the various parenteric fevers. It is now generally recognised that the diagnosis of enteric infections by agglutination tests requires a degree of care and precision, the need for which has become apparent only within recent years. Even if repeated tests are carried out on each patient, so that the rise in agglutinin titre can be successfully demonstrated when it occurs, it is essential that the test should be carried out against each of the members of the typhoid-paratyphoid group of bacteria; moreover, the antigenic complexity of these organisms, and the possibilities of antigenic variations within any single species, must be allowed for if reliable results are to be obtained. It is clear that these conditions have not hitherto been fulfilled.

Table I contains the main statistical data referring to enteric fever in British Guiana, according to the reports of the Surgeon General and Registrar General. The notification of enteric fever as an infectious disease was made compulsory only in 1912. After the introduction, in 1907, of the agglutination reaction as a diagnostic test for enteric fever, a very marked increase in the number of cases recognised seems to have taken place. Rowland (1910) is of opinion that the increase was real and not apparent. Such a thesis appears unlikely, when one considers the figures given in Table I, and with them the general status of sanitation of the Colony, with its population made up of multi-coloured immigrants, none of whom show special immunity to the disease in their countries of origin. The occurrence of a large number of cases, with a *sporadic* distribution, as shown by Rowland in a series of spot maps of the city of Georgetown for the years 1909–1913, leads one to suspect a very large number of undiagnosed cases, atypical, or even ambulant, which, if traced, would form the links between the apparently sporadic cases.

After nearly six years' experience in the Colony, and two years of systematic bacteriological investigation of all cases of febrile affections, not evidently of malarial or other nature (quinine resistant), I have come to the conclusion that, if haemoculture were introduced in the Colony as a routine for the investigation of such diseases, the increase in the number of enteric and parenteric fever cases diagnosed would be enormous.

Table I. *Enteric fever.*

Deaths and Notifications for the City of Georgetown and the whole Colony, 1890 to 1926.

	Whole Colony		City of Georgetown	
Year	Deaths	Notifications	Deaths	Notifications
1890	21	—	10	—
1891	8	—	5	—
1892	15	—	12	—
1893	14	—	10	—
1894	8	—	5	—
1895	7	—	1	—
1896	13	—	7	—
1897	6	—	2	—
1898	11	—	2	—
1899	16	—	—	—
1900	2	—	2	—
1901	7	—	1	—
1902	3	—	2	—
1903	2	—	1	—
1904	6	—	1	—
1905	4	—	1	—
1906	14	—	5	—
1907	8	—	5	—
1908	26	—	13	—
1909	33	—	22	—
1910	57	—	33	—
1911	76	—	44	—
1912	93	308	57	160
1913	106	420	58	254
1914	100	265	45	154
1915	75	419	40	192
1916	91	357	45	190
1917	123	725	44	281
1918	129	637	70	234
1919	111	525	64	178
1920	138	795	80	326
1921	118	489	71	221
1922	92	461	48	135
1923	117	476	59	176
1924	89	413	46	158
1925	79	314	29	80
1926	102	400	16	103

In a country like British Guiana, with an excessively high malarial rate, the diagnosis of all fevers needs considerable care. Bates (1913) has very ably described the difficulties encountered, under similar circumstances, by the American workers in the Panama Canal zone. The axiom that "a fever that continues for more than five days unchecked by quinine is not a malarial fever" proved of inestimable value in Panama; routine bacteriological investigation of all such cases (haemoculture, repeated agglutination tests), led to the detection of an altogether unsuspected number of abortive and light cases of enteric and allied fevers, which would otherwise have been completely

overlooked. Bates, as a routine, considered malaria out of court if the fever was uninterrupted by quinine on the morning of the third day.

In the investigation of such fevers, one should not attach too much weight to the presence of malaria parasites in the blood; a chronic malarial infection (which in the rural districts of British Guiana is more the rule than the exception), takes advantage of any lowering of resistance, and appears as a complication in all kinds of conditions (trauma, post-operative state, childbirth, etc.).

Quinine resistance is by far the best and most reliable criterion. It is, of course, essential that quinine should have been administered in adequate doses. In British Guiana there exists an inexplicable prejudice against quinine; the drug is commonly prescribed in amazingly small doses, and only for short periods; its constant failure has therefore discouraged the inhabitants, who tend to attribute to the drug most of the unpleasant symptoms of the disease. No weight should therefore be given to an uncontrolled history of quinine resistance.

The existence in British Guiana of quinine resistant fevers, of a continued type, has been noted by Kennard (1905), mainly amongst East Indian coolies. These cases showed a daily remitting or intermitting febrile curve, had no malaria parasites in the blood, resisted quinine treatment, and when tested gave a negative agglutination reaction with suspensions of typhoid bacilli, or of paratyphoid A and B. Blood or other cultures were not taken. In his last contribution on the subject, Kennard (1925), on the basis of very unsatisfactory evidence, founded on the crudest bacteriological technique, connects these cases of continued pyrexia with bacteriuria *from a B. coli infection*. The differential diagnosis of the affection is very lightly dismissed as follows:

> With continuous fever, the question of typhoid arises, but I think the general run of the cases, tongue usually clean, frequent presence of a good deal of albumen early, early high temperature and general run of it with its marked ups and downs, little abdominal symptoms, and nature of the stools, is against typhoid irrespective of the germs present; in cases treated with Widal it has proved negative. The absence of malaria parasites shows they are not malarial.

Soon after my arrival in the Colony in 1922, I noted the not rare occurrence of cases of prolonged, irregular or remittent fever, accompanied by a very indefinite symptomatology, and absolutely quinine resistant. Our hospital at the time was rudimentary, and the only tests I could carry out were the Marris test, which gave sometimes positive, but more often ambiguous, results, and the agglutination reaction with T.A.B. suspensions, which proved constantly negative.

In the absence of a more definite term, I grouped such cases under the provisional diagnosis of "Intestinal fever." This designation was not motivated by the occurrence of intestinal symptoms in the disease (which were conspicuous for their absence!) but by the presumption that the disease

belonged to the enteric group, though differing from the usually described forms. In my report for February 1925, I wrote as follows:

Intestinal fever. This designation is somewhat vague, and we use it to indicate a peculiar form of very irregular, continuous or remittent fever. The characters of the disease for the present are negative; that is, there is an entire absence of any characteristic symptom beyond the rise in temperature. The temperature is usually high in the afternoon, with a slight or extremely marked morning remission. In some cases, there is much weakening and loss of weight, in others, the patient is scarcely aware of being ill, and will deny having fever, when the thermometer registers 3 or more degrees above normal. The tongue is more or less coated, and in some cases slight intestinal borborygmi can be noted on the colon when palpating deeply.

We have seen many cases; they occur sporadically both in time and locality. The examination of blood films, even if repeated, has given negative results; the same for the usual laboratory tests for typhoid, from which they can easily be distinguished clinically. Tuberculosis can also be excluded, and the tuberculin test has given uniformly negative results. The temperature usually falls by lysis, or suddenly without apparent reason.

In May 1925, a fully equipped and up-to-date hospital was opened at Mackenzie by the Demerara Bauxite Company; proper laboratory investigation of these cases became possible, and has been carried out as a routine for the past two years. This work has led to the identification of paratyphoid C as a common endemic infectious disease in the Colony, capable of epidemic outbreaks with a high mortality and much disability; it has opened the way to an adequate investigation of the prevalence of enteric fever (*sensu latiore*) in the Colony, and to systematic efforts towards its prevention.

Bacteriological Notes.

During the period October 1926 to June 1928, from a total of 1283 medical cases admitted to Mackenzie Hospital, organisms belonging to the *Enteroidia* group were isolated in 77 instances.

B. typhosus was identified by cultural and serological tests in five instances.

B. paratyphosus A and B were never isolated.

In the remaining 72 cases, a bacillus was isolated which, while showing the cultural characteristics of the *Salmonella* group, could not be identified with the commoner paratyphoid forms.

The following are the general cultural and serological characteristics of the organism. Owing to lack of material, time and proper assistance, and to the impossibility of consulting the medical literature on the subject, this investigation is far from complete; it is at any rate sufficient for general identification of the organism in question.

Morphology.

Shape and size:

On agar slopes: short rods with rounded ends, and disposed in clusters and masses. Size 1μ by $0{\cdot}8\mu$.

In old broth cultures, and on glycerinated potato, short and long rods, size from 1μ to 3μ, and occasionally long threads of 5μ or 6μ.

Capsule absent.

Endospores absent.

Motility in broth, active.

Staining reactions: Gram negative—Ziehl Neelsen negative.

CULTURAL CHARACTERISTICS.

Agar plates. Regular, round, slightly convex colonies with an entire edge, and a smooth surface; yellowish, translucent, moist, homogeneous internal structure.

Agar stab. Abundant growth on surface, scanty along the puncture, diminishing with the depth.

Glycerinated potato. Growth abundant, of butyrous consistence, white tending to brown with age. Medium browned.

Neutral red—glucose agar. Florescent—fragmented by gas production.

Nutrient broth. Uniform turbidity—no odour.

Peptone water. As above.

Lead acetate broth. Blackened in 24 hours.

Litmus milk. 1st day, slightly acid.
2nd ,, very slightly acid or alkaline.
4th ,, alkaline.
7th ,, ,,
10th ,, ,,

FERMENTATION REACTIONS (24 hour cultures).

Peptone water and		glucose	...	Acid and gas
,,	,,	lactose ...	...	Negative
,,	,,	maltose	...	Acid and gas
,,	,,	saccharose	...	Negative
,,	,,	galactose	...	Acid and gas
,,	,,	mannite	...	,,
,,	,,	laevulose	...	,,
,,	,,	dulcite ...	...	,,
,,	,,	arabinose	...	,,
,,	,,	raffinose	...	Negative
,,	,,	sorbite ...	...	Acid and gas
,,	,,	dextrine	...	,,
,,	,,	dextrose	...	,,
,,	,,	inuline ...	...	Negative

Relation to oxygen —Aerobic—Facultative anaerobic.

Indol production —Negative.

Chromogenesis —Negative.

Temperature relation—Optimum 37°. Grows well at room temperature (84°–85° F.).

SEROLOGICAL REACTIONS.

All agglutination reactions were carried out with specific sera for the following organisms, as prepared and supplied by the Oxford Laboratories.

B. typhosus	*Salmonella* Mutton
B. paratyphosus A	*Salmonella* Newport
B. paratyphosus B	*B. enteritidis* (Gaertner)
B. paratyphosus C	

Using these sera, and Dreyer's technique, 60 per cent. of the strains isolated from these patients agglutinated with the paratyphoid C serum in dilutions varying between 1 : 25 and 1 : 250. Negative results were obtained with each of the other sera.

More uniform results were obtained by growing the strains to be investigated in peptone water to which the serum had been added, in dilutions varying between 1 : 100 and 1 : 500. When tested in this way against the paratyphoid C serum, each of 72 strains, isolated by haemoculture or otherwise, gave a characteristic agglutinated growth, most obvious after incubation for 10 hours at 37° C. All other sera gave constantly negative results.

Specimens of serum obtained from the patients were tested against this organism, and also against Oxford Standard suspensions corresponding to the specific sera. In every case the organism we have isolated was agglutinated by the patient's serum, at some stage of the disease, at a dilution varying from 1 : 100 to 1 : 500. In 70 per cent. of the cases agglutination was obtained with *B. paratyphosus* C at a dilution varying between 1 : 150 and 1 : 250. Of the sera which agglutinated *B. paratyphosus* C, 60 per cent. also agglutinated *B. paratyphosus* B, but in lower dilutions, 1 : 25 to 1 : 150. *B. typhosus* and *B. paratyphosus* A were rarely agglutinated, and then in low dilution only.

The agglutinins appeared in the patient's blood at variable periods; usually in the second week, often later. Their persistence is evidently considerable, since agglutination to a titre of 1 : 250 was observed in every case tested at intervals of a year to 18 months after recovery from the disease. Reactions, which were persistently negative during the febrile stage of the disease, frequently became positive soon after convalescence had set in.

The method of vital agglutination was also employed in testing the patients' sera, various dilutions in peptone water being incubated with *B. typhosus*, *B. paratyphosus* A, *B. paratyphosus* B and *B. paratyphosus* C. Using this technique, characteristic agglutinated growth was obtained with *B. paratyphosus* C in every case, while the other bacteria gave consistently negative results. In several cases the reaction appeared earlier in the disease than when the serum was tested against the killed standard suspensions.

The instances in which we have isolated *B. paratyphosus* C from this series of cases are as follows:

By haemoculture in 48 instances.

From the urine in 15 instances.

From the pus of suppurated joints in 2 instances.

From the pus of a suppurative cholecystitis in 1 instance.

From the pus of fixation abscesses in 18 instances.

From the pus of a suppurated retention cyst of the kidney in 1 instance.

Post mortem, the organism was repeatedly isolated from the spleen, the liver, the gall-bladder, the pancreas, and the kidney. Cultures from the mesenteric glands were constantly negative.

From the preceding morphological, cultural and serological findings, we may conclude that the *Salmonella* we have been studying can be identified as *B. paratyphosus* C. This term has been employed to designate various miscellaneous varieties, which, when more accurately studied, have been found to fall in one or other of the better known types of the paratyphoid-enteritidis group. The original Hirschfeld (1919) strains, isolated during the War in the Balkans, for which the term *B. paratyphosus* C was first used, have been the object of considerable controversy as to their exact relationships. In 1920, Schütz recognised the Hirschfeld strain as representing a type within the *Salmonella* group. In 1925, Bruce White noted the serological identity of *B. suipestifer* and *B. paratyphosus* C (Hirschfeld). In 1926, the same author (1926), after a very extensive and careful re-investigation of the subject, carried out tests on a large number of strains, both of porcine and human origin, on the basis of serological and cultural differences, and of geographical distribution, and identified a *suipestifer*-Hirschfeld or *suipestifer-paratyphosus* type composed of four sub-types as follows:

(1) *Sub-type* 1*: American.* Known only from the American Continent, and exclusively from swine.

Cultural characteristics:

(*a*) Fails to blacken lead acetate.

(*b*) Generally fails to ferment arabinose.

(*c*) Generally fails to ferment dulcite in 24 hours.

Includes both diphasic and monophasic non-specific strains.

(2) *Sub-type* 2*: Eastern* (Hirschfeld). So far known only from human disease in India, Mesopotamia, Africa and Balkans, with the exception of one strain probably imported to England from the East.

Cultural characteristics:

(*a*) Regularly and rapidly blackens lead acetate.

(*b*) Ferments arabinose.

(*c*) Ferments dulcite.

Diphasic strains only.

(3) *Sub-type* 3*: Western European.* From paratyphoid and food poisoning in man, and from infections in the pig and monkey.

Cultural characteristics:

(*a*) Blackens lead acetate rapidly.

(*b*) Seldom ferments dulcite when first isolated.

(*c*) Hardly ever ferments arabinose.

Monophasic non-specific strains only.

(4) *Sub-type 4: Glasser Voldagsen.* Only from European diseased swine.
Cultural characteristics:

(*a*) Blackens lead acetate slowly.
(*b*) Ferments arabinose rapidly.
(*c*) Ferments dulcite slowly.
(*d*) Fails to ferment mannite.
(*e*) In fermented media gives a scanty development of gas and grows slowly on ordinary media.

Includes both diphasic and monophasic non-specific strains.

All of our 72 strains, from their first sub-culture after isolation, were active ferments in 24 hours of both dulcite and arabinose, with abundant gas development. All blackened lead acetate in 24 hours.

Our *Salmonella* would therefore find its place in Sub-type 2, *Eastern* (Hirschfeld) of Bruce White's classification of the *suipestifer*-Hirschfeld type. The occurrence of this sub-type in British Guiana is therefore of special interest, as it is the first time it has been reported from the American Continent. Its occurrence on the other hand is hardly surprising, when one considers the enormous immigration to this Colony from the East. Between the years 1838 and 1917, 238,979 East Indians and 14,000 Chinese landed in the Colony. In 1926, the population of the Colony was the following:

Europeans (other than Portuguese) ...	3,229
Europeans (Portuguese)	8,570
East Indians	126,908
Chinese	2,791
Aborigines	9,270
Negroes	121,562
Mixed races	34,004
Other races	510
Total	306,844

Similar conditions exist in Trinidad, with a total population of 339,402 and 127,326 East Indians (1927). In the other British West India Islands, the number of East Indians is much smaller. Jamaica has only 17,318 with a population of 936,927 (1916). In Surinam, immigration from the East has also been very important. With a population of 85,536, there are 20,498 British East Indians and 8298 Dutch East Indians (1913).

Summary.

From 72 cases of pyrexial illness, occurring in British Guiana, an organism has been isolated which has the cultural and serological reactions of *B. paratyphosus* C (Hirschfeld). It seems probable that enteric fever, due to infection with this organism, is now endemic in the Colony, and is an important cause of sickness and death.

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