CONTINUED FEVER DUE TO A GÄRTNER-LIKE *SALMONELLA* OF THE TYPE "DUBLIN."

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(With 2 Charts.)

Introduction.

The three cases briefly reported here (with clinical notes for two of them) were observed in Aberdeen. The *Salmonella* cultures in each of the three were isolated by Smith and identified by him as close relatives of *S. enteritidis* (Gärtner) but not identical with it. Scott received them so described and compared them with the classical strain and with other serological relatives of *S. enteritidis* in his possession. As a result it was established that the three Aberdeen strains, as well as a number of others from various sources, belonged to the *Salmonella* type "Dublin" described by Bruce White (1929). Although this type can produce "food-poisoning," *i.e.* acute gastro-enteritis, there is some evidence that it may have a special tendency to set up continued fever; it is certain, at any rate, that a good many of the cases of "Gärtner septicaemia" encountered in man are really examples of infection with this type and, in two of the published instances, we have been able to prove this by re-examining the causal strain (*vide infra*). Furthermore the type has a special association with bovine animals and consequently with cows' milk. It is included among the group of strains called by Jensen (1913) the "paracolon bacilli" which cause fatal enteritis among young calves in Denmark. Latterly the Danish observers would appear to have confined the name *B. paracoli* to this type. We do not consider, however, that this name *B. paracoli* should have priority; it is misleading as a descriptive appellation and was not correlated with serological analysis which, we consider, is the only safe foundation for distinctions among the *Salmonellas*. We shall, therefore, speak of the type as "*Salmonella dublin*" or *S. dublin* (cf. *S. newport*, *S. reading*, etc.).

Clinical details and bacteriological findings.

Case 1. W. P. (male), aged 38 years, was admitted to hospital as a case of typhoid fever on November 13th, 1925. Previous to admission the chief clinical symptoms were fever, abdominal distension and diarrhoea. On admission his temperature was 99·6° F., pulse rate 120 and respiration rate 36. He was somnolent and listless; the mouth was dirty, the tongue dry, brown in colour, cracked and fissured. Small haemorrhagic areas showed on the soft palate. The heart did not show any abnormality, but there was evidence of consolidation of the upper lobe of the right lung. The abdomen was slightly distended and the

skin showed a profuse crop of rose-coloured spots tending in certain areas to be confluent. The spleen was just palpable but no tenderness or rigidity was demonstrable.

The fever continued and on November 16th the abdomen was still distended and tenderness was elicited to the left of the umbilicus. Since admission the patient had not had diarrhoea, but the stools were loose and dark in colour. On November 19th the patient had improved considerably and for three days the temperature remained normal until on November 22nd a relapse occurred, the temperature remaining at 99·6° to 99·8° F. for a further three days (Chart 1). Thereafter the patient made an uneventful convalescence and was discharged on December 18th, 1925.

Blood for agglutination test and culture was obtained immediately on admission. A Widal test was made and it was found that *S. typhi* was agglutinated in a dilution of 1 in 100, *S. paratyphi* B in a dilution of 1 in 50; no agglutination was obtained with *S. paratyphi* A. Later, when the blood culture was found to contain a non-lactose Gram-negative motile bacillus which fermented glucose and mannite with gas production, an agglutination test was made using this bacillus and *S. enteritidis* (Gärtner) in parallel. The serum agglutinated the former in a dilution of 1 in 200 and the latter in a dilution of 1 in 100. A second blood culture was performed when the relapse occurred on November 23rd and a bacillus similar to the first was again obtained. During the course of the illness the faeces and urine were examined five times but no non-lactose fermenting bacilli were found.

Case 2. I. T. (female), aged 2 years, was admitted to hospital on June 1st, 1926, as a case of erysipelas. Physical examination showed a vesicular rash confined to both arms and legs. There was profuse desquamation on the left buttock and right hand. The left buttock and the dorsum of each foot were swollen and under both great toes there was a pustule. The buccal mucous membrane showed slight ulceration. No evidence of any lesion could be found in the chest or abdomen. The temperature on admission was 102·8° F., the pulse rate 114 and respiration rate 40. On June 6th an incision was made in the left buttock and a large amount of pus was evacuated. Thereafter the temperature subsided and remained at a normal level for three days, when it rose again and continued between 99° and 102° F. for over six weeks (Chart 2). Throughout this prolonged illness the pulse rate ranged from 120 to 132 per minute, the respiration rate remaining comparatively steady around 28–32. There was no diarrhoea and, in fact, rather a tendency to constipation. The heart (apart from the increased rate), the lungs and the abdomen showed no clinical evidence of any abnormal condition. Eventually the temperature subsided to a normal level on July 26th, and the child was discharged from hospital on August 10th, 1926, after an illness lasting over two months. The pus from the abscess in the buttock obtained on June 6th gave a pure culture of *Staphylococcus aureus*. Thereafter the temperature subsided and presumably the septicaemia did not begin till the continued fever became manifest about June 16th.

On June 23rd blood was obtained for culture and agglutination tests. The culture showed a Gram-negative motile non-lactose fermenting bacillus which produced acid and gas in glucose and mannite. The blood serum agglutinated *S. typhi*, *S. enteritidis* (Gärtner) and the patient's own strain in a dilution of 1 in 100. No agglutination was obtained with *S. paratyphi* A or B.

Case 3. I. L. The clinical notes on this boy are not available. He became ill on February 13th, 1929, with a condition which, at first, was diagnosed as influenza. The febrile condition continued, and blood culture on February 19th showed a Gram-negative non-lactose fer-

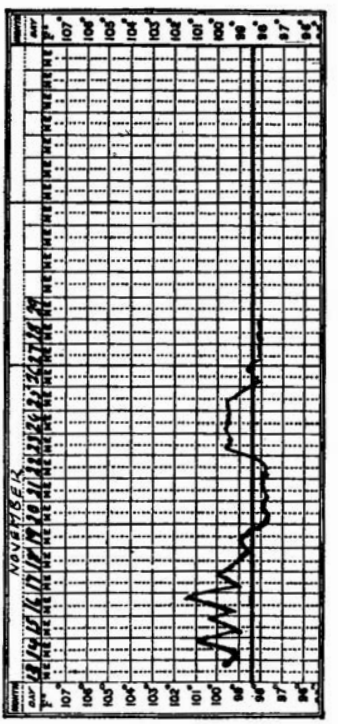

Chart 1.

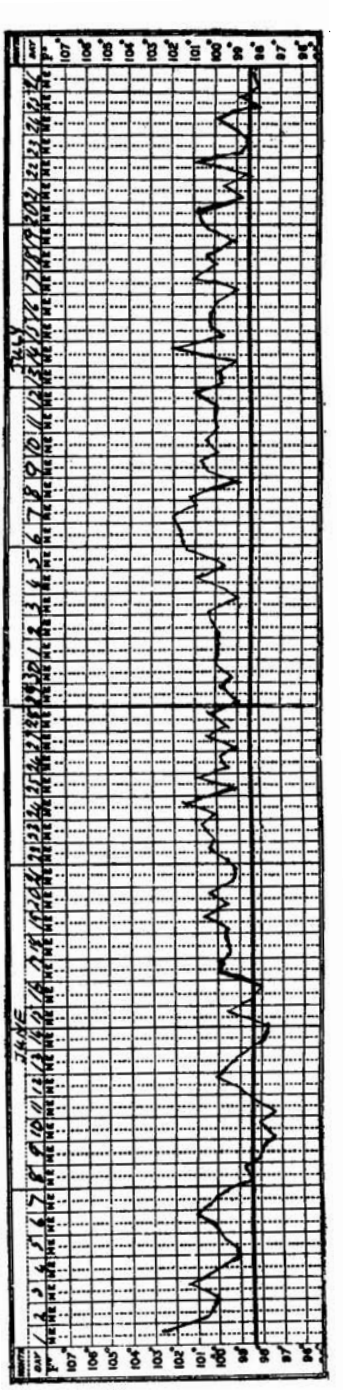

Chart 2.

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menting motile bacillus behaving like the strains isolated in Cases 1 and 2. A sample of faeces obtained two days later showed a similar bacillus.

CULTURAL CHARACTERS.

In our study of these three strains L., P. and T. we have made comparisons with a considerable number of other *Salmonella* strains; these are of very diverse origin but are alike in agglutinating with an anti-Gärtner serum; the majority of these already formed part of the National Collection of Type Cultures and the rest have since been deposited there by us.

In Table I we have divided them, on a serological basis, into set *A* (= 34 typical *enteritidis* strains) and set *B* (= 15 strains established as belonging to the type "Dublin") and have added a note as to the origin of each. Each of these serologically homogeneous sets represents also a cultural unit, and the growth characters of the 49 strains studied are given in two columns, see Table II. Certain differences between individual strains in each set have been noted but they are limited to minor and, perhaps, temporary divergences in the speed of fermentation or the amount of gas produced with certain sugars.

It will be observed (Table II) that all of the *enteritidis* group (*A*) ferment arabinose, usually (but not always) without gas production, while the "Dublin" strains without exception leave this pentose unattacked. Arabinose-negative strains agglutinating with anti-Gärtner serum have long been known (Jensen, 1913); it would appear that most of these, at any rate, were probably serologically distinguishable and really belonged to the *Salmonella* type "Dublin."

The only other distinction noted in Table II is that the "Dublin" type strains are all slow to ferment rhamnose, though they are all capable of producing both acid and gas from it after 24 hours' growth. The fermentation tests were carried out in 1 per cent. bactopeptone water containing 1 per cent. of the fermentable substance and coloured with litmus; the final readings were taken at the end of seven days at 37° C. but in no case did they differ from those taken at 48 hours.

Reference should be made to the fermentation of certain sugars in the phosphate medium of Bitter, Weigmann and Habs (1926), which has been employed by Bahr (1929) to distinguish *S. enteritidis* (Gärtner) from the rat-virus strains such as Danysz virus, Ratin, the Liverpool virus, etc.

This medium is of the following composition: 0·5 grm. di-sodium phosphate, 1 grm. ammonium sulphate, 2 grm. sodium citrate, 5 grm. sodium chloride and 0·05 grm. peptone (Witte) dissolved in 1 litre of distilled water: the sugars, etc., are added in 0·5 per cent. strength (preferably in filtered solution) and the mixture tubed in 5 c.c. quantities and steamed for 10 minutes: the *p*H should be 7·5. One drop of a 24-hour broth culture is sown into each tube and the reaction tested after 16 hours at 37° C. by adding two drops of methyl-red solution (0·5 per cent. in 96 per cent. alcohol).

We can confirm Bahr's statement that the majority, if not all, of the rat-virus strains ferment rhamnose and arabinose in this medium more slowly than the typical *enteritidis* strains. As in the case of the similar slow and fast rhamnose-fermenting groups established by Kristensen and Bojlén (1929)

Table I.

A. Typical enteritidis (*Gärtner*) *strains.*

No.	Designation	Source
1	Original Gärtner (Z. 7)	From Dr L. Bahr, Copenhagen; supposed to be a descendant of the original strain obtained by Jensen from Gärtner in 1889
	N.C.* 410 (18)	The type strain of *S. enteritidis* of the American Museum of Natural History
3	N.C. 75 (Bainbridge)	From the Pasteur Institute, Paris, in 1908
4	N.C. 205 (Danysz)	The Lister Institute strain of Danysz virus
5	*B. danysz*	From Dr L. Bahr, Copenhagen; the strain used by David (1929)
6	*B. ratin*	,, ,, ,, ,,
7	Liverpool virus	,, ,, ,, ,,
8	*B. rattentyphus* (Bonn)	From Dr L. Bahr, Copenhagen
9	Rattenbacillus (Graz)	From Dr L. Bahr, Copenhagen; the strain used by David (1929)
10	Rattenbacillus (Pribram)	,, ,, ,, ,,
11	*B. morratin*	,, ,, ,, ,,
12	Rattenbacillus (Karsten)	From Dr L. Bahr, Copenhagen
13	N.C. 617 (Ratin)	From proprietors
14	N.C. 125 (Limerick)	From food-poisoning (McWeeney, *Brit. M. J.* 1909, **1**, 1171)
15	N.C. 127 (Stokes)	From food-poisoning (France, 1917)
16	N.C. 128 (McNee)	From septicaemia (McNee, 1921, *Lancet*, i, 218)
17	N.C. 2202 (Armitage)	From food-poisoning in New Zealand, 1926
18	N.C. 2203 (273)	From food-poisoning in America, 1926
19	N.C. 2212 (Jerusalem)	From meningitis in Palestine (Stuart and Krikorian, 1926, *J. Hygiene*, **25**, 160)
20	N.C. 2292 (Donnie)	From meningitis in New Zealand, 1926
21	M. 7	From an epidemic in caged mice in 1918 (Scott, London)
22	M. 827	From an epidemic in caged mice in 1920 (Scott, London)
23	G. 1	From an epidemic in guinea-pigs in 1929 (Smith, Aberdeen)
24	N.C. 252 (G. 158)	From a guinea-pig at the Lister Institute
25	N.C. 2109 (Bedson)	From a guinea-pig at the Lister Institute, 1925
26	N.C. 305 (Swine 1)	From a pig
27	N.C. 810	From a rat, multiple lung abscesses, Lister Institute, 1920
28	N.C. 1418	From a rat, Lister Institute, 1922
29	Kidd	From food-poisoning in 1928
30	Messer	From food-poisoning in 1929
31	Payton	From food-poisoning in 1927
32	Pendry	From food-poisoning in 1923
33	Pocklington	From food-poisoning in 1928
34	Turner	From food-poisoning in 1928 (29, 31–34 isolated by Scott)

B. "Dublin" strains.

1	Dublin (Knox)	Pyelitis kidney in case of continued fever (Bigger) (see Bruce White, 1929)
2	N.C. 126 (Newcastle)	Milk epidemic, Newcastle, 1910
3	N.C. 780 (Cork)	Septicaemia (Gregg and Hayes, 1921, *J.R.A.M.C.* **37**, 64)
4	Cassidy	Food-poisoning in Nottingham, 1919 (Dobrashian)
5	L.	From the cases described in this article
6	P.	,, ,, ,,
7	T.	,, ,, ,,
8	Green Cross	From food-poisoning in London; junket suspected, 1928
9	N.C. 2187 (186,707)	From meningitis (Pesch, K. L., 1926, *Zent. f. Bakt. Orig.* **98**, 22)
10	Calf 3502	From Dr L. Bahr, Copenhagen; from cases of calf-dysentery
11	Calf 3508	,, ,, ,, ,,
12	Calf Mjelbo	,, ,, ,, ,,
13	N.C. 577	From Prof. C. O. Jensen, Copenhagen; from cases of calf-dysentery
14	N.C. 578	From Prof. C. O. Jensen, Copenhagen; from cases of calf-dysentery
15	N.C. 579	From Prof. C. O. Jensen, Copenhagen; from cases of calf-dysentery

* N.C. = National Collection of Type Cultures.

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Table II.

	Monosaccharides						
	Hexoses				Pentoses		Methyl-pentose
	Dextrose	Laevulose	Galactose	Mannose	Arabinose	Xylose	Rhamnose
Fermentation tests:							
A. Enteritidis (34 strains)	A. G.	A. G.	A. G.	A. G.	**A. (G.)**	A. G.	A. G.
B. "Dublin" (15 strains)	A. G.	A. G.	A. G.	A. G.	**0**	A. G.	**A. G.** (late)

	Disaccharides			Trisaccharide	Polysaccharides		Alcohols		Glucosides	
	Maltose	Lactose	Saccharose	Raffinose	Dextrin	Inulin	Mannite	Dulcite	Salicin	Inosite
Fermentation tests:										
A. Enteritidis (34 strains)	A. G.	0	0	0	0	0	A. G.	A. G.	0	0
B. "Dublin" (15 strains)	A. G.	0	0	0	0	0	A. G.	A. G.	0	0

	Indol production	Sulphide production (lead acetate broth)	Litmus milk
A. Enteritidis (34 strains)	0	Black	Alkaline
B. "Dublin" (15 strains)	0	Black	Alkaline

among strains of *S. paratyphi* B, no significance as regards pathogenicity can be ascribed to these differences in speed of fermentation and no corresponding serological distinction is perceptible. This peculiarity in fermentation, however, appears to be a relatively permanent property and may find useful application in epidemiological enquiries, *e.g.* in incriminating or exculpating a rat-virus in the case of human infections.

SEROLOGICAL CHARACTERS.

It is not necessary to reproduce here the full range of serological tests required in the definition of the two types, *enteritidis* and "Dublin" (see Bruce White, 1929). We have tested all the strains in Table I for absorption of agglutinin from at least one serum, *i.e.* the serum prepared with the typical Gärtner strain, No 21 (M. 7), and can state that all the *A* strains remove completely its agglutinin for the homologous strain. This serum has a titre of 1 in 50,000 (1 c.c. volume in a 50° C. water bath in 2 hours) and 3 c.c. of a 1 in 50 dilution of it is rendered completely free of agglutinin (tested at 1 in 100) by absorption with the whole 24-hour agar growth on a Petri dish of 3 inches diameter. Similar absorption tests have been performed with sera prepared from other members of the *A* set, namely, No. 1 (original Gärtner), titre 1 in 80,000, No. 13 (Ratin), titre 1 in 10,000, and No. 32 (Pendry), titre 1 in 20,000, with entirely concordant results.

On the other hand, when similar amounts of these *A* (*enteritidis*) cultures have been applied to the serum prepared with the type strain "Dublin" (titre 1 in 30,000), only a slight reduction of titre, to between 1 in 12,000 and to 1 in 20,000, for the homologous strain ("Dublin") has been observed, with,

at the same time, complete removal of agglutinin for all the *enteritidis* strains tested. In the same way, using appropriate and sufficient quantities, the strains in set *B* completely remove the agglutinin for the homologue from the "Dublin" serum, from a serum prepared with L. (titre 6000), with P. (titre 6000), with T. (titre 5000), and from a "paracolon" serum prepared with No. 10 (Calf 3502) of titre 40,000. When similar amounts of these *B* cultures are applied to *enteritidis* sera there is either no perceptible reduction in the homologous agglutinin (as with the M. 7 serum) or a slight drop only, from 10,000 to 5000 (as with the Ratin serum). These results are expressed in tabular form in Table III.

Table III. *Absorption of agglutinin.*

Sera	Homologous titre (floccular agglutination)	Absorbed by								
		Enteritidis (M. 7)	Original Gärtner	Ratin	Pendry	"Dublin"	L.	P.	T.	Calf 3502
Enteritidis (M. 7)	50,000	<100	<100	<100	<100	50,000	50,000	50,000	50,000	50,000
Original Gärtner	80,000	<100	<100	<100	<100	40,000	40,000	40,000	30,000	30,000
Ratin	10,000	<100	<100	<100	<100	5,000	5,000	5,000	5,000	5,000
Pendry	20,000	<100	<100	<100	<100	10,000	10,000	10,000	10,000	10,000
"Dublin"	30,000	12,000	20,000	20,000	12,000	<100	<100	<100	<100	<100
L.	6,000	6,000	6,000	6,000	6,000	<100	<100	<100	<100	<100
P.	6,000	3,000	6,000	3,000	3,000	<100	<100	<100	<100	<100
T.	5,000	4,000	4,000	4,000	3,000	<100	<100	<100	<100	<100
Calf 3502	40,000	20,000	30,000	40,000	30,000	<100	<100	<100	<100	<100

Further remarks on the strains examined.

In Table I a brief note of its origin has been attached to each strain. In the case of some of the strains there are other points of interest. No. 1 of set *A*, the "original Gärtner," has become almost completely "rough" and, though its H-antigen has apparently the full range of components found in smooth *enteritidis* strains, it has lost almost entirely the O-antigen characteristic of the type. The same applies to No. 2 (N.C. 410), the type Gärtner strain of the American Museum of Natural History.

As regards the eight rat virus strains (Nos. 5–12), the results of our serological examination have not confirmed the statement of David (1929) who found that they could be distinguished by absorption tests from the *enteritidis* group; it is probable that differences in technique and especially in the amount of culture employed account for the divergent results. We have no doubt that any serological differences between the "virus" strains which we examined and *S. enteritidis* are not due to differences in the antigen characteristic of the species but to one or both of such causes as "roughness" or loss of heat-labile antigen.

It will be observed that of the 13 strains of recent human origin in set *A*, one (No. 16) is from septicaemia and two (Nos. 19 and 20) are from cases of meningitis, while in set *B*, five (Nos. 1, 3, 5, 6 and 7) are from septicaemia and one (No. 9) from meningitis. The strains, Nos. 3 and 9, were described as "enteritidis (Gärtner)" by their discoverers though, in the former case, the

unsatisfactory result of the absorption test caused the identification to be stated as tentative.

The suspicion that the "Dublin" type may be specially associated with the bovine species and that milk is the usual source of human infection is supported by (1) the fact that it is apparently the cause of the common epizootic dysentery among calves, and by (2) that in the majority of cases, in which it has been isolated from man, milk can be definitely suspected, *i.e.* in connection with strains Nos. 2, 3, 7, 8 and 9.

SUMMARY.

Three cases of continued fever are described in which the *Salmonella* type "Dublin" was isolated from the blood. The cultural and serological behaviour of the three strains so obtained are compared with those of 34 strains of typical *S. enteritidis* (Gärtner) (including strains from commercial rat virus) and with those of 12 other strains of *S. dublin* (including six from calf-dysentery in Denmark). The suggestion is made that the "Dublin" type is of bovine habitat and that cows' milk is the vehicle of human infection.

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