local anaesthesia. The administration of saline solution was continued by slow continuous drip. A portion of gangrenous ileum was found in the sac of a femoral hernia. This was resected but no anastomosis was attempted, rubber tubes being fixed into the ends of the divided bowel. When the proximal enterostomy was draining freely it was joined to the distal tube, but it was found that the proximal ileum was unable to empty itself into the distal portion of bowel via the tube. Ordinary gravity drainage was therefore re-established, but the contents were collected and utilized as in Case I. The patient's condition rapidly improved, and he was well on the way to recovery when, on the third day, he developed an acute chest lesion, from which he died.

This case supports the experimental findings relating to strangulation of short segments of bowel within hernial sacs. The blood loss is small in amount, and toxins escaping into the closed hernial sac are but slowly absorbed. The main factor in this case was the result of the mechanical obstruction with dehydration and alkalosis causing severe tetany, which was rapidly relieved by intravenous saline.

Summary

1. The method of exteriorization of strangulated bowel in patients who are gravely ill is one which can be carried out quickly and with a minimum of shock.
2. Drainage of the bowel must be established, but excision of the affected segment may, if necessary, be left until twenty-four hours have elapsed.
3. When a patient is seriously ill immediate resection and anastomosis increase the risks of peritoneal infection and of recurrent obstruction, since the over-distended proximal bowel may be unable to pass its contents through the new stoma.
4. Operative procedures must be preceded by blood transfusion or intravenous saline infusions according to the type of intestinal obstruction to be dealt with.

THE SERUM TREATMENT OF TYPHOID FEVER

BY

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Antityphoid serum was prepared quite early in the history of modern immunology. Chantemesse (1907) and various workers experimented with sera produced by immunizing animals with typhoid bacilli. However, success did not seem to attend these various early trials. Thus for many years antityphoid serum was neglected for curative purposes, and the antigenic response which typhoid bacilli are capable of eliciting was confined almost entirely to prophylactic inoculation.

However, interest has been revived during 1934 in the possibilities of a curative antityphoid serum through the work of Felix, who has elaborated a hypothesis of a Vi antigenic factor in virulent strains of typhoid bacilli. Felix (1935), using these virulent strains of *B. typhosus*, has immunized horses with living cultures and produced a new serum. Clinical trials with this antityphoid serum, prepared in the serum department of the Lister Institute at Elstree, were carried out in Palestine and in Ireland and were recorded by Felix (1935) and McSweeney (1935). The results were definitely encouraging, for they pointed to a favourable action of the serum on both the toxæmic symptoms of the disease and the pyrexia.

Working with a number of strains of *B. typhosus* isolated from cases of typhoid fever among Chinese patients in Shanghai, we were able to confirm the

observations of Felix and Pitt (1934) concerning the association of the virulence of typhoid bacilli with the inagglutinability by "O" antibody (Robertson and Yu, 1936, *a* and *b*). We then proceeded to immunize a horse with two of our Shanghai strains of high virulence and relative inagglutinability.

The technique consisted of first commencing with injections of 1 c.cm. daily of *B. typhosus* extract prepared according to the method of Felix. We gave this extract for three days and then paused for four days and recommenced, using 1 c.cm. of a suspension of living organisms given intravenously. Living organisms were administered for three successive days and then the animal was rested. Gradually increasing doses of living *B. typhosus* were administered similarly for three days, with rests of four days, for ten weeks. The horse was then bled outright, and in experiments on mice our antityphoid serum was found to confer full protection against infection with highly virulent typhoid bacilli.

In view of the great importance to be attached to the exact quantitative estimation of the two essential antibodies ("Vi" and "O"), on the presence of which the potency of a therapeutic antityphoid serum would seem to depend, and in the absence of a recognized standard for this estimation, a sample of our unconcentrated horse serum was submitted for examination to Dr. A. Felix. According to the report kindly sent us by Dr. Felix, the "Vi" and "O" titres of our serum were almost equal to those of his serum No. 1, which had been used in the clinical trials in Palestine (Felix, 1935).

In selecting cases for clinical trial we were anxious to have the cases as early as possible in the disease—as soon as a completely satisfactory diagnosis had been made. In China, however, a majority of patients tend to visit different doctors and not to come to hospital until at fairly late stages, when they are desperately ill. This greatly lowers the apparent incidence of typhoid fever and raises its mortality in hospital cases. Our object was, so far as possible, only to deal with cases which clinically exhibited all the classical symptoms of typhoid fever, proved positive by Widal test, and subsequently confirmed by a positive blood culture.

We treated in all fifty-two cases of classical typhoid fever, which satisfied the above-mentioned laboratory criteria, with our locally manufactured serum. When the serum was unconcentrated the standard dose for adult patients was 50 c.cm., administered by the intramuscular route. The dose for concentrated serum was 25 c.cm. As a routine this dose was given on three consecutive days. Since, through the courtesy of Dr. Felix, we had a small supply of his concentrated serum available, we were able to treat four further cases with serum prepared at the Lister Institute at Elstree. The standard dose of this concentrated serum was 25 c.cm. given by the intramuscular route.

We did not consider it advisable to use normal horse serum as a control, as it gave very unfavourable results in the hands of Felix (1935) and McSweeney (1935).

A short summary of the main points of interest in the individual cases comprising this small series is reproduced in the following table. When using the phrase "dramatically improved" the intention has been to convey a true impression of the clinical effects, free from any exaggeration, as judged by careful and unbiased observers.

Summary

Of fifty-two Chinese patients who received Lester Institute antityphoid serum thirty cases showed definite improvement, indicated by a drop in temperature and a decrease in toxic symptoms. Seven cases showed reduction in toxæmia but no noticeable effect on the temperature curve. The remaining fifteen cases showed no appreciable effect of the serum.

Case No.	Stage of Disease Treated	Severity of Symptoms	Complications	Diagnosis			Dosage of Serum	Result
				W.B.C.	Widal	Blood Culture		
1. F., age 21	Unknown; probably 2nd week	Severe	Amoebic dysentery	13,000	+	+	3×50 c.cm.	Temperature normal after last dose
2. M., age 20	3rd week	Very severe	Severe haemorrhage	6,250	+	+	3×50 c.cm.	No improvement; death
3. F., age 13	2nd week	Very severe	Probably a perforation	3,800	+	+	3×25 c.cm.	No improvement; death
4. F., age 29	3rd week	Very severe	Nervous symptoms	3,500	+	+ (urine)	3×50 c.cm.	Great improvement at once
5. M., age 16	3rd week	Moribund	Beri-beri	4,500	+	+	3×30 c.cm.	Not improved; fatal
6. F., age 18	2nd week	Severe	—	4,400	+	+	2×50 c.cm.	Greatly improved, immediately convalescent
7. F., age 31	2nd week	Severe	—	5,400	+	+	3×50 c.cm.	Toxaemic symptoms improved
8. M., age 18	3rd week	Very severe	Severe intestinal haemorrhage	2,600	+	+	2×50 c.cm.	No improvement; recovered
9. F., age 43	3rd week	Severe	—	4,100	+	+	1×25 c.cm. 1×30 c.cm.	Toxaemic symptoms improved
10. F., age 22	2nd week	Mild	—	5,100	+	+	2×20 c.cm. 2×30 c.cm.	Dramatically improved
11. M., age 14	3rd week	Severe	Bronchitis	2,600	+	+	3×30 c.cm.	Greatly improved after last dose
12. M., age 23	4th week	Severe	Parotitis	3,200	+	+	3×50 c.cm.	Greatly improved
13. M., age 23	3rd week	Very severe	Herpes on lips	2,000	+	+	3×50 c.cm.	No improvement; recovered
14. M., age 12	2nd week	Very severe	—	7,250	+	+	3×25 c.cm.	Great improvement; convalescent after last dose
15. M., age 14	2nd week	Very severe	Bronchitis, multiple furuncles on neck and face	1,650	+	+	3×30 c.cm.	Great improvement
16. M., age 29	3rd week	Very severe	Bronchitis, intestinal haemorrhage	—	+	+	2×25 c.cm. Felix	No improvement; fatal
17. M., age 14	3rd week	Very severe	—	—	+	+	3×30 c.cm. Felix	Great improvement; convalescent three days after last dose
18. F., age 45	2nd week	Very severe	—	—	+	+	2×25 c.cm. Felix	Toxaemic symptoms improved
19. F., age 35	2nd week	Mild	—	—	+	+	1×25 c.cm. 1×15 c.cm. Felix	Dramatically improved; convalescent three days after last dose
20. M., age 29	4th week	Very severe	Intestinal haemorrhage	—	+	+	2×20 c.cm.	Greatly improved
21. F., age 30	2nd week	Severe	Pneumonia, pyelitis	7,000	+	+	2×50 c.cm.	Toxaemic symptoms improved; no effect on temperature
22. F., age 17	3rd week	Very severe	Pneumonia, beri-beri	8,150	+	+	2×50 c.cm.	Greatly improved
23. F., age 25	2nd week	Very severe	Bronchopneumonia	—	+	+	2×25 c.cm.	No improvement
24. F., age 16	2nd week	Severe	—	—	+	+	2×25 c.cm.	Greatly improved
25. F., age 29	2nd week	Severe	Pyelitis	1,400	+	+	3×50 c.cm.	Dramatically improved
26. F., age 31	2nd week	Severe	—	4,400	+	+	1×25 c.cm. 2×50 c.cm.	Dramatically improved
27. F., age 29	2nd week	Severe	—	7,500	+	+	3×50 c.cm.	Greatly improved
28. M., age 19	1st week	Mild	—	3,800	+	+	3×50 c.cm.	Dramatically improved
29. F., age 33	3rd week	Severe	—	2,550	+	+	3×50 c.cm.	No improvement
30. M., age 34	3rd week	Severe	Diarrhoea	5,050	+	+	3×50 c.cm.	Discharged against advice
31. M., age 34	3rd week	Very severe	Pneumonia, intestinal haemorrhage	4,250	+	+	3×50 c.cm.	General condition improved, temperature remained; died suddenly
32. M., age 21	2nd week	Severe	Decubital ulcer	5,700	+	+	4×50 c.cm.	No improvement
33. F., age 32	3rd week	Severe	—	6,150	+	+	3×50 c.cm.	Toxaemic symptoms improved; little effect on temperature
34. M., age 16	3rd week	Extremely severe	Advanced tuberculosis	1,250	+	+	3×50 c.cm.	No improvement
35. M., age 18	2nd week	Severe	—	4,200	+	+	3×50 c.cm.	Dramatically improved
36. M., age 26	3rd week	Severe	—	6,200	+	+	3×50 c.cm.	Dramatically improved
37. M., age 24	2nd week	Severe	—	4,500	+	+	3×50 c.cm.	Dramatically improved
38. M., age 50	2nd week	Very severe	—	7,150	+	+	3×50 c.cm.	No improvement
39. F., age 17	2nd week	Very severe	Bilateral bronchopneumonia	5,200	+	+	3×50 c.cm.	No improvement
40. F., age 36	2nd week	Severe	—	5,900	+	+	1×25 c.cm. 2×50 c.cm.	Dramatically improved
41. M., age 22	1st week	Moderately severe	—	6,550	+	+	2×50 c.cm.	Dramatically improved
42. M., age 43	2nd week	Severe	—	5,300	+	+	2×50 c.cm.	Dramatically improved
43. M., age 20	3rd week	Very severe	—	—	+	+	2×45 c.cm.	Toxaemic symptoms improved; little effect on temperature
44. F., age 7	2nd week	Severe	—	5,200	+	+	2×20 c.cm.	Convalescent four days after second dose
45. F., age 20	1st week	Severe	Acute bronchitis	6,200	+	+	3×50 c.cm.	Toxaemic symptoms improved; little effect on temperature
46. F., age 23	2nd week	Extremely severe	Pneumonia	2,100	+	+	3×50 c.cm.	No improvement
47. F., age 13	3rd week	Very severe	Bronchitis and tympanitis	3,950	+	+	3×50 c.cm.	Dramatically improved
48. F., age 8	2nd week	Extremely severe	Intestinal haemorrhage	2,600	+	+	3×25 c.cm.	No improvement
49. M., age 16	2nd week	Severe	—	—	+	+	3×45 c.cm.	Greatly improved
50. M., age 21	2nd week	Severe	Pleural effusion	3,350	+	+	3×45 c.cm.	Greatly improved
51. M., age 15	2nd week	Severe	—	6,450	+	+	3×25 c.cm.	Convalescent after last dose
52. M., age 29	5th week	Extremely severe	Severe intestinal haemorrhage	6,250	+	+	3×50 c.cm.	No improvement; died
53. M., age 19	2nd week	Severe	—	1,700	+	+	3×50 c.cm.	Greatly improved
54. F., age 17	1st week	Severe	—	4,850	+	+	1×25 c.cm. 1×50 c.cm.	Convalescent after second dose
55. M., age 4	4th week	Very severe	Pneumonia, otitis, and abscesses	—	+	+	2×25 c.cm.	Convalescent four days after second dose
56. M., age 18	2nd week	Severe	—	4,600	+	+	2×50 c.cm.	Discharged against advice

Of the four cases treated with Felix's Lister Institute serum two showed dramatic improvement. One further case showed lessening of toxæmia. The remaining case showed no change.

It is our impression that the new antityphoid serum is definitely beneficial when given to the typhoid patient during the first or second week of illness in decreasing the toxæmia and shortening the febrile course.

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DYSPHAGIA WITH ANAEMIA IN A MALE

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The association of dysphagia with anaemia was noted over sixty years ago: more recently a third symptom, stomatitis and glossitis, has been added to complete the syndrome usually known as the "Plummer-Vinson syndrome"—no doubt because we owe our first description of the characteristic changes in the oesophagus to A. Brown Kelly and Dr. R. Paterson.¹ The condition is not of great rarity: I have observed twenty-odd cases in a series of just over 500 patients submitted to oesophagoscopy. But most observers agree in describing it as a disorder confined to women; the finding, therefore, of an apparently typical case in a male subject has the interest attaching to the unusual.

Case Report

A man aged 71 came to the out-patient department on August 6th, 1936, complaining of difficulty in swallowing during two months, with no appreciable loss of weight. I was not there then, but it is recorded that the hypopharynx was full of mucus, and there was no evidence of obstruction to a bolus viewed by *x* rays: a lozenge was prescribed. Six weeks later I first saw him; the symptoms were unchanged, but I noticed that he was very pale, with conjunctival pallor; he had never known he was anaemic. He had also glossitis, with loss of papillae except in the centre of the tongue; the insides of the cheeks were sore, and he had a linear scar from each angle of the mouth, and when questioned said that the corners of his mouth had been sore for several years. The blood showed: red blood cells, 5,000,000; haemoglobin, 60 per cent.; Dr. A. D. Fraser reports "anisocytosis fairly well marked, poikilocytosis moderate, polychromasia moderate, microcytosis fairly well marked, megalocytes and nucleated reds absent; erythrocytes show lack of haemoglobin; hypochromic anaemia." Van den Bergh negative, direct and indirect. Test meal: no free HCl in resting juice; one hour after meal combined HCl in 1 c.cm. neutralized by 0.2 c.cm. decinormal soda. Oesophagoscopy: at upper end of oesophagus a thin white demilune web round the posterior aspect reduces the lumen to 8 mm. across. It yielded readily to slight pressure from the endoscope, with just a trace of bleeding. Below this the oesophagus was normal except for

pallor of the mucosa; cardia at 37 cm. from teeth, normal. Immediately following the instrumentation swallowing has become normal. The patient has been sent home, taking 30 grains of iron and ammonium citrate thrice daily; no dysphagia, the soreness of mouth is less, pallor not materially changed.

Pathology

The aetiology is in dispute. Paterson and Brown Kelly² regard the dysphagia as primary, with anaemia due to interference with nutrition; thus following the older descriptions of anaemia occurring in "hysterical dysphagia."

"At a meeting [of the Laryngological Section of the Royal Society of Medicine] in 1919 Brown Kelly and I drew attention to a clinical syndrome in women, the essential feature of which is a gradually increasing inability to swallow, due to spasm of the pharyngo-oesophageal sphincter; often associated with changes in the buccal and pharyngeal mucosa and at a later stage with anaemia, which is to be regarded as a secondary manifestation of the dysphagia. Plummer, approaching it from the physician's point of view, called it hysterical dysphagia, and later Vinson laid stress on the anaemia and splenomegaly.⁵ The blood changes are those of chlorosis and secondary anaemia with considerable reduction in the haemoglobin (Munro Cameron)."⁶

The patients are women and come under observation in middle life with a long history of gradually increasing dysphagia, which eventually confines them to a fluid diet. Mild glossitis with atrophy may be early; later, the tongue is smooth and the buccal mucosa dry and pale.

On the other hand, it has been suggested that the changes in the mouth and pharynx are secondary to the anaemia. Dr. R. S. Johnson³ reports six cases in St. Bartholomew's Hospital. All were women: the anaemia was severe, of secondary type; haemoglobin 32 to 50 per cent.; colour index about 0.5; complexion striking, brownish-yellow, suggesting pernicious anaemia; glossitis and cracks at the angles of the mouth were noted in four; dysphagia in five; complete achlorhydria in all; slight enlargement of spleen in one only; fragility of red corpuscles increased. He considers the changes in the mucosa secondary to the anaemia. With this view I agree. A feature not included in the above accounts is the formation of a thin web at the oesophageal entrance, instead of the spasm mentioned above: in my own experience this is the more usual finding.

Treatment

The essential is the administration of iron in large doses—inorganic preparations are to be preferred; the daily dose of iron and ammonium citrate is 60 to 120 grains for eight weeks or more. It may be necessary to repeat treatment during several years. Where spasm or webbing is present treatment should begin with dilatation of the oesophagus; this rarely needs to be repeated. The prognosis is good, although it is said that later malignant changes in the oesophagus are relatively frequent in these patients.

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- ⁶ *Quart. Journ. Med.*, 1928, xxii, 43.
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