woman aged 50 who presented with melaena. Laparotomy showed her to have a Meckel's diverticulum and a rounded tumour in the wall of her terminal ileum distal to the diverticulum. Resection of the involved segment of ileum was carried out, section showing the tumour to be a leiomyoma.

Summary

We have reviewed briefly the primary tumours met with in the small intestine and report a series of 16 such tumours dealt with in this hospital over the past ten years.

Adenocarcinoma is the commonest of these tumours. It occurs most frequently in the duodenum and upper jejunum. Symptoms occur late owing to the fluid nature of the bowel content at this level. Prognosis is uniformly poor, and this has been our experience. The age incidence of these growths corresponds to the general cancer age, and women were affected more often than men.

A description of the lesions produced by lymphosarcoma and allied conditions is given. Five such cases are reported, and it is suggested that in suitable cases resection of the involved segment followed by radiotherapy is the treatment of choice.

A description is given of the carcinoid or argentaffin carcinoma. The different behaviour of this tumour occurring in the appendix and ileum is discussed, and one such case is reported.

Our thanks are due to other members of the staff of the Essex County Hospital for allowing access to their case records, and to Dr. J. B. Penfold for his helpful criticism.

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ASSOCIATION OF JEJUNAL DIVERTICULOSIS AND STEATORRHOEA

BY

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It seems justifiable to report the following single case of steatorrhoea, macrocytic anaemia, and glossitis associated with multiple jejunal diverticulosis, in view of the considerable theoretical interest of the association and the apparent rarity of the occurrence. No similar case can be found in the literature. Moreover, the diarrhoea was relieved for a period of eight months after a course of chlortetracycline ("aureomycin"), and during this time the anaemia remained in remission without other treatment.

Diverticula of the small intestine between the duodeno-jejunal flexure and the ileo-caecal valve are usually symptomless and are found by chance in the course of a barium-meal examination or at necropsy. Their incidence has been recorded as 9 cases in 2,820 necropsies at King's College Hospital and as 0.31% by Edwards (1939), but it may be commoner than this. Benson, Dixon, and Waugh (1943) state that 122 cases had been recorded at the Mayo Clinic, of which 100 were jejunal, 17 in the ileum, and in 5 cases the diverticula were present in both. They are commoner in older people (Edwards, 1939). They are said on occasion to

give rise to vague abdominal symptoms such as flatulence and postprandial discomfort, but in some instances it may be that the presence of these symptoms from other causes has led to the performance of a barium meal and the discovery of the diverticula.

Complications such as acute intestinal obstruction, volvulus in relation to diverticula (Stiven, 1934), haemorrhage (Braithwaite, 1923; Waterson, 1952), perforation (Butler, 1937), diverticulitis (Butler, 1933), and the syndrome of chronic intestinal obstruction (Phillips, 1953) have all been described. The latter consists of symptoms varying from vague abdominal discomfort to more definite colic, vomiting, and constipation with loss of weight and deterioration in general health. Phillips, in discussing this syndrome, points out that there is no organic obstruction at laparotomy, although distended hypertrophic loops of bowel may be found, and he in fact suggests that there is a "dyskinesia" of the bowel which produces this syndrome and which also causes the pulsion-diverticula. He quotes Benson *et al.* (1943) as stating that non-organic chronic small-bowel obstruction was the commonest observed complication in their series of 122 cases—and that the changes resemble those in small intestine which has been obstructed for a long period. One of two cases which he describes had loose stools.

No reference to their association with deficiency syndromes from failure of small-intestinal absorption can be found in the literature other than a single case report by Montuschi (1949). He reported the case of a man aged 66 with a history of eight years' recurrent abdominal pain and bouts of diarrhoea and four years' oedema of the legs. Investigation showed a lowered plasma albumin and a raised faecal fat. Barium examination revealed multiple diverticula in the small intestine and colon, with precipitate passage of barium through the small intestine and loss of the normal mucosal pattern. It was thought that a low-grade inflammatory process in the diverticula was probably the cause of the small-intestinal hurry which led to deficient absorption of protein.

Case Report

A housewife aged 71 was first seen in December, 1949. She had been in good health until five years previously, when she began to have two or three loose motions a day, the stools being sometimes pale. She did state that her bowels had always tended to be easily upset, but that it was seldom this occurred. Three years before she developed a sore tongue, and shortly afterwards in November, 1946, a blood count showed some macrocytosis and anisocytosis. (Details of blood counts are given in the Table.) On December 20 a barium meal showed a small hiatus hernia. On the second part of the duodenum and on the duodeno-jejunal flexure there were large diverticula, and there were multiple diverticula throughout the jejunum. These showed some stasis in the erect position (Dr. F. R. Berridge). She was apparently diagnosed as suffering from pernicious anaemia, and it was thought that the diarrhoea was due to achlorhydria.

She was treated with a purified liver extract ("ana-haemin") intramuscularly once a fortnight at first, and subsequently monthly for the next three years until she was admitted to hospital. No test meal had been done. Full particulars of her blood counts during this time are not available, but she still had macrocytosis in 1949. Her diarrhoea remained unchanged during this time, and her tongue continued to be sore most of the time, with occasional periods when it did not trouble her. One month before admission she developed much more severe diarrhoea, having 10 watery stools a day and copious vomiting. The

Treatment:	Anaheamin i.m.						Ascorbic Acid, Vit. B, Folic Acid		Nicotinic Acid, Ribo- flavine, Vit. B, Folic Acid	Folic Acid	Plexan, 4 ml. i.m. Weekly
	Nov. 1946	Jan. 1947	May '47	6/1/49	30/12/49	10/1/50	20/1/50	3/2/50	17/3/50	14/7/50	
R.B.C. (mills) ..	4.12	4.15	5.12	4.11	3.64	3.67	3.81	3.7	4.37	4.66	3.76
Hb (g%) ..	15.6	14.1	15.6	14.0	12.8	11.7	13.4	14.0	14.5	15.1	14.0
M.C.H. (γγ) ..	38.0		30.5	34.1	35.2	31.9	35.0	38.0	34.0	32.5	37.3
M.C.V. (cubic μ) ..				109.3	107.2	100.5	110.0	117.0	102.0	94.0	109.6
M.C.H.C. (γ) ..		34.0		31.1	32.7	31.6	31.8	32.2	32.4	34.4	34.1
Reticulocytes (γ) ..					Less than 0.5		0.5	1.3	0.1	1.4	
W.B.C. ..	4,000			Normal	Normal	Normal	Normal		Aniso- cytosis +	Aniso- cytosis +	Normo- chromia. Aniso- cytosis. Macro- cytosis
	Macrocyto- sis. Aniso- cytosis			Some macro- cytosis	Macro- cytosis. Aniso- cytosis	Normo- chromia. Some macro- cytosis					

Treatment :	Plexan, 4 ml. i.m. Weekly	Plexan, 4 ml. i.m. Fortnightly					Chlortetracycline. Total in 9 days = 9.25 g.	No Treatment			
	26/1/51	25/5/51	17/8/51	1/2/52	2/5/52	6/2/53		10/7/53	16/10/53	15/1/54	23/4/54
R.B.C. (mills) ..			4.76	4.87	4.79	4.53		4.75	4.8	4.73	4.2
Hb (g%) ..	13.8	15.0	13.3	14.5	13.6	14.8		13.6	14.0	14.0	13.5
M.C.H. (γγ) ..			28.0	29.8	28.4	32.7		28.6	29.2	29.6	32.1
M.C.V. (cubic μ) ..			88.5	88.5	90.8	99.3		88.5	87.7	91.0	95.0
M.C.H.C. (γ) ..			31.8	33.7	31.3	32.9		32.3	33.4	32.6	33.8
	Normo- chromia. Some aniso- cytosis	Normo- chromia. Normo- cytosis	Normo- chromia. Normo- cytosis	Normo- chromia. Some aniso- cytosis	Normo- chromia. Normo- cytosis	Normo- chromia. Aniso- cytosis		Normo- chromia. Some aniso- cytosis	Normo- chromia. Aniso- cytosis		Normo- chromia. Aniso- cytosis

diarrhoea lasted for 14 days, and the vomiting for a further week, when she was admitted to another hospital and treated with gastric lavage and a fluid diet. The vomiting ceased after three days on this regime. She was transferred to Addenbrooke's Hospital on December 22, 1949, when she gave the above history. She had had no other serious illnesses in the past. Her husband and two children were alive and well and there was no family history of diarrhoea or abdominal illness.

She was a thin, white-haired woman. Her tongue was smooth, and red at the tip and round the sides, but was otherwise normal. Her abdominal wall was very thin and

Radiograph after barium meal, showing multiple duodenal and jejunal diverticula, and a large diverticulum on the duodeno-jejunal flexure.

intestinal peristalsis could be seen. There were no other abnormal physical signs. On December 28 barium meal examination showed multiple duodenal and jejunal diverticula and a large diverticulum on the duodeno-jejunal flexure (see Fig.). Diverticula contained fluid levels in the erect position. Barium flocculated in the jejunum and ileum. Transit time slow, $7\frac{1}{2}$ hours. The calibre of the small gut was wide (Dr. F. R. Berridge). Blood count (see Table) showed a slight macrocytic anaemia.

On January 2, 1950, the serum calcium was 11.1 mg. per 100 ml.; serum phosphorus, 2.8 mg. per 100 ml.; plasma protein, 5.6 g. % (albumin 2.6 g., globulin 3 g.); non-protein nitrogen, 53 mg. per 100 ml.; thymol turbidity, 3 MacLagan units; thymol flocculation, negative. X-ray film of forearm bone with control—no significant abnormality. An amino-acid absorption test was normal. A sternal puncture on January 14 showed: total cell count, 20,000 per c.mm.—megakaryocytes 6 per 10,000 nucleated red cells, M/E ratio 3.2:1; polymorphs—neut. 36.5, eos. 2.6; metamyelocytes—neut. 15.6, eos. 1.8; myelocytes—neut. 9.4, eos. 0.6; premyelocytes, 2.4; myeloblasts, 0.2; lymphocytes, 9.4; plasma cells, 0.2; monocytes, 0.6; normoblasts—late 12.6, intermediate 2.0, early 0.6; megaloblasts—late 4.0, intermediate 1.0, early 0.8; pre-erythroblasts, 0.4; haemocyto blasts, 0.2; megaloblasts of nutritional macrocytic anaemia type (Dr. Martin Hynes). On January 17 a glucose-tolerance test showed: fasting, 0.095%; 30 minutes, 0.176%; 60 minutes, 0.204%; 90 minutes, 0.148%; 120 minutes, 0.132%. A fat balance was unfortunately not completed successfully, and the patient did not wish further investigation.

She was discharged home on a low-fat (50 g.) high-protein diet, ascorbic acid, vitamin B₁, nicotinic acid, and riboflavin; and also folic acid, 10 mg. t.d.s., which was begun on January 17. The reticulocytes on January 20 were only 0.5%, and on the 27th they were 1.8%. She continued with folic acid, 5 mg. b.d., and on February 3 a blood count showed no improvement. By March 17 the red-cell count had risen, and the macrocytosis was less, but the diarrhoea had persisted, and the tongue was still sore, with a smoother appearance than previously. In April, 1950, the folic acid was discontinued for one month, with no change in symptoms. The vitamins were discontinued in

May, and folic acid, 5 mg. b.d., was started again. Symptoms remained unchanged, with the tongue sore most of the time, but the patient felt better in herself. By July 14 the blood count had returned to normal and the macrocytosis had disappeared. She continued with folic acid, and in spite of this in September a blood count showed a fall in the red cells and a return of macrocytosis. Her serum calcium was 9 mg. per 100 ml., plasma proteins 5.8 g.% (albumin 3.6 g., globulin 2.2 g.). The patient complained of feeling generally tired and unwell, and agreed to come back into hospital, which she did on November 27.

A fat balance investigation was carried out, the balance period being four days on a standard 50-g. fat intake, and the result was as follows: dry matter, 6.4% of faeces; total fat, 28.2% of dry matter; neutral fat, 0.8%; free fatty acid, 26.2%; soap fatty acid, 1.2%; fat hydrolysed—93% of total fat. Fat intake was 202 g. over four days, and fat lost 31 g.=15.3% of fat intake. Fasting gastric juice free HCl 0.045%, total 0.073%. After histamine, free HCl 0.273%, total acidity 0.310%. Duodenal juice showed some lipase and tryptic activity, but no quantitative test was attempted. The patient complained of a sore tongue, and it was moderately smooth and reddened. She was treated with two injections of riboflavine, 10 mg., vitamin B₁, 50 mg., nicotinic acid, 50 mg., followed by a further six injections at twice-weekly intervals. Her tongue became extremely sore, and was dark red and beefy in appearance, with complete loss of papillae. She was discharged home, and her tongue remained sore.

In December, 1950, she was started on injections of crude liver extract ("plexan"), 4 ml. twice weekly. Within 14 days the soreness of her tongue disappeared and in a month it looked virtually normal. She continued on injections of plexan, 4 ml., which after a month were changed to weekly, and then to fortnightly after a further two months, until July, 1953. During this time her blood count remained very satisfactory, being normochromic and normocytic. She did, however, continue to have looseness of her bowels with three or four stools a day, and occasionally more severe diarrhoea. At intervals she experienced abdominal discomfort, vague indigestion, and occasional attacks of vomiting lasting a day or two. In May, 1953, she developed more frequent indigestion with vomiting every few days for a period of about a month.

On June 4 she was started on a course of chlortetracycline, 250 mg. six-hourly, which she continued for nine days, receiving 9.25 g. in all. The injections of plexan were discontinued in July. Following the chlortetracycline her stools became more normal over the course of a fortnight, and since July, 1953, she has had two, or occasionally three, normally formed motions each day for the first time for several years. Unfortunately the patient was unwilling to be admitted for a further fat balance investigation. This improvement in her bowels continued until March, 1954. During this period of eight months she had had only three or four slight vomiting attacks. She had no recurrence of soreness of the tongue, and her blood count, carried out at monthly or two-monthly intervals, remained normal. She is a patient who has always complained very readily in the past, but she said that she had felt better since she had the course of chlortetracycline than she had done for years.

This satisfactory state of affairs ceased at the end of March, 1954, when she began to have more frequent attacks of vomiting and developed a sore smooth tongue again. She was started again on weekly injections of plexan, 4 ml., on April 23, and these were continued for three weeks. On April 26 an analysis of one specimen of stools showed that 37.6% of the dry matter was fat. On April 30 she was started on a week's course of chlortetracycline, 250 mg. six-hourly, totalling 7 g. Following this she continued to feel unwell for two weeks, but then began to improve again. Her sore tongue had begun to improve before this, and by May 28 was normal. At the time of writing she appears to be well.

Discussion

It is of interest that although the anaemia responded to refined liver extract and to folic acid, the glossitis showed no improvement. Treatment with crude liver extract, however, resulted in disappearance of the glossitis within a fortnight, and improvement in the patient's feeling of well-being. There was no change in the diarrhoea. Following the course of chlortetracycline her stools became formed for the first time for several years, and she felt better than she had done for a similar period. The anaemia and glossitis also remained in remission without further injections of crude liver extract after the course of chlortetracycline, but this may have been the result of the necessary factors having been stored from the large quantities of crude liver she had received during the previous two years. It does appear, however, that the chlortetracycline exerted some effect on her intestinal function.

Of the various possible mechanisms whereby small-intestinal dysfunction, with impairment of absorption, may be provoked, the presence of infection inside the small bowel is one which has been put forward as responsible in several distinct pathological conditions. Cameron, Watson, and Witts (1949), in experiments on rats, showed that transection of the small gut followed by end-to-side anastomosis, in such a way as to produce a small blind loop which emptied itself downwards, was not followed by anaemia unless there was some stenosis of the opening of the blind loop causing stagnation. If, however, the blind loop was made at the end of the proximal piece of gut, so that stagnation occurred in it, a percentage of the rats so treated developed a macrocytic anaemia. These authors noted that it was important to place the blind loop in the upper or middle part of the small intestine. When the loop was in the lower ileum very few rats developed anaemia. It seems very probable that the steatorrhoea associated with gastro-colic fistula is due to soiling of the small-intestinal contents by material from the large bowel. It has been suggested that the steatorrhoea which sometimes develops after a Polya type of gastrectomy, and which may appear many months after the operation, is the result of stagnation in the afferent loop, with subsequent infection.

The state of affairs existing in multiple jejunal diverticulosis is clearly one in which stagnation and infection in the sacs might be expected to occur. To prove that infection is present in the diverticula is an extremely difficult matter except by the method of direct sampling should the patient require a laparotomy. Taking samples through a Miller-Abbott tube introduces too many possibilities of contamination. In this patient the reversion of the bowel habit to normal after a course of chlortetracycline does suggest that the removal of infection might have been one factor responsible, and it does seem possible that infection in the diverticula may have been in part responsible for the small-intestinal dysfunction.

Summary

A case of jejunal diverticulosis, complicated by steatorrhoea, macrocytic anaemia, and glossitis, is described.

Parenteral crude liver extract produced a complete remission of the glossitis and macrocytosis. Parenteral refined liver extract, oral folic acid, and massive vitamin B therapy had no effect on the glossitis, while the macrocytosis showed a variable response to refined liver extract and folic acid.

Improvement in the diarrhoea and in general health occurred after a course of chlortetracycline, and the glossitis and anaemia remained in remission, without further treatment with crude liver extract, for a period of eight months.

It is suggested that the multiple jejunal diverticulosis was responsible for the steatorrhoea in this case, and

that stagnation and infection in the diverticula may have been the most important factor in producing the small-intestinal dysfunction.

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ANTIBIOTIC SENSITIVITY SPECTRA THEIR USE IN INVESTIGATING EPIDEMICS

BY

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Staphylococcal infections in hospital wards are the cause of considerable morbidity and mortality, and for many years bacteriologists have been devising methods to facilitate the detection of sources of infection. One of the difficulties has always been the fact that coagulase-positive staphylococci are commonly found in the upper respiratory tract and skin of apparently healthy people, and it is not practicable to eliminate all of these. "Unless the epidemic strain has some special characteristic, it is impossible to decide whether, for instance, a carrier of the species concerned is to be incriminated. It is here that the definition of individual 'types' within species has been found so valuable" (*Lancet*, 1947). Serological typing and phage-typing were used by Allison and Hobbs (1947) in their brilliant investigation of neonatal infections. Phage-typing has indeed been a new and successful weapon in tracing the sources of wound infections, but it requires some experience, and it is not used by many routine laboratories. When we were faced with investigation of an epidemic of wound infections in our surgical wards* it was thought that antibiotic sensitivity patterns might help to determine the cause of the trouble.

Investigation

Between September 12 and 24, 1953, five patients developed wound abscesses seven to ten days after an elective operation. The pus from the wounds yielded pure cultures of *Staphylococcus pyogenes*, and these infections appeared to be confined to patients operated on by one surgical team.

Nose and throat swabs were taken from all the nursing staff in the theatre and wards (22 in all), from the anaesthetist, and from two members of the surgical team. (The third member of the surgical team was away for three weeks when this investigation was started, but he had been present at all the operations done on the cases that became infected.) Coagulase-positive staphylococci were found in over half of the nursing staff. It was thus most desirable to determine whether all these staphylococci belonged to the same strain. Sensitivities to penicillin, streptomycin, chloramphenicol, chlortetracycline ("aureomycin"), and oxytetracycline ("terramycin") were determined with standard pads of these antibiotics on blood-agar plates, and three different patterns were obtained from the nursing staff (see Table I). Although the organisms derived from the

wounds all gave the same pattern (Table II), this did not coincide with any of the patterns derived from the nursing staff. The pattern, however, did coincide with that derived from organisms obtained from the nose and conjunctivae of

TABLE I.—*A, B, and C are Antibiotic Sensitivity Patterns of Strains of Staph. pyogenes Obtained from the Nursing Staff. All Coagulase-positive Staphylococci Derived from Them Belonged to One of these Three Strains*

Antibiotic	A	B	C
Penicillin	++	—	—
Streptomycin ..	+	+	—
Chloramphenicol ..	+	+	+
Aureomycin	+	+	+
Terramycin	+	+	—

++ = Very sensitive, + = sensitive, — = resistant.

TABLE II.—*Sensitivity Spectra of Strains of Staph. pyogenes Obtained from the Pus of the Patients (D), and the Nose and Conjunctivae (E and F Respectively) of the Missing Member of the Surgical Team*

Antibiotic	D	E	F
Penicillin	—	—	—
Streptomycin ..	—	—	—
Chloramphenicol ..	—	—	—
Aureomycin	+	+	+
Terramycin	+	+	+

+ = Sensitive; — = resistant.

the missing member of the surgical team (Table II), who had just returned from his holiday at this stage of the investigation. (While on holiday he had suffered from acute blepharitis and conjunctivitis.) Intensive antibiotic therapy was given and his infection was eradicated. There have been no further staphylococcal wound infections in the wards of his surgical team. It should be added that none of the patients operated on while he was on holiday developed staphylococcal wound infections.

Discussion

The value of *in vitro* sensitivity tests in the treatment of infections is still a somewhat controversial subject. The same can be said of our views on the action of antibiotics in their role as antibacterials. The most widely accepted and most plausible theory seems to be the one which ascribes to the antibiotics a power of interfering with some enzyme system which is essential either for bacterial survival or for their multiplication. Where a species of micro-organism displays great variations in sensitivity to an antibiotic, such as, for instance, *Staph. pyogenes*, the organisms that are sensitive would rely for survival or multiplication on some enzyme system which is interfered with by the antibiotic—for example, by poisoning, competition, or blocking—and the ones that are resistant either do not require this enzyme system or have developed an alternative one. It would seem to be a reasonable assumption that a variant strain of one species relies in its metabolism on the same or similar enzyme systems. Antibiotic sensitivity patterns may therefore be useful in tracing strains of bacteria and in finding sources of infection. The determination of antibiotic sensitivity spectra is a simple procedure that can be carried out in routine bacteriological laboratories, and if it can be relied upon to separate different strains of a species of micro-organism this should provide a useful screening test for sources of infection.

The absence of further wound infections after eliminating virulent organisms from the eyes and respiratory tract of a member of the surgical team is, it is felt, strong evidence that he indeed was the source of infection, as is the fact that none of the patients operated on during his absence developed staphylococcal wound abscesses. Antibiotic sensitivity patterns suggested that the staphylococci in the wounds and in his nose were the same strains, and thus showed us where to find the cause of our trouble and how to deal with it.