STAPHYLOCOCCAL DIARRHOEA

WITH AN ACCOUNT OF TWO OUTBREAKS IN THE SAME HOSPITAL

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During the years 1953-5, 31 cases of diarrhoea following antibiotic therapy were investigated in the Radcliffe Infirmary. *Staphylococcus aureus* was cultured from the faeces of 20 of them (Table I). Fourteen of the 31 patients died. Of the 31, 14 had had partial gastrectomies, and seven of these were among the 14 who died (Table I).

Of the total number of cases, 17 occurred in one male surgical ward, where the incidence of the disease reached the proportions of a small outbreak in the spring of 1954 (see Chart). The epidemic nature of this condition has not been stressed in previous reports, though the parts which *Staph. aureus* and the antibiotics play in the genesis of the disease are generally acknowledged.

The epidemiology, bacteriology, diagnosis, and treatment of the condition are discussed below, where the term "staphylococcal diarrhoea" is applied to those cases in which *Staph. aureus* was isolated from the diarrhoeic stools. Special culture methods were used to isolate the *Staph. aureus* to prevent its being overgrown by other organisms (see Appendix).

The term "staphylococcal enterocolitis" has been avoided because evidence was not always available, even at post-mortem examination, that both the small and the large bowel were affected. Similarly, the term "pseudomembranous enterocolitis," which is a descriptive term of pathology and not a disease entity, has also been avoided except in those cases in which pseudomembrane was actually found. From many reports it is seen that pseudomembranous lesions are found in many patients who have not had diarrhoea.

Review of the Literature

Finney (1893) gave what is possibly the earliest report of a similar condition, in a young woman, which developed 15 days after a gastro-enterostomy. She had severe diarrhoea and died, a "diphtheritic" membrane being found over the mucosa of the lower bowel. Descriptions of numerous cases of pseudomembranous enterocolitis have been published (Penner and Bernheim, 1939; Penner and Druckermann, 1948; Dixon and Weismann, 1948). The consensus of opinion of these authors was that shock was probably the cause of pseudomembranous enterocolitis, and no mention was made of bacteria except as secondary invaders.

Pettet *et al.* (1954), at the Mayo Clinic, reviewed 107 cases occurring during the 27 years prior to 1952 and did not think then that the incidence of pseudomembranous enterocolitis had significantly increased since the advent of antibiotics, but they acknowledged the possibility of disturbance by antibiotics of the normal balance of intestinal flora. At the post-mortem examination most of the cases were shown to have a pseudomembrane. *Staph. aureus*, though not specifically sought for, was found in the stools of five of them.

It is difficult to compare these series with those more recently described, because the clinical features are often very different—for example, intestinal obstruction, colonic carcinoma, and generalized peritonitis were common; diarrhoea was often not present; bacteriological examination of the stools was seldom reported; and antibiotics, of course, were not available for many of the early cases.

Kramer (1948) reported what is probably the first case of staphylococcal diarrhoea associated with oral streptomycin.

During the last few years many authors have reported cases of diarrhoea or enterocolitis following the use of antibiotics, more especially the "broad-spectrum" types. Disturbance of the balance of the normal bacterial flora, or its elimination, has usually been thought to be the cause, but more recently infection by *Staph. aureus* has been emphasized.

It is interesting to note, in retrospect, a warning given by the Council of Pharmacy and Chemistry of the American Medical Association (1951): "The new antibiotics, chloramphenicol, aureomycin and terramycin are highly bacteriostatic for many bacteria. Susceptible bacteria are suppressed and monilia and other yeast-like organisms may replace the normal or abnormal bacterial flora. This most frequently occurs in the large bowel and is of little consequence." (There followed a brief warning of possible infections of the lungs and other organs by fungi but no warning of invasion by bacteria resistant to these antibiotics.)

Since then there have been many reports, from both sides of the Atlantic, of fatal intestinal infections with *Staph. aureus* following the use of antibiotics in various conditions: Jackson *et al.* (1951) in treating pneumonia with oxytetracycline ("terramycin"); the same group (Womack *et al.*, 1952) in using oxytetracycline for urinary infections; Hay and McKenzie (1954) in treating dysentery in children with oxytetracycline; Dearing and Heilman (1953) in employing oxytetracycline and chlortetracycline ("aureomycin") in medical and surgical conditions. The last-mentioned authors found erythromycin effective in eliminating *Staph. aureus*, resistant to other antibiotics, from the faeces. From Greece, Choremis *et al.* (1954) reported 22 cases of severe diarrhoea, with 14 deaths, in 195 children with measles treated by antibiotics. Other affected children who did not receive antibiotics had no diarrhoea. Of the 22 cases, only six were studied bacteriologically, and in only two was *Staph. aureus* found in the faeces.

There are several similar reports of deaths, after various operations, due to staphylococcal diarrhoea following antibiotic therapy (Terplan *et al.*, 1953; Fairlie and Kendall, 1953; Wakefield and Sommers, 1953; Gardner, 1953; Williams, 1954; Fowler, 1955). *Staph. aureus* resistant to the antibiotics employed was often cultured from the faeces. Chlortetracycline and oxytetracycline were most frequently used, but in Fairlie and Kendall's series all but one of their five cases (three of them fatal) received penicillin and streptomycin. Pettet *et al.* (1955) described a case of staphylococcal enterocolitis following pre-operative preparation of the bowel with neomycin.

Not all authors agree that *Staph. aureus* and antibiotics together are the chief cause of severe post-operative enterocolitis—for example, Williams and Pullan (1953), although *Staph. aureus* was found in five of their severe cases examined bacteriologically. Their 10 fatal cases all occurred after partial gastrectomy. Dawson-Edwards and Morrissey

(1955) found *Staph. aureus* in only one of their 35 cases of enterocolitis following gastro-intestinal operations, but it was not sought routinely.

The epidemic nature of staphylococcal intestinal infection is illustrated by the report of Todd and Hopps (1955), who recorded two deaths from enterocolitis—one after partial gastrectomy, the other in a case of erythema multiforme. Both patients were in the same ward and died within seven days of one another, both received "broad-spectrum" antibiotics, and both were infected with *Staph. aureus* of the same phage type. The same strain of staphylococcus was widespread over the ward furnishings.

The Radcliffe Infirmary Outbreaks

During six weeks of the spring of 1954, in one male surgical ward (B) of this infirmary, six "good risk" patients developed severe diarrhoea following partial gastrectomy, and four of them died. Their progress after operation was uneventful until the onset of diarrhoea on the second or third post-operative day. A similar time of onset was described by Williams and Pullan (1953). During the next six weeks three more patients in the same ward—one after prostatectomy and two after partial gastrectomy—were similarly afflicted and one died. Unfortunately four cases were not fully investigated bacteriologically, but in retrospect it seems likely from the clinical features that they were staphylococcal infections.

During the following 15 months 20 other patients undergoing various treatments developed diarrhoea of varying severity. All of them, in addition to the above-mentioned 11 early cases, had been treated with antibiotics. The relevant details of these 31 cases are summarized in the epidemiological Chart and in Table I. Seventeen were patients in the same male surgical ward (B). Fourteen had operations for partial gastrectomy, and seven of them died following severe diarrhoea. All these cases were fully investigated bacteriologically.

TABLE I.—*Summary of 31 Cases of Diarrhoea, Giving the Incidence of Staph. Aureus in the Faeces*

Operations Performed	Severe Diarrhoea		Moderate Diarrhoea	Total
	Fatal	Recovered		
Partial gastrectomy ..	7 (1:4)	5 (3:4)	2 (0:2)	14 (4:10)
Other gastro-intestinal operations ..	2 (1:2)	0	1 (1:1)	3 (2:3)
Others ..	5 (5:5)	1 (1:1)	5 (5:5)	11 (11:11)
None ..	0	1 (1:1)	2 (2:2)	3 (3:3)
Total ..	14 (7:11)	7 (5:6)	10 (8:10)	31 (20:27)

Note.—The carriage rate of *Staph. aureus* in the faeces of 49 patients, before and after operation, who did not develop diarrhoea was 12%.
Figures in parentheses are the proportion of the specimens which gave *Staph. aureus* on culture—for example (2:3) indicates that 2 specimens out of 3 cultured were positive for *Staph. aureus*.

Clinical Features.—The cases may be divided into two groups. (A) *The 21 severe cases* :—Severe watery diarrhoea usually developed suddenly, sometimes with a premonitory tachycardia or a fall in blood pressure. The small bowel was distended and hyperactive, although in the later stages it became paralysed. The stools were often of the “rice-water” type, the patient being incontinent. In many cases the temperature rose to 101–102° F. (38.3–38.9° C.) at the onset, but some patients remained afebrile. Within a few hours the patient was collapsed, with circulatory failure, but occasionally he remained calm and almost euphoric. Few of these patients recovered. (B) *The 10 less severe cases* :—These ranged from severe diarrhoea with little systemic upset to milder cases in which the diarrhoea was troublesome for a few days, but ceased spontaneously. Recovery in this group was usual.

Diagnosis

In those cases presenting with tachycardia and a fall in blood pressure, other conditions—for example, pulmonary atelectasis or embolism, coronary thrombosis, a leaking suture line, or internal haemorrhage—were suspected until the onset of abdominal distension and diarrhoea made probable the diagnosis of staphylococcal intestinal infection, especially in those patients who had been given antibiotics.

A specimen of diarrhoeic stool which had been allowed to stand in a glass jar often showed three layers: a lower layer consisting of dirty white flakes of mucus and sometimes mucus membrane; a middle layer of faecal detritus; and a supernatant layer of murky fluid. A Gram-stained film of the faeces often showed large numbers of Gram-positive cocci and pus cells. Cultures of *Staph. aureus* and other pathogens were made from the faeces (and gastric aspirates if a tube was in place), and the sensitivity to antibiotic drugs was determined for all strains isolated.

Typical Cases

Case 11.—This reasonably fit man of 71 years had a Billroth I partial gastrectomy carried out for a chronic duodenal ulcer. Penicillin and streptomycin were given post-operatively. Two days after the operation he developed a profuse watery diarrhoea accompanied by severe systemic upset, fever, and tachycardia. The diarrhoea, with tympanites, persisted for nine days but eventually cleared up. *Staph. aureus* was isolated from the faeces. Treatment was by massive intravenous replacement of the lost fluid, pil. codein., and chlortetracycline, to which the staphylococcus was sensitive. Though this was one of the most severe cases of post-operative diarrhoea the patient recovered.

Case 13.—This fit man, aged 63, had a transthoracic repair and vagotomy for a large intrathoracic stomach. Penicillin and streptomycin were given prophylactically and his condition was satisfactory until the second post-operative day, when his pulse rose to 130 a minute with a fever of 101° F. (38.3° C.). It was thought that he had a pulmonary infection, and oxytetracycline was given. The next day he began to pass melaenic stools and collapsed. He was resuscitated by blood transfusion and laparotomy was then performed. There was marked congestion of the splanchnic veins and

The squares represent the 31 individual cases and the letters in them the seven wards involved. No phage-typing of the strains of *Staph. aureus* was done during the years 1953-4. See also Table II.

the small bowel was purplish in colour. No bleeding-point was found in the stomach or duodenum. He died the same evening. At necropsy was seen the typical appearance of pseudomembranous enterocolitis, all the large and small bowel being affected. There was, in addition, a large chronic gastric ulcer which could have been the source of bleeding. A penicillin-resistant *Staph. aureus* was isolated from the intestinal contents at necropsy.

Case 14.—This man, aged 53, had had a nephrectomy for renal tuberculosis 20 years previously, but was otherwise fit. He was admitted to hospital on February 24, 1955, and an elective Billroth I partial gastrectomy was performed for a chronic duodenal ulcer. The operation and the patient's early progress were straightforward until the evening of the second day, when some abdominal distension was noticed. The pulse rate was 100 all day, the temperature 99–100° F. (37.2–37.8° C.). Early on the third day he developed a profuse offensive watery diarrhoea, appeared very ill, and showed a mild degree of peripheral circulatory failure. A provisional diagnosis of staphylococcal enteritis was made and treatment with intravenous fluids, erythromycin, 300 mg. six-hourly, and oral yoghurt four-hourly was started. He had been fed by jejunal tube for the first 48 hours after operation and had been given penicillin and streptomycin during that time. These measures were discontinued. On this regime his condition improved dramatically and the diarrhoea ceased after four days. No obvious membrane was ever found in the stools, but there were numerous suspicious shreds in most specimens. *Staph. aureus*, resistant to streptomycin, oxytetracycline, and penicillin was found in the faeces and in the nose.

Case 23.—This healthy man, aged 30, was struck by a car and received a moderately severe head injury and dislocations of the left acromioclavicular and knee joints. He was transferred to hospital three days later because of deepening coma, the chief cause for which seemed to be a severe bronchopneumonia with a temperature of 104° F. (40° C.). Nasal swabs and tracheal aspirate showed a *Staph. aureus* sensitive only to erythromycin. He had already been treated with chlortetracycline. Oxytetracycline and chloramphenicol improved his chest condition, but a week later he developed a very severe watery diarrhoea and *Staph. aureus* was grown from the stools. Erythromycin was then given with excellent results and he made a complete recovery.

Treatment

Antibiotic therapy in current use was discontinued. Fluid loss was replaced by intravenous infusions guided by daily biochemical estimations. One patient who survived produced over 47 pints (26.7 litres) of fluid faeces in 12 days, and was given in that time 141 pints (80 litres) of intravenous fluid. If the patient was seriously ill and had not previously received erythromycin, this drug was given (300 mg. six-hourly) by stomach tube without waiting for the bacteriological report. The patient was nursed in an isolation ward in order to minimize the spread of erythromycin-resistant staphylococci. This is extremely important, because Lepper (1953) reported that five months after the introduction of erythromycin into his hospital the nasal carrier rate of *Staph. aureus* resistant to erythromycin rose to 75%.

To several patients yoghurt, which contains lactobacilli, was given in the hope of replacing the pathogenic bacteria (Lancet, 1954a). Rettger and Cheplin (1921) showed that it was possible to create and maintain a lactobacillary intestinal flora in normal subjects by strenuous efforts at feeding cultures of lactobacilli and large amounts of lactose. Although from one patient given yoghurt a lactobacillus was cultured from the stools (Case 20) no evidence of the value of this treatment in staphylococcal diarrhoea was obtained.

Epidemiology

Staph. aureus was isolated from the diarrhoeic stools of 20 of the 31 patients in the present series. Six of the

remaining 11 were not investigated bacteriologically; from the stools of the other five no pathogenic bacteria were isolated (Table II). It should be noted that nine of these cases occurred before the special culture methods for faecal *Staph. aureus* were being used. Since then *Staph. aureus* has been isolated from the stools of 17 out of 19 cases of diarrhoea in surgical patients in this hospital. (It is noteworthy that in any given patient it may not be possible to isolate *Staph. aureus* from every specimen of faeces.) In every case antibiotic therapy had preceded the diarrhoea and in every case the patient's faecal *Staph. aureus* was resistant to the antibiotic he had received. Penicillin and streptomycin were given in 14 cases; penicillin or penicillin and sulphonamides in 10; streptomycin and sulphonamides in one; penicillin, streptomycin, and oxytetracycline in two; penicillin and chlortetracycline in two; penicillin, streptomycin, and chloramphenicol in one; and erythromycin and sulphonamides in one. The usual doses were: penicillin 500,000 units b.d. intramuscularly; streptomycin 0.5 g. b.d. intramuscularly; chlortetracycline, oxytetracycline, and chloramphenicol 250 mg. six-hourly orally.

Of our 31 cases, 17 occurred in ward B and 29 fell into one of two outbreaks. The first outbreak, comprising 10 cases (nine of which were in ward B), occurred in the period April to July, 1954; the second outbreak, comprising 19 cases (eight of which were in ward B), occurred in the period February to July, 1955. It was during the latter outbreak that a more comprehensive epidemiological picture was obtained.

Of the 19 cases in the second outbreak, seven gave *Staph. aureus* of phage type 6/47, three type 7/47/54, two type 77, one each of types 7/47 and 54, and four were not typed. From one case *Staph. aureus* was not isolated. Seven of these 18 strains were resistant to penicillin, streptomycin, chlortetracycline, and oxytetracycline, three in addition being resistant to erythromycin and three to chloramphenicol. Of the remaining five only one was sensitive to penicillin (Table II).

The staff of ward B were swabbed during the second outbreak and *Staph. aureus* type 6/47 with a typical pattern of resistance to antibiotics was found in the noses of the house-surgeon, ward sister, two nurses, and five unaffected patients. Type 54 was also found in the nose and on the hands of one nurse. The majority of the rest of the staff were carrying other strains of *Staph. aureus* in their noses, but none of these strains was isolated from the diarrhoeic stools.

The environment of the patients was also examined. In ward B *Staph. aureus* was isolated without difficulty on three occasions from dust, furniture, soft furnishings, and blankets.

On May 30, 1955, ward B was closed, cleaned, and repainted. On June 30 the ward was again tested and no *Staph. aureus* was isolated from some 40 swabs taken from every situation that might have harboured the organism. Patient No. 24, who had been transferred to an isolation hospital, was then readmitted and nursed in isolation in a side ward. However, in three days the immediate environment of the patient was heavily contaminated with *Staph. aureus* phage type 77 and the same organism was found in other situations in the ward.

In ward C patient No. 16, with a fractured femur, was infected with *Staph. aureus* phage type 6/47 and succumbed. The side ward in which he had been nursed was cleaned and fumigated with formalin. Patient No. 17, eight days later, after a craniotomy, was nursed in the same bed, developed staphylococcal diarrhoea from organisms of the same phage type, and also died.

From 6 of the 19 cases occurring in 1955, *Staph. aureus*, of the phage type corresponding to that grown from their faeces, was grown from the nose prior to the disease developing. In only 2 of the 13 nasal carriers tested was *Staph. aureus*, of the phage type corresponding to that grown from their faeces, grown from the gastric aspirate before the disease developed.

TABLE II.—Summary of 31 Cases of Diarrhoea

Case No.	Ward	Sex and Age	Diagnosis and/or Operation	Stomach Tube	Pre-diarrhoeal Chemo-therapy	Diarrhoea			Faecal <i>Staph. aureus</i> and Phage Type†	Resistance Pattern	Erythromycin Therapy	Outcome
						Day*	Severity	Duration				
1	B	M 38	Billroth I	+	P.	2	Severe	7	N/D	—	—	Recovered
2	S	M 68	Polya	—	P.	2	"	3	N/D	—	—	Died
3	B	M 57	"	+	P.S.	2	"	2	N/D	—	—	"
4	B	M 64	Billroth I	+	P.S.	2	"	8	N/D	—	—	"
5	B	M 67	"	+	P.S.	2	"	9	N/D	P.A.S.T.	—	"
6	B	M 60	Polya	+	P.	3	"	2	—	—	—	"
7	B	M 47	"	+	P.S.	5	"	10	—	—	—	Recovered
8	B	M 66	Billroth I	+	P.S.	3	Mod.	6	—	—	—	"
9	B	M 65	Prostatectomy	+	P.S.	2	Severe	3	+	—	—	Died
10	B	M 47	Billroth I	+	P.S.	2	Mod.	11	N/D	—	—	Recovered
11	B	M 71	"	+	P.S.	2	Severe	9	+	—	—	"
12	Mb	M 62	"	+	P.	3	"	2	N/D	—	—	Died
13	B	M 63	Repair of hiatus hernia	+	P.S.T.	3	"	2	+	P.	—	"
14	B	M 53	Billroth I	+	P.S.T.	3	"	4	+	P.S.T.	+	Recovered
15	V	F 66	S.P. pin femur	—	S.Sul.	13	"	3	+	P.A.S.T.C.	—	Died
16	C	M 85	"	—	P.S.	11	"	1	+	P.A.S.T.C.	+	"
17	C	M 81	G.S.W. head. Craniotomy	+	P.Sul.	5	"	1	+	P.A.S.T.	—	"
18	E	M 63	Laryngectomy	+	P.S.	14	Mod.	1	+	P.A.S.T.	—	Recovered
19	B	M 81	Prostatectomy	—	P.S.	2	"	12	+	Sensitive	+	"
20	B	M 72	Partial ilectomy	+	P.Sul.	6	"	20	+	P.A.S.T.	+	"
21	M	M 68	Polya	+	P.Sul.	1	Severe	3	+	P.A.S.T.	+	Died
22	C	M 67	Extradural haematoma. Craniotomy	+	P.S.T.	2	"	1	+	P.A.S.T.	+	"
23	C	M 30	Multiple injuries	+	P.Sul.	8	Mod.	1	+	P.A.S.T.C.	+	Recovered
24	B	M 57	Excision of papilloma of bladder	—	E.Sul.	1	"	3	+	P.A.S.T.E.	—	"
25	B	M 29	Billroth I	+	P.S.C.	3	Severe	14	+	P.A.S.T.E.	+	"
26	E	F 78	Laryngectomy	+	P.S.	12	Mod.	5	+	P.A.S.T.E.	—	"
27	E	F 71	Carcinoma maxillary antrum	—	P.	15	Severe	5	+	P.S.	+	"
28	L.M.	F 6	Rheumatic fever	—	P.A.	12	"	10	+	P.A.S.T.	—	"
29	L	F 46	Status asthmaticus	—	P.A.	13	Mod.	2	+	P.A.S.T.	—	"
30	B	M 71	Perforated ileum	+	P.S.	4	Severe	7	—	—	—	Died
31	S	F 78	Abdominal pain	—	P.Sul.	4	Mod.	3	+	P.A.T.	—	Recovered

P.=penicillin. S.=streptomycin. C.=chloramphenicol. A.=aureomycin (chlortetracycline). T.=terramycin (oxytetracycline). E.=erythromycin. Sul.=sulphonamides.

* Number of days either after operation or after commencement of antibiotic treatment that diarrhoea began.

† N/D=not done—i.e., not cultured. The phage type where known is given in parentheses.

Aetiology

The present series of cases points to *Staph. aureus* being the chief cause of post-operative diarrhoea in this hospital; it was isolated from the faeces of 20 of the 31 cases. Of these cases 17 were consecutive. Six cases, four of them fatal, were not investigated bacteriologically (Table II).

The arguments brought against *Staph. aureus* as the aetiological agent are as follows: (1) the presence of *Staph. aureus* is not significant of disease, as it is found in 17% of normal adult stools (Brodie *et al.*, 1956); (2) the staphylococci become significant only after the patient has been weakened already by some other initial cause of the diarrhoea; and (3) the resistance of the *Staph. aureus* to the antibiotics in use is not in itself necessarily significant, since its very survival implies resistance.

However, in three severe and three moderately severe cases in this series erythromycin seemed to stop the diarrhoea and cleared the faeces of *Staph. aureus*. This was also the experience of Dearing and Heilman (1953) in 21 of their cases. In three of our cases erythromycin proved ineffective, but two were by that time moribund. The successful use of erythromycin is therefore strong evidence for *Staph. aureus* as the cause of the diarrhoea.

In a given patient it may not be possible to isolate *Staph. aureus* from every specimen of faeces. For example, in one of the worst cases of the series (No. 25) *Staph. aureus* was not isolated from 4 of the 11 specimens of faeces cultured. There may even be cases where, although the *Staph. aureus* is not isolated, it is nevertheless the cause of the condition. Similar difficulty is sometimes experienced in isolating *Salmonella* or *Shigella* organisms from infected faeces.

The relationship between staphylococcal diarrhoea and pseudomembranous enterocolitis is not clear. Penner and Bernheim (1939) and Penner and Druckermann (1948) suggested that the pseudomembrane was caused by submucosal vasospasm resulting from post-operative shock. However, it must be stressed that many of their cases, and those of Pettet *et al.* (1954), did not have diarrhoea. Shock and peritonitis were often present, and in many cases occurred before the advent of antibiotics. The role of bacteria was not thought to be important. Moon's (1938) observation may be relevant here; he noted bloody mucous

diarrhoea with congested oedematous bowel mucosa after severe experimental shock in animals. Possibly some of the cases of necrotizing haemorrhagic jejunitis described by Fick and Wolken (1949) are similar to these animal cases, for profound shock and similar intestinal changes were reported. In addition they found *Clostridium welchii* in all cases. However, in this present series severe staphylococcal diarrhoea occurred in patients who were not previously shocked.

Pseudomembranous enterocolitis has also been described in other conditions—for example, diphtheria and poisoning with heavy metals (Lancet, 1954b). Many fatal cases of diarrhoea following antibiotic therapy and showing pseudomembranous lesions at post-mortem examination have been attributed to staphylococcal infections (Terplan *et al.*, 1953; Wakefield and Sommers, 1953; Dearing and Heilman, 1953). It is probable that formation of pseudomembrane is a non-specific reaction of the body to a variety of noxious and exhausting stimuli, staphylococcal diarrhoea being one of them. However, we believe that *Staph. aureus* is likely to be incriminated more often if special cultural methods are used in investigating cases of diarrhoea following antibiotic therapy.

At the 14 post-mortem examinations which we made in this series a macroscopic pseudomembrane was found lining the intestines in two cases, macroscopic inflammatory changes without pseudomembrane formation in four, and of the other eight, although inflammatory changes had occurred in the intestines, autolysis prevented histological examination in these. An excellent account of the typical pseudomembranous lesions is given by Dawson-Edwards and Morrissey (1955).

We believe that the indiscriminate prophylactic use of antibiotics, chiefly penicillin and streptomycin in combination, was the chief predisposing cause of the diarrhoea in the outbreak in the spring of 1954, when five deaths occurred in one ward. A strain of *Staph. aureus* resistant to the antibiotics in use at the time was presumably able to establish itself in the usually sterile small bowel and to dominate the complex and usually stable flora of the large bowel.

The portal of entry of this resistant organism may have been the mouth or nasopharynx, or any or all of the

processes of ingestion, inhalation, and intubation. The organism itself may have been exogenous or, less often, endogenous (from the nose of the patient himself). The prevalent use of antibiotics, it seems, substantially assisted these organisms to invade the intestines of their victims. In order to appreciate the changes in bacterial population which occur during these abnormal states, it is necessary to consider first the normal intestinal flora.

The normal flora of the human small and large intestine has not yet been fully investigated. Cushing and Livingood (1900) noted that patients with perforations of the lower bowel succumbed rapidly to peritonitis, but that those with perforations of the stomach or upper intestine often recovered well. This observation led them to investigate the bacterial flora of the gut. They took samples direct from the intestines of many animals and patients, and concluded that the upper and middle small intestines were virtually sterile, and that any bacteria present had been ingested. Kendall *et al.* (1927) confirmed these findings.

Bacteriological examination of the contents of the gut at necropsy has been shown to be unreliable because the whole of the small intestine is invaded by coliform bacteria shortly after death (Blacklock *et al.*, 1937).

Cregan and Hayward (1953), of Melbourne, by taking samples direct by syringe from the healthy gut at various levels during abdominal operation, concluded that the whole length of the small intestine contains only a transient flora, chiefly of Gram-positive species that are more commonly associated with the mouth than with the large intestine. However, of 14 specimens from the lower ileum, three contained *Bact. coli* type 1, and one *Bact. aerogenes* type 1—that is, large-bowel organisms. In a second similar series of investigations (Cregan *et al.*, 1953) on 22 patients with gastric lesions, with varying gastric acidity and gastric bacterial flora, they again found few bacteria in the small intestine. *Staph. aureus* was found twice. They concluded that the small intestine has an antibacterial mechanism independent of the gastric barrier.

We have been able to confirm, in a small series, the findings of Cregan and Hayward (1953), using their technique. Eleven aspirates from normal small intestines gave no growth, and five gave scanty growth of mouth organisms—for example, micrococci, *Streptococcus viridans*, and diphtheroids. One of the latter group of five gave a scanty growth of *Bact. coli* also, and gave another scanty growth of *Staph. aureus* sensitive to penicillin.

Colonic bacteria are, however, found in the small intestine in abnormal conditions. For example, *Bact. coli* type 1 (faecal) was cultured from the aspirated intestinal contents of three patients with strangulated or obstructed small bowel and also from one patient with symptomless jejunal diverticulosis.

Broadly speaking, then, the healthy human being has a small bowel which is largely free of bacteria and a large bowel which has an extremely large and complex flora. Although the flow of intestinal contents in the large bowel is unidirectional, organisms can invade it from the anal end, and the last few inches of the small bowel often contains organisms typical to the flora of the large bowel. Thus an exchange of organisms between the large and small bowels can occur, but presumably, under normal conditions, some mechanism maintains the difference in flora between the two.

The oral administration of antibiotics active against coliform organisms can bring about a profound though usually temporary reduction in the coliform flora of the faeces. This has been demonstrated by Zintel *et al.* (1947), Morton and Smith (1948), Hertfort and Standard (1948), Spaulding *et al.* (1949), and Metzger and Shapse (1950). It is difficult to see, however, how antibiotics can influence the susceptibility of the small bowel to infection. Possible reasons for the increased tendency to infection include: (1) a lowered general resistance of the patient due to operation or illness, or possibly due to toxic action of the antibiotic on the protoplasm of the host; (2) a lowering of

local resistance in the intestinal tract by interference with the natural defences—for example, by the removal of gastric acidity, by intestinal ileus, or possibly by the local action of antibiotics themselves on the tissues; (3) suppression of normal intestinal flora by antibiotics, enabling antibiotic-resistant organisms to flourish; (4) an increase in "virulence" of the organism stimulated by exposure to sublethal concentration of antibiotics, or of the changed metabolism of a resistant organism exposed to full concentration, enabling it to infect the small bowel (Garrod, 1951); and (5) the introduction of staphylococci direct into the bowel by means of a transnasal stomach tube.

An experiment illustrative of this increased tendency to infection is described by Freter (1955), who was able regularly to produce cholera in adult guinea-pigs, which are normally resistant to *Vibrio cholerae*, by preparing the animals with oral streptomycin.

Prevention of Staphylococcal Diarrhoea

The most important preventive measures in our view are the restriction of the use of antibiotics and reduction of the numbers of *Staph. aureus* present in the environment.

Since June, 1955, our use of antibiotics has greatly diminished (other routine therapeutic procedures not having been changed) and since then there has been no severe case of staphylococcal diarrhoea in ward B. That the use of the newer antibiotics is no guarantee against staphylococcal enterocolitis is seen from a case following neomycin therapy, quoted by Pettet *et al.* (1955). We feel that these drugs should be used only if specific indications exist, and then only with the patient in isolation. Antibiotics remain effective only as long as bacteria are sensitive to them.

During the period under review, owing to structural alterations there was no ward in the hospital in which septic surgical cases could be isolated. Isolation of such cases in the side wards of general wards was ineffective, *Staph. aureus* spreading rapidly from them to the whole ward area, particularly when it was being excreted in large numbers in the faeces. Thus it is obviously desirable to separate completely infected and "cold" surgical cases, and this should be done wherever possible.

Since October, 1955, the staff of ward B have had hands and noses swabbed every fortnight for the presence of *Staph. aureus*. This was done for the twofold purpose of research into the epidemiology of *Staph. aureus* in the ward and to try to eliminate heavy carriers. Local application of such antiseptics as chlorhexidine ("hibitane") may help to lessen the spread of organisms from these carriers.

The floor of ward B had been treated with spindle oil for some years before staphylococcal diarrhoea became a problem. This method of laying dust has been continued to the present time. Vacuum cleaners with air filters are used to remove any loose dust from the floor.

Since October, 1955, the problem of blankets has also been investigated. The findings will be published elsewhere, and it will suffice to say here that with the ordinary woollen blankets the method of cleaning described by Blowers and Wallace (1955) was adequate, provided that each patient was issued with a freshly laundered set of blankets on admission to the ward.

We feel that mattresses and pillows should also receive attention and that they should probably both be made of foam rubber with sealed air cells and be enclosed in rubber sheeting for easy swabbing with lysol after use by each patient.

The provision of more cubicles, single wards, and smaller nursing units generally will also militate against the spread of staphylococcal infection.

Gastro-intestinal aspiration may be a cause of spread of *Staph. aureus*, and all tubes must be boiled after being used for this purpose. A sterile syringe should be supplied for each aspiration, and any feeds given by this route should also be sterile and handled aseptically.

It will probably never be possible to eliminate *Staph. aureus* completely from patients and staff, but, by the measures outlined above, conditions under which resistant organisms can invade and flourish in post-operative and medical cases may be avoided.

Conclusions

Staphylococcal diarrhoea is a common and often fatal post-operative complication when antibiotics are being used prophylactically as a routine. In the Radcliffe Infirmary it became the major cause of death after elective partial gastrectomy. In medical patients, too, prolonged courses of antibiotics—for example, in chronic respiratory infections—are fraught with danger, especially when given in hospital. We submit, therefore, that the routine prophylactic use of these antibiotics is not justified. The relatively insoluble sulphonamides provide adequate preparation for colonic surgery, and it is unnecessary, and even dangerous, to use antibiotics in order to prepare the patient for operation either on the stomach or on the unobstructed small bowel.

However, if post-operative complications ensue, or if definite indications are present at operation (for example, a grossly soiled peritoneal cavity), the appropriate antibiotic should be used—at full strength and in short courses. Garrod (1955) outlined the principles for the correct use of antibiotics. Their abuse may lead to tragedy.

In conjunction with these measures, every effort must be made to reduce the numbers of *Staph. aureus* in the environment of the patient, not only to avoid surgical sepsis but to allow the safe and effective use of antibiotics when this is necessary.

Summary

Thirty-one cases of diarrhoea are described. Fourteen patients died, seven from one surgical ward. Fourteen cases occurred after partial gastrectomy.

Infection with *Staph. aureus* following antibiotic therapy was the chief cause of diarrhoea in this series.

The literature concerned with enterocolitis and staphylococcal diarrhoea is reviewed.

The epidemiology of two outbreaks of staphylococcal diarrhoea is described. Of the 31 cases, 29 occurred in two short periods in 1954 and 1955.

The aetiology of the condition is discussed and an account is given of an investigation into the bacteriology of the small bowel.

It is strongly recommended that antibiotics should not be used as a routine prophylaxis in abdominal surgery, but should be restricted to cases with special indication and then in isolation.

Measures to reduce the numbers of *Staph. aureus* in the ward environment are discussed.

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APPENDIX: METHOD OF BACTERIOLOGICAL EXAMINATION OF THE FAECES AND GASTRIC ASPIRATES

The faeces and aspirates were plated on to blood agar, one plate for aerobic and another for anaerobic incubation. They were also plated on to nutrient agar containing an added 7% of sodium chloride and inoculated into Robertson's cooked-meat medium containing an added 10% of sodium chloride. The latter was plated out after 24 hours' incubation at 37° C. on to blood agar (aerobic) and salt agar. Suspicious colonies after 24 and 48 hours' incubation were tested by the coagulase test and their sensitivity to antibiotics was determined.

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EXPERIENCE OF THE BURNS UNIT A REVIEW OF 520 CASES

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Colebrook (1950) advocated the establishment of special burns units where difficult and often long-term cases could be treated by trained teams and full use made of special facilities and equipment. In 1952 the Ministry of Health recommended the setting up of special centres in all regions. Burns have been treated at the Basingstoke Plastic Unit since 1940, but not until 1950 was it decided to form a burns unit within the hospital where these cases could be grouped together for the necessary specialized attention. The unit consists of 18 beds, divided into one six-bed ward, one four-bed ward, a five-bed nursery, and three single rooms. A major dressing-room includes a saline-bath unit; a minor dressing-room is available for ambulant and less severe cases, and skin-grafting operations are performed in one of the major operating-theatres normally set aside for that purpose.

Up to the end of 1955, 520 cases had been admitted to the unit, the admission rate gradually increasing up to the present level of 120–130 cases annually.

In Table I the cases are classified according to age groups, and also according to the percentage area of body surface burnt.

The majority of cases are referred direct from neighbouring practitioners or transferred within a few hours