The cells are secretory in type, yet differ morphologically from any ovarian cells known to us.

They have not been discovered in control cases.

They are found only in relatively small numbers and may be extremely difficult to detect. A single section through the ovary is insufficient, as a general rule, to demonstrate them.

The cells may possibly be carcinogenic, secreting a hormone which stimulates some of the cells of the endometrium of the body of the uterus and cervical canal to undergo malignant change. It is hoped that a further search for them will be made in other laboratories.

Our thanks are due to Mr. Bert Cambridge, of the Williamson Laboratory, for his great help, particularly in sorting out microscope slides from bomb debris, and to Mr. Norman K. Harrison, A.R.P.S., of the photographic department, who has offered every possible facility. Miss J. E. Colley has given secretarial help enthusiastically at unusual times of the day, and her knowledge of the literature has been most useful. Miss Joan Wheelwright has followed the work with great interest, instilling the optimism of youth at the most critical phase of the investigation.

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INFANTILE DIARRHOEA AND VOMITING

A CLINICAL AND BACTERIOLOGICAL INVESTIGATION

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This paper reports the results of a combined clinical and bacteriological investigation of infantile diarrhoea and vomiting, and includes a note by Dr. F. O. MacCallum on his virus investigations. In order that cases of infective origin should be presented for bacteriological study the clinical material was drawn in the main from outbreaks of diarrhoea and vomiting and from intercurrent attacks in hospital wards. In addition there were included two series of cases admitted consecutively to the gastro-enteritis units of a children's hospital and of an infectious diseases hospital. In these groups there was sometimes uncertainty

whether cases should be classified as "infective," "dietetic," or "secondary to parenteral infection."

The first outbreak occurred in the nurseries of a maternity unit, and a number of observers took part in its investigation. Subsequently the course of each outbreak and the clinical progress of each case were followed by one paediatrician. Material for bacteriological examination was dealt with at a centrally placed laboratory as soon as possible after collection. In this way a wide area of field investigation could conveniently be covered. The methods and results of the general bacteriological investigation of the cases are given in a later section.

The detailed study by Crowley *et al.* (1941) left little expectation that a bacterial agent might be determined by a quantitative comparison of the faecal flora of affected and unaffected babies. From the outset of the present investigation it had seemed that bacterial studies would need to follow the modern trend towards subdivision of genera by serological, biochemical, and phage-typing methods. Primary culture plates or subcultured strains were therefore sent to laboratories specially equipped for their detailed examination. Similarly, for virus studies, post-mortem tissues and other material were submitted to a laboratory engaged in virus research.

Previous investigators (Costello and Lind, 1939; Sakula, 1943; Sevvit, 1945; Light and Hodes, 1943; Buddingh and Dodd, 1944) have found a variety of bacterial and virus agents associated with infantile diarrhoea and vomiting. Bray (1945) isolated a particular serological type of *Bact. coli var. neapolitanum* from 42 out of 44 cases of infantile "summer diarrhoea." From an early stage of our investigation, work on a certain type of *Bact. coli* provided a promising line to pursue. Sera for its identification were prepared from the *Bact. coli* strains of infants suffering from epidemic diarrhoea of the newborn. The outbreak in which these cases occurred is described under Group A below. The strain is referred to throughout the paper as *Bact. coli* D 433. A description of the serological work, together with an account of the biochemical activities and other characters of the strain, are given in a later section.

The main purpose of this paper is to report the association of *Bact. coli* D 433 with certain groups of cases of infantile diarrhoea and vomiting and its absence in control groups of healthy and sick babies. Work on similar lines was published by Giles and Sangster in March, 1948. They reported the isolation of a serologically homogeneous strain of *Bact. coli* from over 90% of cases of primary infective gastro-enteritis admitted to hospital during an outbreak in the city of Aberdeen in 1947.

Cases of Infantile Diarrhoea and Vomiting

Clinical and bacteriological investigations were made on the following groups of infants suffering from diarrhoea and vomiting: one outbreak in a maternity unit (Group A); two outbreaks in a mothers and babies' hostel (Groups B and C); one outbreak in a residential nursery (Group D); intercurrent cases of diarrhoea and vomiting in a children's hospital (Group E); routine admissions to two gastro-enteritis units (Groups F and G); and endemic diarrhoea and vomiting in a residential nursery (Group H).

Group A

An outbreak of epidemic diarrhoea of the newborn occurred in February and March, 1947, in the 90-bed maternity unit of a Derbyshire hospital. In all, 20 babies contracted the disease and 14 of them died. At the onset of the illness the age of 19 of the babies was from 6 to 20 days, and that of one baby, retained for the treatment of minor sepsis, was 43 days. All the babies had received early glucose feeds.

Fifteen were fully bottle-fed and four partially breast-fed at the time when the illness began; one baby, apart from early glucose feeds, had been fully breast-fed from birth.

The outstanding symptom was diarrhoea with frequent watery green or yellow stools, preceded in some cases by a period of lethargy, reluctance to feed, and loss of weight. Vomiting also occurred in all cases. Parenteral infection was limited to one case of early bronchopneumonia, some subcutaneous abscesses, and a few minor skin infections. All the babies became dehydrated, most of them severely so.

Nine babies were available for examination during the active stage of the disease, and *Bact. coli* D 433 was isolated from all of them. Five had developed symptoms after discharge from the maternity unit and were readmitted for treatment in the emergency gastro-enteritis unit. The duration of illness at the time of swabbing varied from two to five days. In eight cases the strain was isolated from the rectal swabs and in one case from the upper respiratory tract only.

Group B

A severe and sudden outbreak of diarrhoea and vomiting occurred in a mothers and babies' hostel in Middlesex between Sept. 7 and 18, 1947. The hostel has accommodation for 14 mothers and their babies. They are usually admitted direct from maternity hospitals after the lying-in period. The babies are cared for by their mothers under the supervision of a small staff of nurses. Of the 12 babies living in the hostel at the time 11 developed the disease. The one baby who remained healthy was fully breast-fed. The others were all bottle-fed babies who had thrived since birth and were in good health at the start of the outbreak. Their age distribution was as follows: under 1 month, 3; 1 month, 3; 2 months, 2; 3 months, 2; 4 months, 1. One other baby, the 9-months-old non-resident child of the daily cleaner, also contracted diarrhoea and vomiting; he was taken into the kitchen each day for his midday meal.

The main symptoms were diarrhoea and vomiting, with dehydration. In several cases the onset was heralded by lethargy and reluctance to take feeds. The stools were green and watery, with mucus but no blood (except as a terminal event in one fatal case). Vomiting occurred in all but two cases; it was severe in four. There was no evidence of parenteral infection at the start of the illness, but secondary infection occurred in several cases during its course. Some degree of dehydration occurred in all the 12 cases; it was slight in two and severe in the remainder. Two cases may therefore be classed as mild and 10 as severe. Seven babies were given intravenous therapy, and these recovered. There were three deaths.

Rectal swabs were taken, at times varying from the second to the eighth day of illness, from 10 of the 12 sick babies in this outbreak. *Bact. coli* D 433 was present in all of them.

Group C

A second and less severe outbreak of diarrhoea and vomiting occurred in the same hostel eight months after that of Group B. Eight of the 17 babies exposed to infection developed the disease between May 13 and June 6, 1948. Seven of the eight were bottle-fed, and one, a mild case, was breast-fed. Seven of the babies were 1 month old and one was 2 months. The clinical features were similar to those of the previous outbreak, but with two exceptions the cases were comparatively mild.

The onset of illness was more insidious than in the previous outbreak, and in three cases was characterized by lethargy and reluctance to feed. The stools were green and mucoid—watery in the severe cases and relaxed in the mild ones. Vomiting occurred, but was never a severe feature. Three of the babies had no more than slight diarrhoea of a few days' duration, accompanied in one by loss of weight and in the others by a temporary interruption of weight gain. Ordinarily these very mild cases might not have been regarded as infective diarrhoea, but it was considered that they were part of the outbreak and therefore mild examples of the disease. The remaining five babies were more severely ill; two became dehydrated, and one of these died.

Bact. coli D 433 was isolated from the rectal swabs of the eight babies with diarrhoea and vomiting. The swabs were taken in five cases on the first, second, or third day of illness, and in the other three cases on the twelfth, fourteenth, and fifteenth days. Rectal swabs had been taken from three babies before the onset of symptoms. *Bact. coli* D 433 was isolated from one baby on seven occasions during the nine days preceding onset and from the other two babies on the preceding one and four days.

Group D

An investigation was made of an outbreak of diarrhoea and vomiting in a residential nursery in Hertfordshire. It has accommodation for 40 children, including a nursery unit for 12 babies. At the end of December, 1947, two babies died from diarrhoea and vomiting; these are not included in the series. Four others developed the disease between Feb. 13 and 15, 1948. They were all bottle-fed. Their ages were as follows: 1 month, 1; 2 months, 2; 3 months, 1. The symptoms were severe diarrhoea with green watery mucoid stools and vomiting. No parenteral infection was found at the start of the illness. All the babies became dehydrated. One baby died after an illness of eight days.

Bact. coli D 433 was present in the rectal swabs of the four cases. The swabs were taken from the fourth to the sixth day of the illness.

Group E

An investigation was made of 23 babies who developed intercurrent diarrhoea and vomiting while undergoing in-patient treatment in a children's hospital in London. The occurrence of seven cases in one ward during a period of two months, and of two or three cases in quick succession in three other wards, suggested the possibility that some, if not all, of them were of an infective type. The babies were all nursed in single-cot cells.

The period of study was from late January to early May, 1948. The babies were all bottle-fed or on mixed feeding. Their ages were as follows: under 3 months, 5; 3 to 5 months, 8; 6 to 8 months, 6; 9 to 11 months, 3; over 1 year, 1. They had been admitted to hospital for a variety of conditions—i.e., feeding difficulty, rumination, congenital defect, eczema, surgical operation, etc. The attack of diarrhoea and vomiting was characterized by the onset of watery diarrhoea, accompanied in most cases by vomiting. Parenteral infection at onset was found in only two cases. Seventeen of the babies became severely ill and 16 were given intravenous therapy; the other babies had moderate or mild attacks. Two of the babies died.

Bact. coli D 433 was present in the rectal swabs of 21 of the 23 cases of intercurrent diarrhoea and vomiting. The swabs were taken at times varying from the first to the ninth day of illness.

Group F

An investigation was made of 26 cases of diarrhoea and vomiting admitted consecutively between Feb. 4 and March 31, 1948, to the gastro-enteritis unit of a children's hospital in London. The unit consists of one double-cot and eight single-cot cells. Twelve of the 26 babies had developed intercurrent diarrhoea and vomiting while in other wards of the hospital or shortly after their discharge from them. These cases have already been included in Group E.

The other 14 infants with diarrhoea and vomiting were admitted from outside at the request of medical practitioners. They were all bottle-fed or on mixed feeding. Their ages were as follows: under 3 months, 5; 3 to 5 months, 3; 6 to 8 months, 4; over 1 year, 2. On admission nine of the babies had been ill for periods varying from one to six days and, five for three weeks or more; three had suppurative otitis media, one severe proctitis, and one a history of recent coryza. Seven were severely ill and were given intravenous therapy.

Bact. coli D 433 was present in the rectal swabs of six of the 14 cases; with few exceptions the swabs were taken on the day of admission to the unit. Of these six babies three had contracted diarrhoea and vomiting in other hospitals, two during outbreaks in residential nurseries, and one, a sporadic case, at home. The eight babies from whom the strain was not isolated had developed the disease at home.

Group G

An investigation was made of 24 cases of diarrhoea and vomiting admitted consecutively during May, 1948, to a gastro-enteritis unit, consisting of 48 single-cot cells, in a London infectious diseases hospital. From each baby a rectal swab was taken in the receiving-room before admission to the unit, and a nasopharyngeal and repeat rectal swab on the following day within the unit.

Two of the 24 babies were partially breast-fed; the remainder were either bottle-fed or on a mixed diet. Their ages were as follows: under 3 months, 7; 3 to 5 months, 11; 6 to 8 months, 3; 9 to 11 months, 3. Three had contracted the disease while in another hospital, four while in a residential nursery, and 17 at home. A history of contact with other cases of infantile diarrhoea and vomiting was found in nine instances.

The clinical picture and the severity varied considerably. Diarrhoea was the main symptom in all cases, and vomiting occurred in all but a few, although it was marked in only five. Parenteral infection was found on admission in eight babies (upper respiratory tract infection, 5; bronchopneumonia, 2; vaccination reaction, 1). On admission 17 cases were classified as mild and seven as severe; in the latter group six were sufficiently dehydrated to need intravenous therapy. Seventeen made uneventful recoveries, four (one of whom died) had severe relapses, and three developed secondary parenteral infections (bronchopneumonia, 2; skin sepsis, 1).

Twenty-one of the 24 babies were admitted during the first week of the disease, two in the second week, and one, with a relapse and pneumonia, in the seventh week. *Bact. coli* D 433 was present on admission in three of the seven severe cases and in two of the 17 mild ones. There were no obvious clinical features to distinguish those cases in which the strain was found. Two of the five babies in whom *Bact. coli* D 433 was present had contracted diarrhoea and vomiting while undergoing treatment in another hospital; the other three were admitted direct from home.

Group H

A mild type of endemic infantile diarrhoea and vomiting was investigated in a large residential nursery in London. Accommodation is provided for 120 children under 3 years of age, including about 40 bottle-fed or breast-fed babies. There is a large turnover of children, with frequent admissions and discharges. On arrival some of the babies are in poor physical condition and are under weight. Rises in incidence of the endemic diarrhoea and vomiting occur from time to time. A period of comparative freedom from the disease was followed by an increase in the number of cases during March and April, 1948.

Investigations were made of 14 cases occurring consecutively during this time. The babies affected were all either bottle-fed or on mixed feeding. Their ages were as follows: under 3 months, 8; 3 to 5 months, 3; 6 to 8 months, 1; 9 to 11 months, 1; over 1 year, 1. Diarrhoea and vomiting, usually of insidious onset, were the main symptoms. Parenteral infections at this stage were found in only two of the babies. Eight showed clinical evidence of dehydration, but only three were severely ill. There were no deaths.

Rectal swabs were taken from the 14 babies at times varying from the first to the sixth day of illness. No *Bact. coli* D 433 was isolated from them.

Control Groups of Babies

Rectal swabs were taken from a control series of 208 babies (Groups K and L). Their ages were as follows: under 3 months, 122 (including 79 under 1 month); 3 to 5 months, 42; 6 to 8 months, 35; 9 to 11 months, 9. Seventy-seven were breast-fed, 43 partially breast-fed, and 88 either bottle-fed or on mixed feeding. Those who had received no more supplementary feeding than water or glucose feeds during their early days have been included in the breast-fed group.

Group K: Healthy Babies.—One hundred and seventy-five healthy babies were examined during the period February–June, 1948. Sixty-seven of them were attending infant-welfare clinics in North and South London, 29 were in residential nurseries in North London and in Hertfordshire, 10 were attending clinics for congenital defects in Central London, and 69 were in the newborn babies' nurseries of three maternity hospitals in East and North London and in Middlesex. No *Bact. coli* D 433 was isolated from the rectal swabs of these 175 babies. After an interval of at least two weeks an inquiry was made about the progress of each baby. Thirteen of them could not be traced. None of the other 162 had developed diarrhoea and vomiting, but it was reported that six neonatal babies had had mild digestive disturbances with relaxed stools.

Group L: Sick Babies.—Thirty-three sick babies were swabbed in the receiving-room of a children's hospital in London immediately before their admission for conditions other than diarrhoea and vomiting. Seventeen of them were examined in May and June, 1948, and 16 in October and November, 1948. No *Bact. coli* D 433 was isolated from their rectal swabs. The clinical progress of each baby was followed for a fortnight after admission; none of them developed diarrhoea and vomiting during this time, but five of them had some relaxed stools while in hospital.

Incidence of *Bact. coli* D 433

The accompanying Table shows that *Bact. coli* D 433 was present in all the 31 cases of infective diarrhoea and vomiting which were swabbed in four outbreaks of the disease

Table showing Incidence of *Bact. coli* D 433 in Cases of Diarrhoea and Vomiting and in Control Groups of Babies

Group	Place	Description of Group	No. of Babies Swabbed	<i>Bact. coli</i> D 433	
				No. of Babies Positive	Percentage of Babies Positive
A	Maternity unit	Epidemic diarrhoea of the newborn. 20 cases. 14 deaths	9	9	100
B	Mothers and babies' hostel	Severe outbreak. 12 cases. 3 deaths	10	10	100
C	Mothers and babies' hostel	Second and less severe outbreak in same hostel as Group B. 8 cases. 1 death	8	8	100
D	Residential nursery	Severe outbreak. 4 cases. 1 death	4	4	100
E	Children's hospital	Intercurrent cases among sick babies. 17 severe and 6 moderate or mild cases. 2 deaths	23	21	91
F	Gastro-enteritis unit 1 (children's hospital)	Routine admissions. 7 severe and 7 moderate or mild cases. No deaths	14	6	43
G	Gastro-enteritis unit 2 (infectious diseases hospital)	Routine admissions. 7 severe and 17 mild cases. 1 death	24	5	21
H	Residential nursery	Endemic diarrhoea and vomiting. 3 severe and 11 mild cases. No deaths	14	0	0
K	Clinics, maternity units, and residential nurseries	Healthy babies	175	0	0
L	Receiving-room of children's hospital	Sick babies on admission for conditions other than diarrhoea and vomiting	33	0	0

(Groups A–D) and in 21 out of 23 intercurrent cases in a children's hospital (Group E). The strain was not, on the other hand, isolated from any of the 14 cases of endemic diarrhoea and vomiting in a large residential nursery (Group H). *Bact. coli* D 433 was present in six of the 14 cases admitted direct to gastro-enteritis unit 1 (Group F), but was found in only five of the 24 cases admitted to gastro-enteritis unit 2 (Group G). It was not isolated from any babies in the control group, which consisted of 175 healthy babies and of 33 sick babies suffering from conditions other than diarrhoea and vomiting.

The great majority of the babies from whom *Bact. coli* D 433 was isolated had severe attacks of diarrhoea and

vomiting, with enough dehydration to need intravenous therapy. Some of the cases in which it was found were, however, mild examples of the disease.

An analysis of the age distribution of the 63 babies in whom *Bact. coli* D 433 was present gave the following results: under 3 months, 33; 3 to 5 months, 15; 6 to 8 months, 11; 9 to 11 months, 4. The first age group included 13 babies in the neonatal period, eight of whom were involved in the outbreak of epidemic diarrhoea of the newborn (Group A). The ages of the babies in the outbreak of Group B were of interest in that they ranged from 25 days to 9 months. The limits of age, taking the whole series of cases showing *Bact. coli* D 433, was 10 days for the youngest baby and 11 months for the oldest.

Further Observations on Cases

1. *Necropsies*.—Post-mortem examinations were carried out on 13 babies of Groups A-E. The seven neonatal babies all showed hyperaemia of the intestines, particularly of the small intestine; in all but one case there was some enlargement of the mesenteric glands. Two small membranous lesions of the gastric mucosa were found in one of these seven babies, and a few large superficial erosions of the small intestine in another. No evidence of parenteral infection other than one case of early bronchopneumonia was found. Among the group of six older babies four showed some hyperaemia of the small and large intestines; the alimentary tract of the other two appeared normal. In five of these cases the liver showed fatty change. The only parenteral infections found were pneumonia and mastoiditis in one case. A sample of the contents of the small intestine was taken at necropsy from four of the neonatal and three of the older babies. *Bact. coli* D 433 was present in all these specimens. It was also present in the mastoid antra of the baby with mastoiditis. The interval from the onset of diarrhoea and vomiting to death varied from three to 27 days. One of the 13 dead babies had not been swabbed during life.

2. *Nasopharyngeal Swabs*.—Nasopharyngeal as well as rectal swabs were taken from 88 of the babies suffering from diarrhoea and vomiting. *Bact. coli* D 433 was isolated from the nasopharyngeal swabs in 12 cases; 11 of these yielded the strain in the rectal swabs also. Five of these 12 were suffering from epidemic diarrhoea of the newborn (Group A).

3. *Chemotherapy*.—Sixteen babies were on courses of sulphonamides (sulphadiazine, sulphamezathine, sulphasuxidine, or phthalyl sulphathiazole) and three on penicillin treatment when *Bact. coli* D 433 was isolated from their rectal swabs.

4. *Infant Feeding*.—An analysis was made of the feeding of those babies from whom *Bact. coli* D 433 had been isolated. It was found that on the day of swabbing and during the previous few days they had received a variety of dried-milk preparations to which had been added sucrose, glucose, lactose, or dextrimaltose. Expressed breast milk or diluted Hartmann's fluid had been given to a few of them. Two of the babies were fully breast-fed and three partially breast-fed.

5. Later Swabbing of Babies with Diarrhoea and Vomiting

(a) *Clinical Progress and Bact. coli. D 433*.—In gastro-enteritis unit 1 a study was made of the association between the clinical progress of the cases and the finding of *Bact. coli* D 433. From the 20 babies concerned, rectal swabs were taken on admission and on each subsequent Monday from early February to the end of March, 1948. Eight

of the babies were negative to *Bact. coli* D 433 on admission and six of these became positive during their illness. The first positive swab was discovered at times varying from the 10th to the 30th day after admission. The finding of *Bact. coli* D 433 was in one case associated with a severe exacerbation of diarrhoea and in three others with mild relapses. Of 12 babies who were positive to *Bact. coli* D 433 on admission nine became negative during their stay in the unit. The stools of three had settled by this time, but those of the other six were still relaxed. The first negative swab occurred at times varying from the ninth to the 34th day of illness.

(b) *Re-examination of Cases in Groups A-D*.—Eighteen other babies (Groups A-D) from whom *Bact. coli* D 433 had been isolated in the first swab were re-examined during the course of their illness. It was not possible to correlate exactly the clinical progress of the cases with the finding of *Bact. coli* D 433. It was observed, however, that in some cases loose stools continued after the rectal swabs had become negative, and that in others the stools had settled while the result was still positive.

(c) *Clinical Relapses*.—Four babies admitted to gastro-enteritis unit 2 during April and May, 1948, had at first mild or moderate attacks of diarrhoea and vomiting, accompanied in one case by bronchopneumonia. While in hospital they had relapses of their diarrhoea and vomiting, during which they all became dehydrated. Three were given intravenous therapy and one of them died. *Bact. coli* D 433 was not isolated from their rectal swabs during the initial attacks, but was present in all four during their relapses.

6. *Cases Other than Diarrhoea and Vomiting*.—During the course of the investigation 14 babies admitted to the gastro-enteritis units were found to have illnesses other than diarrhoea and vomiting. No *Bact. coli* D 433 was isolated from their rectal swabs.

7. *Other Outbreaks of Diarrhoea and Vomiting*.—*Bact. coli* D 433 was present in rectal swabs or stools received from a limited number of cases of diarrhoea and vomiting which occurred in other outbreaks during 1948. The residential nurseries in which they arose were situated in three counties. The results of these examinations, taken together with those listed in the Table, show a distribution of *Bact. coli* D 433 over a wide area. In all, it was isolated from cases of diarrhoea and vomiting in Derbyshire, Middlesex, Hertfordshire, Berkshire, Leicestershire, Sussex, and London.

Adult and Baby Contacts

A number of adult and baby contacts of infective diarrhoea and vomiting were examined for the presence of *Bact. coli* D 433 in their faeces or rectal swabs. Some individuals were direct contacts and others were indirect contacts exposed only to mediate infection or to possible carriers of the infecting agent.

Adult Contacts.—Faeces (or rectal swabs) were obtained from 84 adult contacts of infantile diarrhoea and vomiting. Specimens were taken, usually once only from each person, either during or shortly after an outbreak of the disease. Four of the contacts reported diarrhoeal attacks during the course of the investigation of Groups A, B, and H. No *Bact. coli* D 433 was found in their specimens, but in two instances the diarrhoea was not reported until recovery was complete. The other 80 adult contacts were associated with Groups B, C, D, and E, and none of them reported any attack of diarrhoea. *Bact. coli* D 433 was isolated from only four of these 80 persons—a daily cleaner whose baby had an attack of diarrhoea and vomiting, a laundress whose duties included the washing of soiled napkins, and two mothers, one of whom

was the mother of a case. On re-examination of the laundress and the cleaner six and 11 days later, respectively, no *Bact. coli* D 433 was found in their faeces.

Baby Contacts.—Rectal swabs were taken from 34 baby contacts of cases of diarrhoea and vomiting from which *Bact. coli* D 433 had been isolated. Eleven of the baby contacts were associated with the neonatal outbreak (Group A), nine with the outbreaks in the mothers and babies' hostel (Groups B and C), seven with that in a residential nursery (Group D), and seven with cases of intercurrent diarrhoea and vomiting in a hospital ward (Group E). The rectal swabs were obtained once only from 26 of the baby contacts and on several occasions from the other eight. Nine of the 34 baby contacts were positive to *Bact. coli* D 433. Three of these nine were associated with Group A, one with Group B, and five with Group C. Four of the nine babies were breast-fed, two partially breast-fed, and three bottle-fed. The remaining 25 were negative to *Bact. coli* D 433; seven of these were breast-fed, four were partially breast-fed, and 14 either bottle-fed or on mixed feeding. The progress of the 34 babies was followed for a further fortnight, and all remained free from diarrhoea and vomiting. Rectal swabs were also taken from 28 baby contacts of cases of endemic diarrhoea and vomiting (Group H) in a residential nursery. No *Bact. coli* D 433 had been isolated from the babies suffering from the disease and none was found among the baby contacts.

Subsequent Investigations in Nurseries and Hospital Wards

Rectal swabs were taken some months later from infant occupants of the nurseries and wards in which cases of diarrhoea and vomiting associated with *Bact. coli* D 433 had been investigated. The groups present at the later date consisted, with few exceptions, of different babies from those originally there.

(a) On three occasions examinations were made of groups of babies in the maternity nurseries in which epidemic diarrhoea of the newborn (Group A) had occurred in February–March, 1948. (1) Three months after the outbreak, in June, 1947, 20 neonatal babies in the nurseries were swabbed. No *Bact. coli* D 433 was isolated from them. Their subsequent progress was not followed. (2) Fourteen and 17 months after the outbreak, in May and August, 1948, two further groups of neonatal babies in these nurseries were examined. The groups consisted of 21 and 30 babies respectively, making a total of 51. The results were unexpected, for a strain of *Bact. coli* which was closely related antigenically to *Bact. coli* D 433 but which failed to produce gas in “sugars” was isolated from 21 of them. Particulars of this anaerogenic strain are given below. A clinical follow-up of the 51 babies was made 2½ weeks after each swabbing. Fourteen had suffered from mild transient diarrhoea; from 10 of these 14 the anaerogenic strain had been isolated. It was evident that the babies were free from severe epidemic diarrhoea of the newborn. It is uncertain whether any significance should be attached to these minor diarrhoeal attacks, which may possibly have been no more than digestive disturbances common in the neonatal period.

(b) The infant community of the mothers and babies' hostel were swabbed three months after the second outbreak of diarrhoea and vomiting (Group C) and that of the residential nursery in Hertfordshire three and six months after the outbreak (Group D). There had been no cases of diarrhoea and vomiting in the intervening months. The number of babies present was 13, 10, and 8 respectively. No *Bact. coli* D 433 was isolated from the rectal swabs. Progress reports for the ensuing fortnight showed that none of the babies developed diarrhoea and vomiting during this time.

(c) Thirty-one sick babies accommodated in wards where intercurrent diarrhoea and vomiting had occurred in January–May, 1948, were swabbed in August, 1948. The intervening period had been a quiescent one. No *Bact. coli* D 433 was isolated from the rectal swabs of these babies. Their clinical records for the following fortnight showed that one of them

had developed diarrhoea and vomiting during this time, and that the others had remained free from the disease.

Report of Virus Investigations by Dr. F. O. MacCallum

Attempts made to isolate a virus from material obtained from four fatal cases of diarrhoea and vomiting yielded negative results.

1. Post-mortem material was obtained from two babies, aged 9 and 17 days, who had died from epidemic diarrhoea of the newborn (Group A). They had been ill for three and five days respectively. Suspensions of brain, small intestine, and intestinal contents were filtered through collodion membranes which had an A.P.D. of 750 mμ. The filtrates were then inoculated into mice, cotton-rats, guinea-pigs, and young swine. Intracerebral passages were made, using 100 mice. The mice were killed after various intervals and brain suspensions injected into further mice. Eight passages were made, with negative results. Six intracerebral passages using 18 guinea-pigs were negative. Four intranasal passages, using 20 guinea-pigs, of the consolidated lung of an intracerebrally inoculated guinea-pig were negative. Four intracerebral passages using 20 cotton-rats were negative. The original swine were inoculated intranasally and orally, and then three passages were carried out with brain intracerebrally, with lung intranasally, and with intestine orally. Seventeen swine were used, and the results were negative.

2. Post-mortem material was obtained from twin babies, aged 3 months, who had died from diarrhoea and vomiting (Group B). They had been ill for 7 and 8 days. Mice were inoculated intracerebrally with brain, intranasally with lung, and orally with intestine. The material was unfiltered. Two passages using 16 mice gave negative results. Similar inoculations in four cotton-rats and four young rabbits gave negative results. Three passages in 18 guinea-pigs were negative.

General Bacteriological Investigations

The number of cases of infantile diarrhoea and vomiting listed in the Table is 106. Rectal swabs from 85 of these were examined on two to four occasions for non-lactose-fermenters and from 18 on one occasion only. Nasopharyngeal and rectal swabs from 88 of the 106 cases were submitted to general bacteriological examination.

Nasopharyngeal swabs consisted of curved swabs which were passed under the uvula to the posterior pharyngeal wall. They were inoculated on to horse-blood–digest-agar plates, which were incubated aerobically. In most cases rectal swabs were taken through a narrow glass anal cannula for their protection from skin contamination. Culture media used were horse-blood digest agar (one plate incubated aerobically and one anaerobically), horse-blood digest agar + 1 in 1,000 chloral hydrate for inhibition of swarming by *Proteus* (Gillespie, 1948), plain digest agar + 7.5% NaCl for isolation of staphylococci (Chapman, 1945), and desoxycholate-citrate medium (Hynes, 1942) or Difco “bacto S S” agar for isolation of non-lactose-fermenters.

No salmonellae or shigellae were isolated from the rectal swabs of the 103 cases examined for non-lactose-fermenters. Thirty-six of the 88 babies from whom nasopharyngeal and rectal swabs were taken had, prior to swabbing, either had diarrhoea and vomiting for more than seven days or had received chemotherapeutic drugs. They have therefore been excluded from the following analysis of the general bacteriological results. The swabs from the remaining 52 babies were taken in 18 cases on the first or second day

of illness, in 21 on the third or fourth day, in 11 on the fifth or sixth day, and in 2 on the seventh day. The distribution of organisms in the 52 nasopharyngeal swab cultures was as follows: alpha- and non-haemolytic streptococci, 48; *Staph. pyogenes*, 30; *Neisseria*, 23; *Bact. coli*, 18; diphtheroids, 7; *Haemophilus*, 5; pneumococcus, 5; yeasts, 3; aerobic spore-bearing bacillus, 1; *Chromobacterium*, 1; paracolon bacillus, 1. The distribution of organisms in the 52 rectal swabs was as follows: *Bact. coli*, 50; *Streptococcus*, 41; *Staph. pyogenes*, 16; *Proteus*, 16; *Lactobacillus*, 15; *Micrococcus*, 15; paracolon bacilli, 5; *Fusiformis*, 3; *Clostridium*, 2; yeasts, 2; aerobic spore-bearing bacillus, 1.

Bact. coli was present in abundance in 47 of the 52 rectal swabs. The detailed examination of the *Bact. coli* strains is described below. Organisms of the *Proteus* group were isolated from 16 of the 52 rectal swabs, but in abundance from only 11 cases. *Proteus* was not isolated from any of the babies with epidemic diarrhoea of the newborn (Group A) or from those with diarrhoea and vomiting in two other outbreaks (Groups B and C). It was, on the other hand, present in the rectal swabs of all the babies in Group D, but it was also present in the seven unaffected baby contacts in this outbreak.

Only seven of the 14 cases with endemic diarrhoea and vomiting (Group H) were suitable for inclusion in the general bacteriological analysis, and *Proteus* was grown from the rectal swabs of three of them; the organism was also found in 16 of the 28 baby contacts in the nursery. Paracolon bacilli were present in the rectal swabs of five of the 52 babies; three of these five were suffering from epidemic diarrhoea of the newborn. Paracolon bacilli were isolated from the nasopharyngeal swab of one of them. *Staph. pyogenes* (i.e., coagulase-positive staphylococci) was present in the nasopharyngeal swabs of 30 and in the rectal swabs of 16 babies; in 15 of the latter it was isolated from the nasopharyngeal swabs also.

Staph. pyogenes strains isolated from the cases of the first two outbreaks (Groups A and B) were examined for phage type by Dr. V. D. Allison. The distribution of the phage types in the nasopharyngeal swabs was type 7/47 (one baby), type 47 (one), type 52A (one), and type not found (five); in the rectal swabs it was type 7/47 (one), type 47 (one), type 52 (one), type 52A (one), and type not found (two). On account of the variety of phage types in the first two outbreaks, and of the low incidence and sparsity of *Staph. pyogenes* in the rectal swabs in general, phage typing was not continued. The phage types determined in the first two outbreaks were not those commonly found in staphylococcal food-poisoning outbreaks—i.e., type 6/47 and type 42D (Allison, 1949).

Gale (1944) found large numbers of Group D streptococci with an unusually high tyrosine decarboxylase activity in the stools of cases in certain outbreaks of neonatal diarrhoea. A detailed examination was therefore made by Dr. P. M. F. Shattock and Miss M. E. Sharpe of streptococci isolated from the babies with epidemic diarrhoea of the newborn. Group D streptococci in small numbers were isolated from the rectal swabs of only three of these babies. Nine strains derived during this outbreak from these rectal swabs and from the intestinal contents of two other babies after death, together with two strains from the upper respiratory tract, were examined. They were found to be: *Str. faecalis*, 3; *Str. faecalis* var. *liquefaciens*, 3; *Str. faecalis* var. *zymogenes*, 3; unclassified, 2. These strains were found to be of several serological types. Their tyrosine decarboxylase activity varied from a high figure to nil.

Scanty Group B streptococci were isolated from the rectal swabs of two other neonatal cases in this outbreak. *Clostridium* was found in only two of the 52 rectal swabs.

Thirty-four stools from cases of diarrhoea and vomiting were examined microscopically. Abundant bacteria were seen, varying numbers of epithelial cells, rarely more than a few leucocytes, and very occasionally a few red blood cells. No flagellate protozoa were observed. Stools from the 24 cases admitted to gastro-enteritis unit 2 (Group G) were examined for *Giardia lamblia*, each on two occasions, by Mr. L. G. C. Maslen, but none was found. The ether concentration method was used.

Blood was taken, at times varying from the second to the seventh day of illness, from the internal jugular vein of eight babies with *Bact. coli* D 433 in their rectal swabs. Six had severe and two moderate or mild attacks of diarrhoea and vomiting. Cultures were prepared in liquid digest broth and incubated aerobically, anaerobically, and under CO₂ at 37° C. for 14 days. With the exception of two contaminated anaerobic cultures, no growth was found.

In summarizing the general bacteriological results of the rectal swabs it may therefore be said that no recognized pathogen was isolated, that *Proteus* and *Staph. pyogenes* (of phage types other than those of food-poisoning staphylococci) were each present in about one-third of the cases, that *Clostridium* was rarely found, and that Group D streptococci were not conspicuous in the outbreak of epidemic diarrhoea of the newborn. *Bact. coli* was the most frequently occurring organism, and, with the exception of a profuse growth of *Lactobacillus*, *Proteus*, or *Streptococcus*, on some plates, it yielded the most abundant growth.

Serological and Other Investigations of *Bact. coli* Strains.

Lovell (1937), working on the types of *Bact. coli* isolated from diseased calves, identified his strains by the precipitin reaction. Bray (1945), using the agglutination reaction suitable for the identification of the somatic antigen, isolated a particular serological type of *Bact. coli* var. *neapolitanum* from cases of infantile "summer diarrhoea." Kauffmann and his collaborators, using agglutination tests, identified the O or somatic, the H or flagellar, and the K antigens of the *Bact. coli* group: the K antigen may be of the L type (surface) or A or B types (capsular or surface), which are distinguished by their susceptibility to heat treatment. These workers were able to establish a diagnostic coli antigenic schema of O groups, subdivided into types and classified by their O, H, and K antigens. Giles and Sangster (1948) used their techniques for the identification of a serologically homogeneous strain of *Bact. coli* from over 90% of their cases of gastro-enteritis. Detailed information regarding the serology of the coli group may be found in the review of the subject by Kauffmann (1947) and the monographs by Vahlne (1945) and by Knipschildt (1945).

The methods used by these Scandinavian workers have been followed for the examination of *Bact. coli* strains isolated in this investigation. The first strains of *Bact. coli* to be investigated were derived from the outbreak of epidemic diarrhoea of the newborn (Group A). Primary blood-agar plates were inoculated with nasal, nasopharyngeal, throat, and rectal swabs taken from nine babies in the active stage of the disease, two in the convalescent stage, 11 baby contacts, and four babies at first suspected of epidemic diarrhoea of the newborn but later found to have ailments other than this; the intestinal contents of four babies who died from epidemic diarrhoea of the newborn were taken at necropsy and similarly plated. Colonies suggestive of *Bact. coli* were picked from all those

plates on which they were found, the number picked depending on the number of colonial forms present. Each strain was then tested for its fermentation reactions on a variety of "sugars," the production of indole, urease, and H_2S , utilization of citrate, Voges-Proskauer and methyl red reactions, liquefaction of gelatin, gas production at $44^\circ C.$, and haemolysis (using the method described by Vahlne). In this way 178 strains of *Bact. coli* were isolated. The subsequent serological investigation of these strains will be described later.

For the preparation of sera, eight strains of *Bact. coli* isolated from active cases of epidemic diarrhoea of the newborn (Group A) were used. Six of these strains had been isolated from the rectal swabs of six babies, one from the nasopharynx of one of these babies, and one from a subcutaneous abscess of another of them. This abscess had formed at the site of a subcutaneous injection. These eight strains were chosen because in their biochemical reactions they showed some slight variation from one another and were representative of other strains found.

O sera were made in rabbits, using as antigen an overnight broth culture steamed for $2\frac{1}{2}$ hours. K sera were made, using a living culture which had grown overnight on a thick 0.1% glucose-agar plate, a suspension of about 500 millions per ml. in quarter-strength Ringer solution being employed as inoculum. O and K sera were made from each of the eight strains. One of the rectal strains was motile, and from this an H serum was made using a formalized overnight broth culture. Thus, a total of 17 sera were prepared. Cross-agglutination and reciprocal-agglutination absorption reactions were carried out between these 17 sera and the eight strains of *Bact. coli* used for their production. From the results obtained it was obvious that five of the strains were serologically identical; of these, three had been isolated from rectal swabs and the fourth and fifth from the nasopharynx and rectal swab respectively of another baby.

This serological type is referred to as *Bact. coli* D 433. It is non-motile, therefore O and K sera only were used for its identification. It was tested with *Bact. coli* sera kindly supplied by Dr. G. Vahlne, and was found to be different from any of the 25 O groups of the diagnostic coli antigenic schema of Kauffmann, Knipschildt, and Vahlne. The organism is not capsulated, so that the A antigen was not considered. The presence of an L antigen could not be demonstrated, but a B antigen may be present, though more work is needed for the proof of this point. Dr. F. Kauffmann in a personal communication states that he believes *Bact. coli* D 433 has a surface antigen of the B type and that both the O and the B antigens differ from those of other strains in the schema. The strain of *Bact. coli* isolated by Giles and Sangster (1948) was tested and found to be identical with *Bact. coli* D 433.

The titre of the *Bact. coli* D 433 O serum was 1 in 6,400 and of the *Bact. coli* D 433 K serum 1 in 800. It was considered that these titres were high enough to show any differences between *Bact. coli* D 433 and related serological types which might subsequently be investigated. All the 178 strains already isolated in connexion with the outbreak of epidemic diarrhoea of the newborn (Group A) were then tested against each of the 17 sera. The results suggested that *Bact. coli* D 433 might be related to the outbreak in that it was isolated from the nine active cases examined, from the four cases at necropsy, and from three of 11 contacts; it was not isolated from the two convalescent cases of the disease or from the four cases other than epidemic diarrhoea of the newborn.

The *Bact. coli* D 433 O and K sera, already prepared with strains from cases of epidemic diarrhoea of the newborn, were used for the subsequent identification of *Bact. coli* D 433 among the sick babies and contacts and controls of Groups B-L. Material from these babies was plated on blood-agar. From all plates on which "coliform" colonies appeared four discrete colonies were tested with *Bact. coli* D 433 K serum by the slide-agglutination method. One agglutinable colony was then taken from each "positive" plate and its characteristics investigated. Without serological tests it was not possible to identify colonies of *Bact. coli* D 433 either on blood agar or on desoxycholate-citrate-agar plates. If *Bact. coli* D 433 colonies were overgrown with *Proteus* they were sometimes found to be inagglutinable by the slide method. In this event it was usual to test discrete colonies on duplicate primary plates of blood agar + 1 in 1,000 chloral hydrate; if these were not available, colonies subcultured on to this medium from the primary blood-agar plates were tested.

In all, 133 cultures of *Bact. coli* D 433 were investigated; they were derived from clinical cases of diarrhoea and vomiting and their contacts. All the strains were non-motile. All fermented lactose, glucose, maltose, mannitol, and sorbitol, with the production of acid and gas, after overnight incubation at $37^\circ C.$ The fermentation of sucrose, salicin, and dulcitol was occasionally rather slower, but the majority of strains gave acid and gas in these "sugars" in four days. All strains were V.P. -, M.R. +, produced indole, failed to utilize citrate, gave acid and gas in MacConkey broth when grown at $44^\circ C.$, and failed to liquefy gelatin or to produce H_2S . The large majority of the strains when grown on 10% horse-blood-agar plates showed no ring of haemolysis round well-isolated colonies, though there was always haemolysis in the area of confluent growth. Each strain was subjected to the haemolysis test; only six strains gave a positive result. All strains were agglutinated to titre by *Bact. coli* D 433 K and O sera. Representative strains from each group of babies investigated were used for absorption tests and completely removed all agglutinins to the homologous strain.

We have already stated that an anaerogenic strain of *Bact. coli* was isolated from a number of newly born babies accommodated in the maternity nurseries where over a year before epidemic diarrhoea of the newborn had occurred. This strain produced acid but no gas in lactose, glucose, maltose, mannitol, and sorbitol, failed to ferment sucrose and dulcitol, and gave variable reactions in salicin. The other biochemical reactions were the same as those of *Bact. coli* D 433. The O and K antigens of the two strains were identical, but the anaerogenic strain possessed in addition an H antigen and in this respect differed from *Bact. coli* D 433.

Four motile aerogenic strains of *Bact. coli* having the O and K antigens of *Bact. coli* D 433 were isolated during the investigation. These strains were derived from the rectal swabs of four babies, two of whom had mild attacks of diarrhoea and vomiting and were included in Group E and Group H respectively. The other two were healthy babies. The first of these was included in Group K (healthy controls) and the second was among the neonatal babies swabbed in the maternity nursery where epidemic diarrhoea of the newborn had occurred 14 months previously; their progress reports for $2\frac{1}{2}$ weeks after swabbing showed that they remained free from diarrhoea and vomiting during this period. The biochemical reactions of these strains showed no constant difference from those of *Bact. coli* D 433, though two strains failed to ferment maltose in

24 hours but did so later. In view of their motility these strains have not been classed as *Bact. coli* D 433. It has not been possible to assess their significance, particularly as they have been so few in number.

Thirteen strains of *Bact. coli* isolated from calf scours were tested. The biochemical reactions of some strains were similar to those of *Bact. coli* D 433, but all the strains differed from it serologically.

Pathogenicity tests were carried out, using 18-hour broth cultures of *Bact. coli* strains, by intravenous and intraperitoneal inoculation, with and without mucin, of mice of various ages and by the intramuscular inoculation of guinea-pigs. One strain of *Bact. coli* D 433, two strains from calf scours, one strain from a subcutaneous abscess, and one strain from a healthy child were tested. All the strains were pathogenic to animals, but no marked difference in degree of pathogenicity could be detected between them.

Discussion

Among over a hundred cases of infantile diarrhoea and vomiting no recognized intestinal pathogen was detected and virus studies of four fatal cases yielded negative results. A serological type of *Bact. coli*, referred to as *Bact. coli* D 433, was first identified during an outbreak of epidemic diarrhoea of the newborn in a maternity unit. It was present in all of the nine babies available for examination during the active stage of the disease. The same serological type was subsequently isolated from all of 22 cases of diarrhoea and vomiting examined during two outbreaks in a mothers and babies' hostel and one outbreak in a residential nursery. The results thus showed a constant association between *Bact. coli* D 433 and cases of undoubted infective origin.

Clinically, the characteristic feature of the cases in these outbreaks was diarrhoea and vomiting, leading to dehydration. Parenteral infection at the onset was limited to one case of bronchopneumonia. The strain was also isolated from 21 (91%) out of 23 sick babies who developed diarrhoea and vomiting during in-patient treatment in a children's hospital. In this group only two of the babies showed any evidence of parenteral infection at the start of their attacks. The circumstances in this series suggested that some, if not all, of these intercurrent cases were of an infective type.

Lower association rates between clinical cases and *Bact. coli* D 433 were found among the routine admissions to two gastro-enteritis units. These units accept cases from a wide area on the recommendation of medical practitioners, and therefore admit babies with diarrhoea and vomiting of possibly varying aetiology. In the first unit, six (43%) of the 14 cases yielded the strain. The clinical history of five of these six babies suggested that the attacks were of an infective type. In the second and larger unit *Bact. coli* D 433 was found in only five (21%) of a series of 24 babies admitted with diarrhoea and vomiting. The strain was not detected among the 14 babies examined in a large residential nursery. Their attacks of diarrhoea and vomiting were insidious in onset, and 11 of them were mild in type. The series of cases was spread over a period of two months and appeared to be due to a rise in incidence of the diarrhoea and vomiting endemic in this nursery rather than to an outbreak of the disease: it differed, therefore, in this respect from the sharp outbreaks which were investigated among other infant communities. Among a control series of 208 babies *Bact. coli* D 433 was not found.

The majority of the babies in whom *Bact. coli* D 433 was present had severe attacks of diarrhoea and vomiting.

The relatively large number of severe cases associated with the strain may have been due, however, to the selection of this type of case for investigation. An unselected series of cases might have shown a different incidence of the strain in relation to severity. *Bact. coli* D 433 was in fact found in some mild examples of the disease such as those of the second outbreak in the mothers and babies' hostel.

The distribution of *Bact. coli* D 433 was not closely confined to one area or to one season of the year. The strain was found in counties as widely separated as Derbyshire and Sussex, and was isolated during all seasons from the winter of 1947 to the summer of 1948. It was not restricted to one age group among the cases, for the strain was present in babies ranging in age from 10 days to 11 months. It is interesting to note that *Bact. coli* D 433 was present both in young babies with epidemic diarrhoea of the newborn and in older babies with infective diarrhoea and vomiting.

Consideration was given to the possibility that *Bact. coli* D 433 may have owed its existence in the stools to some common factor in the feeding of those babies from whom it was isolated. An analysis of the feeds which were being given at the time of swabbing and during the previous few days showed, however, that the babies had received a variety of preparations and several types of added sugar. A small number were fully or partially breast-fed. Similarly, the administration of chemotherapeutic drugs could not be held responsible for the appearance of the strain, since 42 of the 63 sick babies from whom it was isolated had not received this form of treatment.

A diarrhoeal condition is evidently not essential for the existence of *Bact. coli* D 433; this was shown by the fact that the strain was isolated from a number of adult and baby contacts who remained free from intestinal disturbance. The possibility that the serological type may result from alimentary-tract conditions pertaining to all diarrhoeal states seems to be ruled out by the fact that it was not found in a number of babies with watery diarrhoea. More difficult to determine is whether the strain, present in small numbers and therefore passing undetected in the stools of the normal infant, may grow out freely under particular intestinal conditions associated with only certain forms of diarrhoea. Before reaching a decision on this matter a readier method than slide agglutination will be required for the detection of small numbers of *Bact. coli* D 433 on culture plates.

Relapses are a common occurrence during the course of diarrhoea and vomiting. Five babies were admitted to gastro-enteritis units with mild or moderate diarrhoea and vomiting. While under treatment they developed severe relapses with dehydration. *Bact. coli* D 433 was not isolated from them during their initial attacks, but it was found in all of them during their relapses. It seems possible that the relapses were in fact attacks of infective diarrhoea and vomiting acquired within the unit and superimposed on some milder primary condition.

In the later stages of the work a *Bact. coli* strain closely related antigenically to *Bact. coli* D 433 was isolated from babies in the maternity nurseries in which epidemic diarrhoea of the newborn had occurred more than one year before. It differed from *Bact. coli* D 433 in the possession of an H antigen and in producing no gas in "sugars." Some of the babies from whom it was isolated suffered from a mild and transient diarrhoea, but they were evidently free from diarrhoea of the severe epidemic type. Four aerogenic motile strains having the O and K antigens of *Bact. coli* D 433 were isolated from four older babies, two with

diarrhoea and vomiting and two healthy. The significance of these related strains of *Bact. coli* cannot as yet be assessed, but further work may bring an answer to this problem.

Another and more important problem is the possible status of *Bact. coli* D 433, when confirmed by biochemical and serological test, as a causative agent of infective diarrhoea and vomiting. Its close association with clinical cases in certain outbreaks of diarrhoea and vomiting and its absence from control groups of babies suggest that it may play some part in the genesis of the disease, but further work is necessary before any definite conclusion can be reached. Possible lines of research are animal transmission experiments, pathogenicity and toxicity tests, laboratory investigation of the strain for further distinguishing characteristics, closer correlation between the clinical findings and the detection of the strain, and studies of possible dual virus and *Bact. coli* causation.

Summary

A clinical and bacteriological investigation of infantile diarrhoea and vomiting was carried out. The clinical material was drawn from one outbreak of epidemic diarrhoea of the newborn (Group A), two outbreaks of diarrhoea and vomiting in a mothers and babies' hostel (Groups B and C), one outbreak in a residential nursery (Group D), intercurrent cases among sick babies in hospital (Group E), two series of admissions to gastro-enteritis units (Groups F and G), and endemic diarrhoea and vomiting in a residential nursery (Group H).

No recognized intestinal pathogen was isolated, and virus investigation of fatal cases yielded negative results.

Bact. coli sera, prepared from strains isolated from cases of Group A, led to the identification of a particular serological type, referred to as *Bact. coli* D 433. It was isolated from all nine cases examined during life in this outbreak.

The same sera were subsequently used for the identification of *Bact. coli* D 433 among the other groups of babies studied. It was isolated from all 22 cases (100%) of Groups B, C, and D, from 21 (91%) of the 23 cases in Group E, from 6 (43%) of the 14 cases in Group F, from only 5 (21%) of the 24 cases in Group G, and from none of the 14 cases in Group H.

Bact. coli D 433 was not isolated from any of the 208 babies of the control groups.

Five babies with mild or moderate diarrhoea and vomiting has severe relapses while in gastro-enteritis units. *Bact. coli* D 433 was not isolated from them during the initial attacks, but was present during the relapses.

Bact. coli D 433 was isolated from cases in seven counties and during all seasons of the year. The youngest baby in whom it was found was aged 10 days and the oldest 11 months.

Bact. coli D 433 was isolated from four of 84 adult contacts and from nine of 34 baby contacts examined in connexion with Groups A-E.

Bact. coli D 433 was not isolated from rectal swabs taken three to six months later from 82 infant occupants of nurseries and wards in which cases of diarrhoea and vomiting (Groups A-E) had been investigated. Fifty-one newborn babies, occupying the maternity nurseries in which epidemic diarrhoea of the newborn (Group A) had occurred, were swabbed more than a year after the outbreak. From 21 of them an anaerogenic motile *Bact. coli* strain was isolated which was closely related antigenically to *Bact. coli* D 433. Ten of these babies suffered from a mild diarrhoea the significance of which is at present undetermined.

Whether, the serological type of *Bact. coli* has any aetiological significance in diarrhoea and vomiting is undecided. Lines for further research on this matter are indicated in the discussion.

We wish to acknowledge our thanks and indebtedness to the following: Dr. R. Cruickshank and Professor A. A. Moncrieff for their encouragement and advice; the Medical Committee of the Hospital

for Sick Children, Great Ormond Street, London, for facilities for research in the wards and laboratories, and Dr. B. E. Schlesinger for his interest in the work; Dr. R. G. Cooke for facilities to make investigations in the Derby City Hospital; Dr. S. Dundon and Dr. R. E. Glennie for voluntary and invaluable service in the gastro-enteritis unit for neonatal diarrhoea; Mrs. W. S. Willett (working for the Public Health Laboratory Service) for the preparation of the *Bact. coli* sera and for much other bacteriological work during the early stages of the investigation; Dr. G. R. Osborn and Dr. M. Lécutier for permission to include their post-mortem findings; the medical officers of health of the areas in which investigations were made; the medical superintendents, medical officers, matrons, sisters, and nurses of the hospitals, nurseries, and welfare clinics concerned.

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WHAT IS SOCIAL MEDICINE?*

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It is usually assumed that the expression "social medicine" is of relatively recent origin. Dr. René Sand (1948) has shown, however, that it was used exactly 100 years ago by Dr. Jules Guérin, writing in the *Gazette Médicale de Paris*. The idea of social medicine therefore is certainly not new. The only new thing about it is the reawakening of thought which realizes that here is something of fundamental importance that has been forgotten in certain circles.

If, in the past, clinicians have forgotten the importance of the environment in determining disease, hygienists have perhaps been too limited in their outlook and interpretation. Social medicine attempts to link together clinical medicine and preventive medicine in the hope of benefit to both. It is my purpose to try to illustrate the existence of a common ground between the two.

If we are to understand fully the meaning of and need for social medicine it is necessary to trace briefly the history of medicine as a whole and its relation to other branches of human activity.

To the Greeks medicine meant the art of healing; it achieved importance because of the necessity for curing a sick person of disease. The emphasis was therefore on the treatment of disease, and little or nothing was known of aetiology. Preventive medicine was certainly studied by Hippocrates, and his writings are full of sound reasoning concerning the spread of epidemics. Preventive medicine, however, could make no real advance until the basic sciences of physiology and bacteriology had been developed. Throughout the Middle Ages no advancement was made in

*A paper read to the West of England Branch of the Society of Medical Officers of Health at Bristol on Nov. 20, 1948.