mechanism of producing ventricular block, but it is certain that they affected the circulation of the cerebrospinal fluid and the diffusion of streptomycin injected subthecally.

Comment

We cannot close this paper without remarking on the relative frequency of infection by intestinal organisms in infants. In many circumstances saprophytic organisms in the digestive tract of the newborn become pathogenic and produce bacteriaemia, septicaemia, and meningitis. It is significant that in 18 months we have been able to observe in the Clinique Médicale des Enfants 41 cases of this type of infection, 25 of which developed meningitis. The signs of these infections are often obscure at first sight, and many of the cases can be discovered only by the careful examination of infants suffering from toxaemia and subacute fever with alimentary disturbances.

A search must be made for the organism in blood, marrow, stools, urine, pus from the ear, cerebrospinal fluid, nasopharyngeal secretions, and pus from any metastatic suppuration in the skin. Repeated blood culture is extremely important. The occurrence during a gastro-intestinal illness of an inexplicable alteration in the patient's general condition or, as we have shown, a polymorphonuclear leucocytosis, is a diagnostic sign of great importance. The possibility of meningeal infection must always be considered, and lumbar puncture, repeated if necessary, must be done as a routine measure. At the same time it must be remembered that the cerebrospinal fluid may be normal or be little changed.

Summary

An account is given of 41 cases of infection in the infant by intestinal organisms, seen over a period of 18 months. Of these cases 16 had septicaemia alone and 25 developed meningitis.

The clinical features of the condition are discussed, and an account is given of treatment with streptomycin given by the intramuscular, oral, intrathecal, and intraventricular routes.

A method of assaying the sensitivity of organisms to streptomycin *in vitro* is discussed.

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The family allowances scheme has now been in operation for three years. The Ministry of National Insurance states that about 2,941,000 families of two or more children are receiving allowances varying between 5s. and £3 5s. a week at a total cost of £60 million a year. Family allowances are a payment of 5s. a week for every child after the elder or eldest below the age limit, which is usually 15 (school-leaving age), but is extended to July 31 following the sixteenth birthday where full-time education is continued and in cases of apprenticeship. During the three years the Ministry has received nearly three and a half million claims to family allowances, of which fewer than 100,000 have had to be rejected. The 2,941,000 families receiving allowances contain children within the qualifying ages as follows: two children, 1,850,000; three children, 688,000; four children, 247,000; five or more children, 156,000. The family drawing the largest allowance of £3 5s. a week consists of 14 children within the age limits. In the last year over 290,000 new claims to allowances resulted in payments for over 300,000 children. In the same period the total number of allowances in payment and the number of children for whom allowances are paid increased in each case by over 100,000.

STREPTOMYCIN TREATMENT OF INFANTILE DIARRHOEA AND VOMITING

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Crowley *et al.* (1941), in a survey of the literature and from their own findings, concluded that no single specific aetiological agent could be incriminated in infantile diarrhoea and vomiting. A wealth of facts relating to the clinical and metabolic changes arising in that condition has been accumulated and has made treatment more rational and effective; none the less, modern medical science has not yet provided the answer to the challenge of this illness. It is therefore not surprising that almost every chemotherapeutic agent introduced during the last decade has been tried in the treatment of infantile diarrhoea and vomiting in the vain hope that it might offer a satisfactory solution to the problem.

Recently streptomycin has been used and a number of encouraging results have been published. James, Kramer, and Armitage (1948) treated 30 children aged from 6 days to 13 months with streptomycin by mouth, on the basis of their finding in the stools *Proteus vulgaris*, to which they attributed pathogenic significance. They pointed out that some of their cases not associated with *Pr. vulgaris* also improved on streptomycin. There were no deaths in their series, and convalescence was particularly rapid. In a control group of eight cases *Pr. vulgaris* was isolated from the stools of five infants; all recovered, though at a slower rate. The total dose of streptomycin was 2 g., given over a period of seven days. No toxic effects were noticed, and *Pr. vulgaris* was rapidly cleared from the gut as a result of treatment.

Pulaski and Amspacher (1947) reported an epidemic involving 13 infants, three of whom died; the successful outcome in the ten who recovered was attributed directly to streptomycin. The dosage used in all the cases was 0.1–0.2 g. of streptomycin per kilogram of body weight by mouth for two to ten days. Loeschke and Cochlovius (1949) attributed recovery from infantile gastro-enteritis to streptomycin in 9 of 13 cases. They gave 25–75 mg. five to eight times daily by mouth. Their bacteriological findings were *Bact. coli, Pr. vulgaris, Pseudomonas pyocyanea*, and *Streptococcus faecalis*. A reduction in the number of Gram-negative organisms isolated generally followed the oral administration of streptomycin. Leisti (1947) recorded his results in 46 infants suffering from diarrhoea; 38 were full-term babies, eight of whom died; 8 were premature infants, all of whom recovered. Streptomycin was given in a dosage of from 40,000 units (40 mg.) to 160,000 units (160 mg.) intramuscularly daily for one to eight days. Goettsch, Cobley, and Mulloy (1948) obtained excellent results in 44 cases of parenteral gastro-enteritis. There were three deaths in their group, which they felt could not be attributed to failure of streptomycin. Their dosage was 0.5 g. intramuscularly and 0.5 g. orally for seven to ten days

In the present investigation special attention was given to the presence in the stools of a serological type of *Bact. coli* var. *neapolitanum* (abbreviated in this paper to B.C.N.) and *Pr. vulgaris*, the object being to correlate the clinical effects of treatment with bacteriological findings. Organisms of the *Salmonella* and *Shigella* groups were absent in this series of cases. Bray (1945), Bray and Beavan (1948), Giles and Sangster (1948), and Taylor, Powell, and Wright (1949) have all described this particular serological type of *Bact. coli* associated with a high percentage of cases of infantile diarrhoea and vomiting. Dr. C. Giles kindly placed at the disposal of one of us (G.M.) antisera and subcultures of his alpha and beta types of *Bact. coli*, from which our own antisera were prepared (the alpha type corresponding to B.C.N.). Full details of the bacteriological investigations and findings will be published later.

Stools were cultured before streptomycin was given and just before or after the end of treatment. No case was considered to be negative for B.C.N. until at least 30 colonies had been tested specially. The streptomycin sensitivity of B.C.N. strains was tested on plates, using strips of filter-paper soaked with 1 mg. per ml. of streptomycin.

Results of Treatment

Cases of non-specific infantile diarrhoea and vomiting admitted to hospital, as well as those developing the disease after admission, were divided into three groups. One group was treated with streptomycin by intramuscular injection, a second group by oral administration, while every third case, regardless of its severity, acted as a control and formed the third group.

Two standard schemes of dosage were employed for both the intramuscular and the oral route of administration. The first was to give 20 mg. of streptomycin per lb. body weight per day, divided into doses given at four-hourly intervals day and night for five to seven days; the second was to administer 100 mg. at four-hourly intervals for 24 hours and 75 mg. at four-hourly intervals for the remainder of the period, which varied from four to six days. The total dosage used for a single case therefore rarely exceeded 3 g. Five to seven days' treatment was regarded as adequate for assessment of failure or success.

All patients were given fluids, whether receiving streptomycin or not. The following fluids were used: plasma, blood, 5% glucose in N/5 saline, Hartmann's solution, 2.5% or 5% casydrol intravenously, according to the requirements of the individual infant. Feeding was started after 24 or 48 hours with a diluted skimmed lactic acid milk, gradually increasing the concentration of the formula if improvement was maintained. During the starvation period Hartmann's or Darrow's solution was given by mouth.

The clinical condition of each patient was classified as mild, moderate, or severe, according to the degree of dehydration, character of stools, persistence of vomiting, and initial loss of weight. The existence and the nature of parenteral infection were noted.

The effect of treatment was assessed by the clinical response. Some cases improved rapidly and recovered during the course of streptomycin treatment, and it was these which had to be considered as possibly benefiting from streptomycin therapy. Others showed no improvement during the period when streptomycin was given, but recovered eventually; these were considered not to have responded to streptomycin. Fourteen (19%) of the patients died.

Two levels of dosage have been mentioned, but as there was no apparent benefit from the higher dosage no differentiation has been made in analysing the results.

Table I sets out the number of cases, classed according to clinical severity and the response to treatment. The control group and the cases as a whole are included for comparison.

The details of individual cases are shown in Tables II, III, and IV.

Bacteriological Observations

Of the 79 cases in this series, B.C.N. was isolated from the faeces at the first examination in 50 (63%). It was more commonly present in severe cases (76%) than in moderate and mild cases (50%). The difference is statistically significant, as it is just over twice the standard error. Of severe cases in which the organism was found, 42% ended fatally (13 of 31 cases). In comparison, of the severe cases which did not have the organism 10% were fatal (1 of 10 cases). This difference is also significant statistically, being more than twice the standard error.

One may therefore conclude that in this series there was a significant correlation between severity of case and the presence of B.C.N., and also between the probability of death in severe cases and the presence of this organism.

TABLE I.—*Details of Cases showing Clinical Severity and Response to Treatment*

	Intramuscular Treatment				Oral Treatment				Control				Total			
	Total Cases	Rapid Improvement	Delayed Improvement	Died	Total Cases	Rapid Improvement	Delayed Improvement	Died	Total Cases	Rapid Improvement	Delayed Improvement	Died	Total Cases	Rapid Improvement	Delayed Improvement	Died
Clinical condition of all cases:																
Severe	16	3	8	5	14	5	3	6	11	8	—	3	41	16	11	14
Moderate ..	7	6	1	—	10	8	2	—	14	14	—	—	31	28	3	—
Mild	1	1	—	—	2	2	—	—	4	4	—	—	7	7	—	—
Total ..	24	10	9	5	26	15	5	6	29	26	—	3	79	51	14	14
Cases with parenteral infections:																
Severe	7	2	3	2	4	2	—	2	3	3	—	—	14	7	3	4
Moderate ..	3	3	—	—	3	3	—	—	4	4	—	—	10	10	—	—
Mild	1	1	—	—	1	1	—	—	2	2	—	—	4	4	—	—
Total ..	11	6	3	2	8	6	—	2	9	9	—	—	28	21	3	4
Cases without parenteral infections:																
Severe	9	1	5	3	10	3	3	4	8	5	—	3	27	9	8	10
Moderate ..	4	3	1	—	7	5	2	—	10	10	—	—	21	18	3	—
Mild	—	—	—	—	1	1	—	—	2	2	—	—	3	3	—	—
Total ..	13	4	6	3	18	9	5	4	20	17	—	3	51	30	11	10

TABLE II.—*Intramuscular Streptomycin Treatment of Infantile Diarrhoea and Vomiting*

Case No.	Age	Sex	Clinical Condition		Bacteriology of Stools		Result
				Parenteral Infection	Before Treatment	After Treatment	
3	6 weeks	F	Severe		B.C.N. (S.)	B.C.N. (S.)	N.I.*
8	11 months	M	Moderate	Upper resp. infection	*Pr. vulg.*	*Pr. vulg.*	Improved
9	3 weeks	F	,,		B.C.N. (R.)	Negative	N.I.
10	10 weeks	F	Severe		*Pr. vulg.*	*Pr. vulg.*	N.I.
11	3 ,,	M	,,		B.C.N. (R.)	B.C.N. (S.)	Died
12	3 ,,	F	,,		B.C.N. (S.)	B.C.N. (S.)	Improved
17	3 ,,	M	,,	Otitis media	B.C.N. (S.)		Died
18	10 ,,	F	Mild	Upper resp. infection	*Pr. vulg.*	*Pr. vulg.*	Improved
19	3½ months	F	Moderate		*Bact. coli* (beta) (S.)	Negative	,,
23	4 ,,	F	Severe		*Pr. vulg.* *Bact. coli* (beta) (S.)	No *Proteus* *Bact. coli* (beta) (R.)	N.I.
26	2½ ,,	M	,,	Otitis media	*Pr. vulg.* *Bact. coli* (beta) (R.)	Negative *Pr. vulg.*	Improved
27	5 weeks	M	,,	,, ,,	B.C.N. (S.)	B.C.N. (R.)	N.I.
32	1 year	F	,,	,, ,,	B.C.N. (R.)		Died
34	4 months	F	Moderate		B.C.N. (R.)	B.C.N. (R.)	Improved
45	7 ,,	M	,,	,, ,,	B.C.N. (S.)	B.C.N. (R.)	,,
47	3 weeks	M	Severe		B.C.N. (S.)	B.C.N. (R.)	N.I.
50	5 months	F	,,	Mastoiditis	B.C.N. (S.)		Improved
54	2 ,,	F	Moderate		B.C.N. (R.)	B.C.N. (R.)	,,
59	4 weeks	F	,,	Pneumonia	Negative	Negative	,,
67	2 months	M	Severe		Negative	Negative	N.I.
76	5½ ,,	M	,,		B.C.N. (S.)	B.C.N. (R.)	Died
77	6½ ,,	F	,,	Pyelitis	B.C.N. (R.)		N.I.
84	2 ,,	M	,,		B.C.N. (R.)		Died
86	18 ,,	F	,,	Otitis media, pyelitis, pink disease	B.C.N. (S.)	B.C.N. (R.)	N.I.

* N.I. = Not improved, but recovered later on routine treatment. S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

These findings may not, however, apply generally, and in themselves may not indicate a causal relationship.

The organism was often found in mild and moderate cases. It also persisted in recovered cases, even those which had been clinically severe. Of 50 recovered cases it was found in 27 (54%), which was a very small reduction compared with the initial incidence of 63% if a causal relationship existed.

About half the cases from which the organism was isolated before treatment yielded streptomycin-resistant strains (24 of 50 cases, 48%). Strains which were initially sensitive often became resistant during treatment, a change which was noted in 12 of 16 cases (Tables II and III). Five of these 12 cases recovered satisfactorily.

The findings as a whole may be regarded as not supporting an aetiological relationship of this organism to infantile diarrhoea and vomiting. They indicate, too, that streptomycin therapy had little effect in eliminating the organism from the bowel.

Pr. vulgaris was isolated initially in 10 cases, in 6 cases being associated with B.C.N. or the beta type of *Bact. coli*. Seven of the 10 cases were classified as severe. This organism appeared to have a minor significance in this series. It was not present in any of the patients who died.

Discussion

Our investigations confirm the frequent occurrence of a special type of *Bact. coli*, referred to as B.C.N., in the stools of infants suffering from infective gastro-enteritis, though this association was less common in our cases than in the series reported by Bray and Beavan (1948), Giles, Sangster, and Smith (1949), and Taylor, Powell, and Wright (1949). No evidence has yet been forthcoming to prove the pathogenic importance of any of the varieties of *Bact. coli* shown to be associated with infantile diarrhoea.

B.C.N. was isolated from 25 of 32 cases arising after admission to hospital: in all probability these were the result of cross-infection, a conclusion that was supported

TABLE III.—*Oral Streptomycin Treatment of Infantile Diarrhoea and Vomiting*

Case No.	Age	Sex	Clinical Condition		Bacteriology of Stools		Result
				Parenteral Infection	Before Treatment	After Treatment	
2	2 weeks	F	Severe		B.C.N. (S.)	B.C.N. (S.)	Died
5	5 months	F	Moderate		Negative	Negative	Improved
13	5 ,,	M	Mild	Otitis media	B.C.N. (S.)	B.C.N. (R.)	,,
15	7 weeks	M	Severe	Bronchitis	B.C.N. (R.)	B.C.N. (R.)	N.I.*
28	3½ months	F	,,		B.C.N. (S.)	B.C.N. (S.)	N.I.
30	3 weeks	M	Moderate	Pneumonia	Negative	Negative	Improved
31	2 months	F	,,		B.C.N. (R.)	B.C.N. (R.)	,,
40	5 ,,	M	Severe		Negative	Negative	,,
46	6 weeks	M	Moderate	Bilateral otitis media	B.C.N. (S.)	B.C.N. (R.)	,,
48	5 ,,	M	Severe		Negative	B.C.N. (R.)	N.I.
49	3 months	M	,,		B.C.N. (R.)	B.C.N. (R.)	Improved
51	14 days	M	Moderate	Upper resp. infection	B.C.N. (S.)	B.C.N. (R.)	,,
53	3 weeks	F	Severe		B.C.N. (R.)	B.C.N. (R.)	Died
55	4 ,,	M	Moderate		Negative	B.C.N. (R.)	N.I.
57	3 ,,	F	,,		Negative	B.C.N. (R.)	Improved
58	9 ,,	M	,,		B.C.N. (S.)	B.C.N. (R.)	,,
60	5 ,,	M	Severe		B.C.N. (R.)	B.C.N. (R.)	,,
62	6 ,,	M	,,		B.C.N. (R.)	B.C.N. (R.)	,,
63	3 ,,	M	Moderate	Bronchopneumonia	B.C.N. (R.) *Pr. vulg.*	B.C.N. (R.) No *Proteus*	,,
64	9 months	M	Severe	Bronchitis	B.C.N. (R.)		Died in 24 hrs.
65	3½ ,,	F	,,	Pneumonia	B.C.N. (R.)	B.C.N. (R.)	Improved
68	14 days	M	Mild		Negative		,,
72	7 months	F	Severe	Bilateral otitis media	B.C.N. (R.)		Died
74	4 weeks	M	,,		B.C.N. (R.)	B.C.N. (R.)	,,
75	11 ,,	M	Moderate		B.C.N. (S.)	B.C.N. (R.)	N.I.
79	6 ,,	M	Severe		B.C.N. (S.)	B.C.N. (R.)	Died

*N.I. = Not improved, but recovered later on routine treatment. S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

TABLE IV.—*Control Cases of Infantile Diarrhoea and Vomiting on Routine Treatment*

Case No.	Age	Sex	Clinical Condition		Bacteriology of Stools		Result
				Parenteral Infection	Before Treatment	After Treatment	
4	1 year	M	Moderate		*Bact. coli* (beta) (S.)		Improved
6	3½ months	F	,,		B.C.N. (S.)		,,
7	9 ,,	F	,,	O.R.I.	Negative	B.C.N. (R.)	,,
14	3½ ,,	F	,,	Otitis media	B.C.N. (S.) *Bact. coli* (beta) (S.)	Negative	,,
16	10 weeks	M	Severe	,, ,,	Negative *Pr. vulg.*	Negative *Pr. vulg.*	,,
20	15 months	M	Moderate		Negative	Negative	,,
22	7 weeks	F	,,	,, ,,	B.C.N. (R.)		,,
25	4 months	M	Severe	,, ,,	B.C.N. (S.)	B.C.N. (S.)	,,
29	1 month	F	,,		Negative		Died
35	6 months	F	Moderate		B.C.N. (S.)	Negative	Improved
37	6 ,,	F	,,	Pyelitis and pneumonia	Negative	,,	,,
39	2 ,,	M	Mild		*Bact. coli* (beta) (S.)		,,
42	5 weeks	M	Moderate		B.C.N. (S.)		,,
43	10 ,,	F	,,	Upper resp. infection	Negative		,,
44	9 months	F	Mild	Pneumonia	Negative		,,
52	9 ,,	M	Severe		B.C.N. (R.)		Died in 24 hrs.
56	3 weeks	F	Mild		Negative	,,	Improved
61	4 months	F	Moderate		B.C.N. (S.)	,,	,,
66	10 ,,	M	Severe		B.C.N. (R.)	,,	,,
69	7 ,,	F	Mild	Bronchopneumonia	Negative	,,	,,
70	8 ,,	M	Severe		B.C.N. (S.)		,,
71	5 ,,	M	,,	Upper resp. infection	*Bact. coli* (beta) (S.) *Pr. vulg.*		,,
78	8½ ,,	M	Moderate		B.C.N. (R.)		,,
80	11 weeks	F	Severe		B.C.N. (R.)		Died
81	4 months	F	Moderate		B.C.N. (S.)		Improved
82	4 ,,	M	Severe		Negative		,,
83	4 weeks	F	Moderate		*Bact. coli* (beta) (R.)	,,	,,
85	2 months	M	Severe		B.C.N. (S.) *Pr. vulg.*	Not received	,,
87	3 weeks	M	,,		B.C.N. (R.)	B.C.N. (R.)	,,

S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

by the more frequent isolation of streptomycin-resistant strains later in the investigation. This may be accounted for by survival of resistant strains only in patients under treatment or by cross-infection with a B.C.N. strain originally sensitive but resistant after treatment.

Bacteriological investigation thus would not seem to justify streptomycin therapy, though the presence of B.C.N. in a severe case of infantile diarrhoea and vomiting may be regarded as a warning signal and a pointer to a more serious prognosis.

Clinical improvement in some patients receiving the antibiotic seemed to be attained at a more rapid pace than in those treated by standard measures. Especially was this so in cases associated with a parenteral infection: stools returned to normal in a shorter time and the upward trend in the patient's general condition appeared steeper. In agreement with this are the favourable results recorded by Goettsch, Cobley, and Mulloy (1948) in their cases of parenteral gastro-enteritis.

In a number of our cases streptomycin was followed by a spectacular improvement—in others it failed completely. Even detailed analysis of the case histories has not furnished clinical or bacteriological indication for the use of the antibiotic. In each individual case the result of streptomycin therapy was also unpredictable.

Summary

The results of streptomycin treatment of infantile diarrhoea and vomiting are discussed.

Streptomycin was given to 26 cases orally, and to 24 intramuscularly, while a control group of 29 cases received no antibiotic.

The dosage of streptomycin was either 20 mg. per lb. body weight per day for five to seven days, or 600 mg. for the first 24 hours, followed by 450 mg. daily for a further four to six days.

The results do not indicate that streptomycin exerts any specific therapeutic effect.

The frequent association of a special type of *Bact. coli* (B.C.N.) with infantile diarrhoea and vomiting was confirmed, being found before treatment in 50 out of a total of 79 cases, but no evidence was obtained that it was of any aetiological significance.

Our thanks are due to Professor Gaisford for his encouragement and valuable criticism; to Professor Maitland for allowing facilities in the department of bacteriology and for help with bacteriological problems; and to Drs. S. K. Guthrie, R. I. Mackay, and N. Wells for permission to include some of their cases in our investigation.

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Food Investigation, 1947, is a report from the Department of Scientific and Industrial Research (H.M.S.O., price 6d.) which is written for the non-specialist. It describes work which has been done on whalemeat during an expedition to the Antarctic by the factory ship *Balaena*. It was found that the whalemeat was much improved in quality if the whale was bled and cooled down rapidly. The practice recommended was to make an incision in the main blood vessels in the neck and to slit the belly wall so that the cold sea-water could circulate. In this way the meat could be kept in good condition for 18 to 24 hours. Research on meat, fruit, and potatoes continued during the year, and at the Torry Research Station quicker and more convenient methods of freezing were studied. Lobsters are apparently better frozen cooked than raw. Rapidly frozen cooked lobsters can be stored for eight months with little change in flavour and texture.