symptoms. Alternatively, she might have been a case of haemoglobin E trait (or even thalassaemia trait) with anaemia due to some entirely different cause.

Case 2 had haemoglobin E and about 5% haemoglobin F in his blood and showed signs of severe anaemia. He was evidently a case of thalassaemia-haemoglobin E disease, but the relatively low figure of 5% is in contrast to the values of 20-40% obtained in Siamese by Chernoff (quoted by Lehmann, 1957). The absence of demonstrable haemoglobin A is in keeping with the findings of other workers that the presence of the thalassaemia gene interferes with the expressivity of the gene responsible for the production of haemoglobin A.

Cases 3 and 4 were unaffected and showed only haemoglobin A in their bloods. It follows that neither of the parents of this family could be homozygous for either the haemoglobin E gene or for the gene (or genes) responsible for thalassaemia. Analysis of the parents' bloods showed the presence of haemoglobins E and A in the father, and only haemoglobin A in the mother. Hence the appearance of haemoglobin F in Cases 2 and 5 may have been due either to a mutation or to inheritance from one of the parents.

The suggestion of mutation is a purely academic one, since all indications are that mutation from a normal gene

FIG. 2.—Genetic representation of the family.

to abnormal at any given locus takes place only once in 100,000 gametes, so that it is only in cases like those of the ABO and MN groups, where most members of families have been tested, or in congenital diseases like haemophilia, where the resulting disease has striking manifestations, that instances of human mutation may be expected to be found. Moreover, the presence of two separate identical mutations in a single sibship is extremely unlikely and would occur in only one in 10,000,000,000 families for each gene. Hence one of the parents in the family studied must have been a carrier of the thalassaemia gene. It is perhaps reasonable to infer that the gene is present in the mother, because had it been present in the father he would have shown at least some of the rather severe manifestations of thalassaemia-haemoglobin E disease. We therefore regard the mother as a carrier of the thalassaemia trait with non-penetrance of the thalassaemia gene: that she was not entirely normal was indicated by the increased resistance of her red blood cells to haemolysis. Accordingly we have constructed the genetic table as illustrated in Fig. 2.

A possible racial origin of haemoglobin E cannot be ascertained as yet. This abnormal haemoglobin probably arose in South-east Asia as the result of a single mutation and was then disseminated from this focus. With regard to Ceylon, the Sinhalese as well as the Veddahs are of partial Bengali extraction, and it is possible that the haemoglobin E found in Veddahs and Sinhalese originated in Bengal.

Mackey and Vivarelli (1954) suggested that sicklers are more prone to develop falciparum malaria than non-sicklers. Allison (1954) and Raper (1955) reported statistically significant differences in the incidence of malaria in carriers of the sickle-cell trait and those without the trait. Others (Moore, Brass, and Foy, 1954; Archibald and Bruce-Chwatt, 1955) could not confirm the differences. No statistical investigation has been done so far to determine

whether carriers of haemoglobin E were more resistant to malaria than those without haemoglobin E. Na-Nakorn, Minnich, and Chernoff (1956) reported that haemoglobin E offered no protection against malaria. Still, it is interesting to note that the incidence of haemoglobin E in Ceylon is largely confined to areas which had been hyperendemic for malaria prior to 1945 (de Silva *et al.*, 1957).

Summary

Clinical, haematological, and genetic manifestations of haemoglobin E syndromes in a Ceylonese family are described. In this family, the father carried the haemoglobin E trait, three children were affected with thalassaemia-haemoglobin E disease, whilst the mother and two other children showed only normal adult haemoglobin in their bloods.

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FRAMYCETIN IN INFANTILE GASTRO-ENTERITIS DUE TO PATHOGENIC ESCHERICHIA COLI

BY

R. LOUWETTE

AND

A. LAMBRECHTS

Université de Liège. Clinique des Maladies de l'Enfance

Framycetin sulphate ("soframycin") is an antibiotic produced by a strain of *Streptomyces* which was isolated by Decaris in 1947 (Decaris, 1953). Given parenterally, this substance is highly toxic to the kidneys and the eighth cranial nerves (Massénat-Deroche, 1954), a fact which has retarded its clinical use. When given by mouth, however, it is harmless at the prescribed dosage levels, since it is very poorly absorbed from the gut.

In vitro its action on various strains of pathogenic *E. coli* is far superior to that of chloramphenicol and the tetracyclines. It is both bacteriostatic and bactericidal (Massénat-Deroche, 1954).

Various investigators have reported on its usefulness in infective infantile gastro-enteritis (Marquézy *et al.*, 1955; Laplane *et al.*, 1955; Cathala *et al.*, 1954; Schneegans *et al.*, 1955, 1956; Boyer and Tissier, 1955; Pierret *et al.*, 1956; Shidlovsky *et al.*, 1955-6).

Several of us (Hainaut *et al.*, 1957) have already reported on the effectiveness of neomycin in the treatment of gastro-enteritis due to pathogenic *E. coli*. In the present paper we have endeavoured to compare the activity of framycetin with that of neomycin, using the same experimental conditions and applying identical criteria.

Material

Our trials of framycetin were carried out on the one hand during a local epidemic due to *E. coli* O.55:B5 in the premature babies' wing of the Clinique Pédiatrique Universitaire, and, on the other, on a group of infants admitted for gastro-intestinal disturbances. We report only on the cases in which bacteriological investigation confirmed the presence of pathogenic *E. coli* in the stools.

We have used framycetin in the form of a flavoured water-soluble powder. Daily doses, divided into two portions, varying from 125 to 250 mg., were given according to the patients' weight (50 mg./kg.). This treatment was administered for 3 to 12 days. Generally a five-day course was sufficient. For three gastro-intestinal cases we had to combine framycetin with chloramphenicol by mouth for various associated infections (otitis, bronchopneumonia, pyelonephritis).

Twenty-five infants were treated. Their ages ranged from 7 days to 7 months and their weights from 1,400 to 6,900 g. Of these, 14 were premature babies (from 1,400 to 2,200 g.) and 8 others were undernourished.

Culture of the stools, before treatment, yielded the following results: *E. coli* O.55:B5 in 20 cases, *E. coli* O.26:B6 in 2 cases, *E. coli* O.119:B9 in 2 cases, *E. coli* O.111:B4 in 1 case.

How gravely ill these babies were can be gauged from the severity of the diarrhoea and dehydration, which we graded as follows: 14 infants passed numerous watery stools (more than eight daily), whereas in 11 cases the stools had the same character but were less frequent; 15 infants presented with moderate dehydration; 10 infants were very dehydrated—amongst these, five showed severe neurotoxicity.

Results

In order to assess the results of treatment and compare them with our trials with neomycin, we adopted the same criteria as before—that is: (1) the time taken to clear the pathogenic agent from the stools (bacteriological examinations were carried out before and repeatedly during treatment by the Institut Provincial de Bactériologie); and (2) clinical considerations: (a) the rate of disappearance of dehydration, (b) the time required for the stools to become normal in number and appearance, and (c) the duration of vomiting.

1. Culture of the stools became negative within three days in 22 babies and within five days in 2. Only one remained positive after five days' treatment. This infant's stools were still positive for *E. coli* O.55:B5 six weeks later, but there was no sign of gastro-enteritis.

2a. In most cases the fluid balance was restored by drinking. Only five children received intravenous infusion because they were in a highly toxic state. Apart from a single infant who continued to be in that state for 72 hours, all were normally hydrated after 48 hours.

2b. The gastro-intestinal disturbances recovered rapidly. The stools returned to normal within 48 hours in 18 infants. After 72 hours only one still had diarrhoea; he was a premature baby whose stools remained soft and granular for 12 days in spite of prolonged therapy and negative stool cultures. The stools resumed their normal appearance in this case only after a concomitant urinary infection had been cured, the latter having caused periodic bouts of fever. Another infant, who had improved rapidly in 36 hours, relapsed on the fourth day of treatment; this case was cured in turn by neomycin therapy.

2c. Administration raised no problem. No digestive upset resulted. Of 12 infants who had severe vomiting at the start, in only 2 did it not subside within 24 hours. After 48 hours all vomiting had ceased, and in no case did it recur during treatment.

To find out whether framycetin might be nephrotoxic, we carried out extensive urine analyses and made several estimations of the blood urea level, both during and after treatment; all readings were strictly normal.

Conclusion and Summary

Framycetin has a very favourable action on gastro-enteritis due to pathogenic *E. coli* in premature babies and in infants. Our investigations were mainly concerned with *E. coli* O.55:B5. Framycetin is well tolerated and does not appear to be toxic at the dosage used—50 mg. per kg. per day by mouth for five days as an average. It acts with the same speed and potency as neomycin, which we have used in gastro-enteritis caused by *E. coli* O.111:B5 and O.55:B5. Diarrhoea, dehydration, and vomiting disappear very rapidly and often after two days' treatment; stool cultures usually become negative within three days.

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The need to advance our knowledge of mental health and illness was urgent, said Viscount MONCKTON at the meeting of the Mental Health Research Fund on March 25. Nearly half our hospital beds were occupied by the mentally sick, and mental sickness constituted by far the greatest problem of medicine to-day. An advance in knowledge in this field would do more towards the happiness of mankind than any other improvement in the standard of health or of living. Nevertheless he must say that the interest which had been stimulated in the subject had not been matched by corresponding generosity in voluntary gifts from the public generally. No doubt the sum spent on research in the field of defence and in scientific work for peaceful purposes was enormously greater than that spent on medical research. And it would be easy to criticize the Government for not devoting more of what could be spent on research to medical research. But he had been too lately released from the Government stable to be ready to make that sort of criticism without going on to say what research now being done should be abandoned to make way for this. There were limits to what the Government could spend, even on medical research.