

failed to confirm the results obtained by Simpson and Wood (1935) in a similar experiment on children. As judged by the increase in weight of the rats, the cod-liver oil had a decidedly beneficial effect, the halibut-liver oil plus dried milk had a slightly better effect, whilst the virol was almost without influence as compared with the control rats receiving no supplement. As judged by the percentage of the ash content of the bones of the rats, all three supplements were equally without effect. This suggested that the mixed diet was deficient in the elements required for calcification.

A second experiment was carried out on six groups of rats, all of which were fed liberally with the same mixed diet and given six drops each of a good sample of cod-liver oil daily—a very large dose for a rat. One group received no other supplement, three were given graded doses of a mixture of salts of calcium and phosphorus, and two had graded doses of milk.

The salt mixture had no significant influence on the increase in weight of the rats, but the doses of milk had a distinctly beneficial effect.

The graded doses of salt mixture produced graded results in the percentage of ash in the bones, ranging from 42.83 per cent. for the lowest dose (0.02 gramme) to 52.12 per cent. for the highest dose (0.18 gramme), which is about the normal percentage for rats such as these. The bones of the rats given no supplement contained 39.7 per cent. ash. This proves quite clearly that the ordinary mixed diet of the poorer classes is seriously deficient in the elements required for the calcification of bone.

The lower dose of milk, 5 ml., produced 45.74 per cent. of ash in the rats' bones; the higher dose, about 15 to 16 ml., produced 52.03 per cent. of ash. A comparison of the submaximal effects from the lower dose of milk and the lower doses of salt mixture showed that the milk apparently contained 0.76 gramme of calcium per litre. As this is less than the average calcium content (1.12 grammes per litre) of cows' milk it is concluded that the calcium of cows' milk is no more easily available for the rat than the calcium of inorganic salts.

The serious shortage of calcium in the mixed "poorer-class" diet was confirmed by analysis of typical bulked days' rations as given to the rat.

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SONNE DYSENTERY

BY

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Although for some years Sonne dysentery has been known in paediatric circles as one of the bugbears of children's hospitals, there are many busy practitioners who have seen nothing of the disease and remain unfamiliar with its characteristics. In view of the present epidemic in London and the home counties a brief account of the disease may perhaps be considered opportune.

Bacillary dysentery may be described with sufficient accuracy as consisting of three types, due respectively to (a) the Shiga bacillus, (b) the Flexner group of bacilli, and (c) the Sonne bacillus. The differentiation of these three types is ultimately a bacteriological matter, but clinically there are important general differences between them. Shiga dysentery, the most serious and fatal type, is practically non-existent among the ordinary population of London, and probably of the country: in seventeen years no example of this infection has occurred at the Paddington Green Children's Hospital. Flexner-group dysentery, as compared with Sonne dysentery, is less common but more severe, prolonged, and dangerous. Sonne dysentery, with which we are here concerned, is therefore the commonest of the three types but runs the mildest and shortest course.

Epidemiological Features

Sonne dysentery, although probably commonest in the summer months, may occur at any time of the year. No age is exempt from it, and while it is most frequently seen in young subjects, infants do not seem to be preponderantly affected. In these two particulars it differs from the so-called epidemic gastro-enteritis, which is essentially a summer disease and strictly confined to infants.

The disease spreads with such ease and rapidity that it is tempting to think that transmission may be by air-borne infection. There is, however, as yet no clear proof that transmission can occur by any means other than the ingestion of the specific bacillus, the ultimate source of which is the infectious faeces of the patient. Thus, as in typhoid fever, patients and those in attendance on them must be regarded as the source of contamination of food, drink, feeding utensils, etc. Transmission in the same way by flies is a possibility.

Outbreaks of Sonne dysentery usually arise in a children's ward from the admission of a case in which the stools are not typical of the disease on inspection. Thus very mild cases and convalescent cases constitute the chief danger. D. Nabarro and A. G. Signy (1932) report that children who have recovered from an attack may continue to pass Sonne bacilli in the faeces "for months." This must, I think, be very rare, and it does not seem that the chronic carrier constitutes a problem of importance among children. The bacilli may disappear from the stools within as short a time as ten days from the onset of symptoms, and in my experience, in the absence of any relapse, tests have always proved negative by the end of three or four weeks. The incubation period is from one to eight days, usually two or three days.

Morbid Anatomy

Necropsies on cases of Sonne dysentery are so rare that I have not been able to obtain any first-hand information

on the morbid anatomy of the disease. Doubtless there is an inflammatory congestion of the mucosa of the colon, and the character of the symptoms suggests that this may be at its most severe in the lowest part of the intestine. The conspicuous presence of blood in the motions must indicate some degree of superficial ulceration of the mucosa, but the rapid recovery which ensues makes it clear that there can be no gross ulcerative changes.

Clinical Features

Describing first a typical case, the disease develops with great rapidity, with the onset of fever up to 102–3°, abdominal pain with colic and perhaps tenesmus, and purging. The stools are loose and contain obvious quantities of blood and mucus. Pus is also present on microscopic examination. The passage of blood and mucus without faecal material is exceptional, but may occur in between the typical actions. The bowels during the first twelve hours are moved perhaps every hour, or even more frequently. Abdominal pain may be severe, but is not excruciating as in intussusception. Vomiting may be absent throughout; but it is common at the early stage of the disease for some vomiting to occur with each action of the bowels, clearly due to the general intestinal turmoil going on. In exceptional cases (*vide infra*) vomiting is a prominent symptom. By the second day the more violent symptoms are subsiding, and by the end of the third day the temperature is falling rapidly, the blood is disappearing from the stools, pain is lessening and the number of stools is diminishing. The patient is left feeling considerably weakened by the attack. The constitutional disturbance seems to arise not so much from toxæmia as from dehydration, loss of sleep, and starvation. For the next few days some mild diarrhoea remains, the motions being unformed and showing the presence of some mucus; blood, however, is only now to be found by microscopic examination, and even this soon disappears. From this time onwards there is usually rapid recovery, so that by the end of about ten days from the onset the child is as well as before the attack.

In mild cases the symptoms are less severe and the motions, although containing mucus, may show no obvious blood; but on microscopic examination blood and pus cells are constantly to be seen. A similar condition of the stools may be found in cases convalescent from a typical attack, and in both these conditions there is considerable danger that the true nature of the disease may pass unrecognized.

In exceptional cases vomiting may apparently be troublesome, and R. E. Smith (1931) has raised the question whether there may not be a gastric type of Sonne infection. Further observations are required to settle this point, but it might well be kept in mind in connexion with epidemics of unexplained vomiting, especially in institutions.

Course and Prognosis

The usual short course of the disease has been described. Relapses within a week of recovery are occasionally seen. Complications and sequelae seem to be practically unknown. The length of time during which the stools may remain infectious has been discussed. Danger to life may arise in the case of weakly infants who acquire the disease; otherwise the infection appears to carry no death rate.

Diagnosis

The clinical diagnosis of Sonne dysentery is not difficult in typical cases. In infants and young children intussus-

ception must be considered. This is essentially an obstructive condition, whereas Sonne dysentery is a diarrhoeic disease and pus is present in the stools. Further, the positive points in favour of intussusception are absent in dysentery—namely, the characteristic temporary collapse with the crises of abdominal pain, the presence of a tumour felt through the abdominal wall or per rectum, and the diagnostic radiographic picture with an opaque enema. In older children and adults Sonne dysentery has to be distinguished from other forms of infective diarrhoea and food poisoning, and this rests upon the bacteriological examination of the stools. The danger of overlooking mild, convalescent, and atypical cases has been emphasized.

The bacteriological diagnosis of the disease is of the utmost importance, and a reliable report can be obtained in eighteen hours. A swab may be taken of the rectal mucosa, in which case the specimen must reach the bacteriologist with practically no delay; but usually a specimen of the faeces is submitted to examination. Here again it is important that the specimen should be as fresh as possible, and although it is difficult to lay down a precise rule I should not myself rely upon a negative report if the stool were twenty-four hours old before being planted out. In order to obtain as satisfactory and pure a growth of the bacillus as possible a piece of mucus is picked out of the stool, gently washed free of faecal material in normal saline, and spread by means of a swab over a small area of a warm dry plate of lactose-litmus-bile-salt-agar or similar medium. Any surplus material is removed from the surface, and from this area, by means of a spreader, the rest of the plate is planted out by quartering. Eighteen hours later a suspicious colony is removed and emulsified in water on a slide. A loopful of Oxford specific agglutinating serum for the Sonne bacillus is added, and if the test is positive macroscopic clumping is seen within a minute. Confirmatory sugar reactions will take an additional twenty-four hours, but in expert hands the results of the Oxford serum tests seem entirely reliable. A similar technique with other types of Oxford sera leads to the recognition, if needed, of Flexner-group and Shiga dysentery, the typhoid and paratyphoid, Gaertner and *aertrycke* infections. Sero-diagnosis from the patient is not helpful, at all events in early stages of the disease.

Treatment

Sonne dysentery is a notifiable disease. Preventive measures to check its spread can hardly be relied upon to be completely successful. In the early and most contagious phase of the infection the patient may require attention every half-hour, and in practice it seems impossible to institute measures which will with certainty prevent the infection of other children in a ward. Where practicable, therefore, the patient should be isolated. When this cannot be done those in attendance on the patient must not handle other children, and in particular must have nothing to do with the preparation of their meals. To protect herself the nurse should wear surgical gloves. In houses the lavatory should not be used by infected people. It is customary to obtain three negative tests of the stools before regarding the case as free of infection.

Remedial treatment should be undertaken in the expectation that the worst of the disease will be over in three days. Thus the indications are to relieve pain and prevent dehydration. The customary anti-dysenteric treatment by repeated doses of sodium and magnesium sulphates does

neither of these things and is best avoided, nor should any other form of aperient be prescribed. Opium is the most useful drug in cases of this disease, and it may be taken with bismuth or a reliable brand of kaolin. Fluids should be given so far as the vomiting permits, and as soon as there is a desire for food a bland diet may be ordered. In debilitated patients special measures to combat the dehydration may be required. The use of anti-dysenteric serum is neither necessary nor of value in cases of Sonne dysentery.

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THE ABSENCE OF ANTI-GONADOTROPIC SUBSTANCES IN THE BLOOD SERUM OF MAN INJECTED WITH GONADOTROPIC EXTRACTS

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Recent work has demonstrated that the prolonged administration of gonadotropic hormones to animals produces a state of insensitivity, so that the initial hypertrophy of the gonads disappears and may even be followed by atrophy (Collip, 1934). Moreover, the serum of an animal injected for about three months with a gonadotropic extract acquires the property of inhibiting the action of the gonadotropic extract when both are separately injected into a test animal, such as the immature rat; when the serum alone is injected into a normal adult animal it may cause atrophy of the reproductive organs (Rowlands, 1937). These phenomena are due to the production of anti-gonadotropic substances in the blood as a result of the continued administration of the gonadotropic extract.

These facts might be of clinical importance in the treatment of patients for a prolonged period with gonadotropic hormones. Should such anti-gonadotropic substances be formed in the human it would appear advisable to intersperse rest periods of several months, during which the patient receives no treatment, to enable him to re-acquire sensitivity and to prevent any possible damage to the gonads. On the other hand, should there be no indication of the production of such substances as a result of prolonged treatment these rest periods would be unnecessary. In the elucidation of this problem samples of blood from nine patients with undescended testes who were receiving treatment with gonadotropic hormones were tested for anti-gonadotropic activity.

Methods

The patients were injected intramuscularly twice a week with extracts of human urine of pregnancy (pregnyl or antuitrin S) or with extracts of pig anterior pituitary (ambinon or antuitrin gonadotropic). Details of their treatment are given in Table I.

TABLE I.—*The Treatment of the Patients with Gonadotropic Preparations*

Case No.	Age (Years)	Preparation	Dose (Rat Units, R.U.) twice weekly
1	19	Pregnyl	1,000
2	12	Pregnyl	500 for first 9 weeks, then 1,000
7	14	Pregnyl	1,000
8	20	Pregnyl	1,000
9	12	Pregnyl	500
10	14	Pregnyl	500
5	13	Antuitrin S	200
3	14	Ambinon	50
4	10	Antuitrin gonadotropic	30 for first 14 weeks, then 50 for 9 weeks

Where possible a sample of blood was obtained before treatment and thereafter at intervals of one to two months for as long as was practicable in each case (Table II). About 20 c.cm. of blood was obtained from the basilic vein, and kept in a sterile flask at 0° C. until the following morning, when the serum was separated. The activity of the serum was measured by its capacity to neutralize, in the immature rat, the power of a gonadotropic extract similar to that injected into the patient. Each sample of serum and gonadotropic extract was injected into a group of five immature female rats (40–50 grammes) once daily for five days; the two injections were given on opposite sides of each animal. The rats were killed twenty-four hours after the last injection, and the ovaries dissected, fixed in Bouin's fluid, and weighed the following day from 70 per cent. alcohol.

A gonadotropic extract from human urine of pregnancy (UP10) was used in testing, of which a total dose of 1 mg., divided over five days, produces ovaries weighing 35 mg. in the immature rat. The weight of the normal ovaries of rats of this body weight is 10–12 mg. The activity of the other extracts used is given in Table II.

TABLE II.—*The Effect of Serum from Patients Treated with Gonadotropic Extracts on the Action of Similar Extracts on the Immature Rat Ovary*

Case No.	Date of Sample after First Injection (Weeks)	Assay			
		Substance	Amount (mg.)	Amount of Serum (c.cm.)	Weight of Rat Ovaries (mg.)
1	0	UP10	1	1.25	34
1a	5	"	1	1.25	44
1b	11	"	1	1.00	27
2	11	UP10	1	1.25	40
2a	15	"	1	2.00	33
2b	19	"	1	1.50	22
2c	25	"	1	1.90	26
2d	29	"	1	1.50	30
7	7	UP10	1	1.50	29
8	13	UP10	1	1.00	39
8a	20	"	1	0.80	47
8b	28	"	1	0.75	32
9a	6	UP10	1	1.00	34
9b	13	"	1	1.00	34
5	0	—	—	1.50	12
5a	4	UP10	1	0.75	32
5b	10	"	1	1.00	39
—	—	Saline extract of pig Ant. pit. AP43D	1 gm.	—	43
3	16	"	1 gm.	1.25	65
—	—	AP43D	25	—	27
3a	21	"	25	1.50	44
—	—	AP44	25	—	32
3b	26	"	25	1.50	35
4a	13	AP43D	25	0.75	32
4b	19	AP44	25	1.90	39
—	—	AP51	25	—	21
9 & 10	0	"	25	2.50	27