are encouraged. The newly healed skin may feel tight, but this can be relieved by rubbing in lanolin, as recommended by Wakeley (1942). The hand and wrist may temporarily feel weak as a result of the immobilization of the muscles.

FIG. 5.—Burns of hands of man aged 32 immobilized for 3 weeks; grafted and immobilized for 10 days.

FIG. 6.—Same patient as Fig. 5. Movements 8 weeks after accident.

Discussion

It has been found possible to treat burns by methods similar to those successfully applied to the treatment of other wounds. Burns are particularly liable to become infected, on account both of their size and of the impossibility of removing dead tissue. The incidence of infection can be reduced only by exposing the lesions as infrequently as possible. In a busy general hospital dressings can be carried out with proper aseptic precautions only if they are done at long intervals, thus permitting time and care to be taken over them. Where infection does take place systemic disturbances resulting from it may be controlled by immobilization of the affected region. The benefits to be derived from the immobilization of a series of infected burns have been described by Roulston (1941). Immobilization of the hand does not necessarily lead to stiffness, provided care is taken to place the fingers in a good position. Nevertheless, it would be unwise to continue such immobilization for periods exceeding 4 to 6 weeks.

It is sometimes stated that part of the treatment in the later stages of a deep burn should include the cleaning of the raw areas by means of frequent wet dressings before applying skin grafts. It seems doubtful whether a case so treated, with all the risks of cross-infection attendant on the frequent changes of dressings, fares any better than one given a single cleaning just before laying on the grafts. The mere presence of bacteria upon the surface of the wound is no indication as to the possibilities of success with skin grafts.

When a large number of cases have to be dealt with simultaneously there is a great advantage in being spared the

necessity for the frequent changing of dressings in all the cases. A case of extensive burns is in need of careful and continuous nursing during the first few days. Such attention is the more easily given when there is no need to interfere with the local lesion.

Summary

The principles which govern the treatment of burns as wounds are outlined.

A simple technique of treatment, which includes the use of plaster-of-Paris casts for burns of the hand and forearm, is described. If plaster is applied, elevation of the limb is essential, to prevent oedema, and the hand must be placed in the correct "position of function."

The value of immobilization, infrequent dressing, and the prevention of oedema is pointed out.

Burnt hands do not become stiff merely as a result of immobilization, provided that this is carried out correctly for a limited period.

In spite of the presence of infection with *Ps. pyocyanea*, skin grafts will "take" on granulating burns that are dressed infrequently.

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SULPHAGUANIDINE IN NEONATAL EPIDEMIC GASTRO-ENTERITIS

BY

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Since the virtues of sulphaguanidine in the treatment of alimentary infections were discovered by Marshall and his colleagues (1940, 1941) this sulphonamide compound has won general recognition as the most effective drug hitherto employed in the treatment of a variety of intestinal infections. It has greatly lessened the severity of the symptoms and the duration of illness in the various types of dysentery, and has been very successful in infective gastro-enteritis in infancy and childhood. The principal object of this paper is to record the excellent results achieved with this drug in epidemic gastro-enteritis in the newborn, the most lethal of the commoner neonatal infections.

Epidemiology of Neonatal Gastro-enteritis

Outbreaks of infective gastro-enteritis occur periodically in all maternity hospitals in which opportunities for cross-infection among the infants arise owing to imperfect architectural and nursing arrangements. In all epidemics the vast majority of affected infants are bottle-fed. The publicity given to the prevalence of the disease in the maternity hospitals in New York City by Rice and his collaborators (1937) has focused attention on the appalling waste of infant life in maternity hospitals from this preventable alimentary infection. These workers reported 505 cases of epidemic diarrhoea in 11 maternity hospitals in New York in the 2½-year period July, 1934, to Dec., 1936, the incidence being the very high one of 14%. The earlier literature contains surprisingly few references to such a common disease. The paper based on the largest series of cases, and the only one of note emanating from this country, was published from this hospital in 1936

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by Craig. The impetus given to the study of the disease by Rice *et al.* has accounted for the appearance of numerous publications in the U.S.A. (Abramson and Frant, 1938) and this country (Ormiston, 1941; Crowley *et al.*, 1941) in the last few years. These have shown that few maternity hospitals are exempt from periodic epidemics of neonatal gastro-enteritis. The complacent attitude towards this grave infection is attributable to the long intervals which usually occur between successive outbreaks. The causal bacterium or virus still eludes identification. Some believe, however, that normal inhabitants of the bowel may cause the disease by assuming pathogenic properties, as in epidemic gastro-enteritis in lambs. Outbreaks have been attributed to *B. proteus vulgaris*, *B. coli mutabile*, *B. lactis aerogenes*, and other commensals. Special bacteriological assistance has been given in many of the cases in this series, and no organisms of the enteric or dysenteric groups or any other pathogens have ever been isolated. Rice *et al.* and others, particularly in the U.S.A., believe that this disease is confined to the first month of life, but it may be that feeble resistance to infection in the early weeks rather than a distinctive aetiology accounts for the more severe features of gastro-enteritis in the newborn.

Incidence and Mortality Rate

Six epidemics and a few sporadic cases, comprising a total of 102 infants with gastro-enteritis, have occurred in the Simpson Maternity Hospital, Edinburgh, during the three years 1940-2. For some unaccountable reason there were more epidemics and a higher incidence of the disease during this period than for many years. The incidence was approximately 1.5%. There were 50 mature and 52 premature infants, the incidence in premature infants thus being very much higher than in mature infants. Universal bottle-feeding is the chief reason for the greater incidence in premature infants. The nurseries in this hospital are visited daily by an experienced paediatric staff, and a clinical chart and a record of each infant are kept. A series of uniform observations has thus been made, and it is unlikely that more than a few very mild cases have been overlooked. Cases of gastro-enteritis complicating thrush infection of the upper alimentary tract have been carefully excluded. A post-mortem examination was made by Dr. Agnes Macgregor in all of the 58 fatal cases. Fig. 1 shows the mortality rate in each of the three

FIG. 1.—Mortality rate in gastro-enteritis before and after the introduction of sulphaguanidine.

years, 1942 being divided into the period before the introduction of sulphaguanidine therapy and the period after its commencement. The dramatic fall in the mortality rate in 1942 can be attributed almost entirely to the introduction of this drug. The greatly improved results did not justify the use of controls. The accompanying table shows the relation of the mortality to the maturity in treated and untreated infants.

Table showing Relation of Mortality to Maturity in Infants Treated with Sulphaguanidine and those Untreated

		Treated		Untreated	
		No.	Mortality	No.	Mortality
Mature infants—over 5½ lb.	..	11	0	39	69%
Premature infants:					
(a) 5½–4 lb., incl.		11	0	19	84%
(b) Under 4 lb.		8	38%	14	86%

Clinical Features

The first signs of gastro-enteritis usually appear after the first week of life, but they occasionally develop earlier. A sudden failure of appetite is the first sign of illness. Diminished vitality, a tired sickly appearance, and pallor follow within a few hours. Diarrhoea as a rule develops within a few hours of the onset, but may be delayed for 24 hours. The stools are watery in most cases. They are usually yellow, but may be greenish, and mucus is occasionally present. Blood sometimes appears in severe cases. The stools frequently exceed 10 a day and are sometimes uncountable. Signs of dehydration usually appear by the second day, and rapidly become severe in the absence of appropriate treatment. Approximation and overlapping of the cranial bones with a reduction in the size of the anterior fontanelle are often earlier signs of dehydration than a pinched facies. The weight course shows a sudden reversal, and the loss amounts to several ounces daily. Fever is an inconstant feature, but there is often a moderate degree either at the outset or at a later stage. Vomiting is absent in many cases; it tends to be a much more pronounced feature in some epidemics than in others, and the diarrhoea is sometimes milder when the vomiting is severe, suggesting a predominantly upper alimentary infection. Abdominal distension is common after the first two or three days. Screaming attacks may be caused by colic.

In the absence of appropriate treatment the dehydration and weight loss progress rapidly, and pallor, weakness, and anorexia soon become extreme. Sclerema, a grave terminal sign, occasionally supervenes. In a state of such extreme weakness the aspiration of vomitus readily occurs, causing bronchopneumonia, which is often the terminal event.

Treatment

Not a moment should be lost in starting treatment in such an acute disease; for severe toxæmia, a prolonged illness, much difficult nursing, and possibly a fatal issue may thus be forestalled. Even such a potent drug as sulphaguanidine cannot be expected to give good results when it is not administered until the illness has lasted several days; but it is never too late to introduce it in liberal doses, as therein lies the main hope of recovery.

(a) *General.*—The following routine, in conjunction with sulphaguanidine therapy, has given very satisfactory results. It has the virtue of simplicity.

An initial purge has been dispensed with when diarrhoea has become established. Milk is entirely withheld, and 5% lactose or dextrimaltose water is given *ad lib.* every one and a half hours. If fluid amounting to 4 oz. per lb. of birth weight per day is not taken, the total must be made up to this amount by gavage. Such an ample fluid intake is essential to replace the excessive loss, and to ensure adequate renal elimination of that part of the sulphaguanidine absorbed from the gut and prevent its crystallization in the renal tubules and urinary tract. When there is much vomiting the sugar should be given in 1/5 normal saline instead of water. In severe cases the fluid may have to be introduced by stomach-tube for several days. A thin male catheter (No. 18 French) attached to the barrel of a 10-c.cm. or 20-c.cm. syringe may be used for this purpose. Only sugar and water or diluted saline should be given until the appetite returns; this may not occur for from several days to a week. It is a great mistake to introduce any milk until the general condition shows considerable improvement and the feeds are taken with some eagerness. Apprehension is often shown over such prolonged withholding of milk, but in the absence of a return of appetite there is no indication whatever for giving it sooner, and better progress is made without it.

The above regime, coupled with sulphaguanidine therapy, obviates the need for the parenteral administration of fluid except on rare occasions. Only one of the 30 cases treated with adequate doses of sulphaguanidine was given fluid parenterally. The frequent subcutaneous administration of saline was a routine procedure with former methods of treatment, and intravenous fluid was sometimes required in addition. The comparative ease with which severe dehydration can be prevented when sulphaguanidine is given is a measure of its efficacy.

The necessity for introducing milk gradually when the appetite returns must be emphasized. It is customary in this

hospital to give it in alternate feeds in the form of either half-strength breast-milk or 1/12 sweetened condensed milk. The number of dilute milk feeds is slowly increased until milk is being given at every feed. Then the feeds are gradually strengthened according to the demands of the appetite. When convalescence is well established fresh milk should be substituted for sweetened condensed milk. The re-establishment of milk feeding in a premature infant is shown in Fig. 2.

FIG. 2.—Clinical chart of baby, birth weight 5½ lb. Epidemic gastro-enteritis developed on the eleventh day. The chart shows the course of the weight, temperature, and stools, and the treatment by starvation and with sulphaguanidine.

(b) *Sulphaguanidine*.—It is of the utmost importance to give full doses. Owing to its slow absorption from the bowel, and the necessity for achieving a high concentration therein, larger doses of this sulphonamide should be given than of the others. In this series of cases the mature infants received an initial dose of 0.75 g. tabloid sulphaguanidine, B.W. & Co., followed by 0.5 g. every four hours, and premature infants an initial dose of 0.5 g. followed by 0.25 g. every three hours. The latter dose is well tolerated by very premature infants provided ample fluid is given. These doses are continued for several days until there is pronounced clinical improvement with a return of appetite. It is then gradually reduced, being stopped a few days later (see Fig. 2). It was continued for as long as a fortnight in some of the cases in this series.

(c) *Prophylactic*.—Immediate isolation of all infants suspected of infective gastro-enteritis is an essential precaution in maternity hospitals. This dangerous disease should be suspected when an infant which has been feeding and progressing satisfactorily loses its appetite and shows diminished vitality and pallor. Confirmation of the diagnosis should be followed by strict precautions, to limit the extent and duration of the outbreak. There should not be any new admissions to the nursery in which the case occurred until all the contacts have been discharged. These contacts should be watched very closely for the first signs of the disease. Unless such strict measures to stamp out the infection are taken at its first appearance—and they are often neglected—an epidemic which will drag on for weeks or months may occur. Frant and Abramson (1938) have drawn up an excellent code of hygiene for the prevention and control of this and other infections in hospital nurseries.

Toxicity of Sulphaguanidine

Sulphaguanidine is one of the less toxic sulphonamides owing to its slow absorption from the bowel. This property enables very much higher concentrations to be attained in the bowel than in the circulation and other tissues of the body. About 20 to 25% of the drug is excreted in the urine. Acetylation does not occur in the intestine, but 20 to 50% of the assimilated drug is conjugated. After oral administration the maximal

concentration in the blood is reached in about four hours, and most of the drug is excreted within 24 hours. Stickney, Heilman, Bargen, and Dearing (1942) found, in a series of 70 patients who were mostly adults, that with an average dose of 0.1 g. per kilo of body weight given every four hours the maximal concentration of free drug in the blood usually did not exceed 4 mg. per 100 c.cm., and seldom reached the level of 6 mg. per 100 c.cm.

The maintenance of a high fluid intake is important to eliminate the possibility of excessive concentration of the drug in the urine, with crystallization in the urinary tract. The urine of infants receiving the drug often contains a few characteristic crystals in the form of parallelogrammic plates, and needles occurring singly and in sheaves, but these should never be abundant.

A recurrence of frequent defaecation, which appeared to be a delayed toxic effect of sulphaguanidine on the bowel, occurred in 8 of the 30 infants. This phase began 8 to 10 days after starting with the drug, and subsided a few days later. The stools were small in bulk and normal in appearance. In some cases the drug was still being given, in others it had been discontinued for a few days. The diarrhoea had usually been controlled for a few days before the increased frequency of defaecation recurred. A return of frequent stools, provided they are normal, is no indication for continuing or resuming either drug or starvation treatment, as convalescence is uninterrupted.

In their series of 70 cases, mentioned above, Stickney *et al.* observed the following undesirable reactions: nausea 4, dermatitis 3, headache 2, indigestion 2, vomiting 1, and haematuria 1. The estimation of toxicity in the newborn must of course depend on the observance of signs such as dermatitis, vomiting, and haematuria. Agranulocytosis seems to be a rare complication with sulphaguanidine, but should always be watched for on account of its seriousness.

Comment

In computing the comparative death rates in cases treated with sulphaguanidine and those untreated, four infants who received the drug have been excluded. These four were among the first to be treated with the drug, and were given only half the dose which was afterwards found to be necessary for an optimal effect. Moreover, treatment of two of them was not begun until the fourth day. All four died, and it seems irrational, from a comparative standpoint, to include them in the group of cases all of which were treated in the standard manner recommended here.

The mortality rate in the series of 30 cases treated with sulphaguanidine would probably have been still lower if there had not been so many very premature infants. There were 11 mature and 19 premature infants, and 8 of the premature infants weighed less than 4 lb. at birth. The three fatal cases all belonged to the latter group. In addition to extreme prematurity two of the infants who died had complications which might have determined the fatal issue. One showed clinical signs of intracranial haemorrhage which were confirmed at necropsy, when both subdural haemorrhage from a fairly large tentorial tear and subarachnoid haemorrhage were found. It is reasonable to assume that this complication substantially reduced the chances of recovery from the gastro-enteritis which supervened on the tenth day. The other infant seemed to be responding well to treatment when its condition suddenly deteriorated, six days after the onset of the disease, and signs of bronchopneumonia developed. A necropsy showed that aspiration of vomitus had caused the pneumonia. As this infant was improving and beginning to feed well it would probably have recovered if the unfortunate accident of aspiration, which is commoner in premature infants, had not occurred.

Much work remains to be done on the action of various sulphonamide compounds in neonatal gastro-enteritis. More experience with sulphaguanidine is needed, and the action of sulphapyridine, sulphathiazole, and other compounds requires investigation. Sulphapyridine and sulphathiazole are valuable therapeutic agents in bacillary dysentery and some other alimentary infections, and may be beneficial in neonatal gastro-enteritis, but they are likely to prove more toxic to the newborn infant than sulphaguanidine.