designed to relieve vasospasm or to promote vasodilatation will be valuable, particularly at an early stage. When there is clinical evidence of raised tension in the anterior tibial compartment surgical decompression would seem to be reasonable, if by so doing survival of the limb is not prejudiced.

Summary

Two cases in which the clinical features of the anterior tibial syndrome followed arterial embolism are described. Pathogenesis, diagnosis, and treatment are briefly discussed.

I am indebted to Dr. E. T. Baker-Bates (Case 1) and to Dr. C. S. McKendrick (Case 2) for permission to report these cases.

REFERENCES

- Carter, A. B., Richards, R. L., and Zachary, R. B. (1949). *Lancet*, 2, 928.
 Edwards, J. W. L., Jones, N. B., McConnell, R. B., Pemberton, H. S., and Watson, D. C. (1952). *British Medical Journal*, 2, 808.
 Ferguson, F. R., and Liversedge, L. A. (1954). *Ibid.*, 2, 333.
 Haimovici, H. (1950). *Angiology*, 1, 20.
 Horn, C. E. (1945). *J. Bone Jt. Surg.*, 27, 615.
 Horn, J. S., and Seviitt, S. (1951). *Ibid.*, 33B, 348.
 Hughes, J. R. (1948). *Ibid.*, 30B, 581.
 — (1949). *Lancet*, 2, 1150.
 Mufson, I. (1952). *Angiology*, 3, 392.
 Pearson, C., Adams, R. D., and Denny-Brown, D. (1948). *New Engl. J. Med.*, 239, 213.
 Phalen, G. S. (1948). *Ann. Surg.*, 127, 112.
 Psaki, R. C., and Shields, C. D. (1952). *Arch. phys. Med.*, 33, 153.
 Sirbu, A. B., Murphy, M. J., and White, A. S. (1944). *Calif. west. Med.*, 60, 53.
 Tillotson, J. F., and Coventry, M. B. (1950). *Proc. Mayo Clin.*, 25, 223.
 Vogt, P. R. (1943). Quoted by Horn (1945).

THE ROLE OF SULPHONAMIDES IN THE INFECTIVE DIARRHOEAS OF AFRICAN CHILDREN

BY

LORNA G. MACDOUGALL, M.B., Ch.B., D.C.H.
 Medical Officer, King George VI Hospital, Nairobi

The problem of diarrhoea in infancy and childhood has been the subject of much research; owing to the multiplicity of causes a very careful clinical, bacteriological, and biochemical assessment may be required before an accurate diagnosis can be made and effective treatment selected.

In many tropical and backward countries immediate laboratory services are not always available, medical personnel is limited, and clinical examination alone may fail to reveal the presence of more than one disease. The discovery of otitis media or pneumonia in a child presenting with diarrhoea does not preclude the fact that there may be a coexisting bacillary dysentery even in the absence of blood and mucus in the stools.

The problem of selecting treatment is equally complex if one is to provide a satisfactory standard of therapy within the economic limits of a rapidly developing community.

In infantile gastro-enteritis in which no pathogenic organisms are isolated from the stools, sulphonamides are considered to be of doubtful value, and a regime of graduated feeding and parenteral fluids (with or without the more recent antibiotics) still forms the basis of treatment. In bacillary dysentery sulphonamides are widely used and the "non-absorbable" compounds have been accepted as the standard treatment in many countries.

Present Investigation

The original object of the present experiment had been to assess the efficacy of the "absorbable" sulphonamide sulphadimidine ("sulphamezathine"), as compared with the "non-absorbable" compounds, sulphaguanidine and phthalylsulphathiazole ("thalazole"), in the treatment of bacil-

lary dysentery in children. As it proved impracticable to await the result of a stool culture before beginning treatment, it was decided that all cases presenting with diarrhoea as their main symptom should be included in the trial.

Although the scope of the trial was thus widened to include many possible diseases and the scientific limitations were fully realized, it was hoped that the results might be of some value to others in assessing the efficacy of sulphonamides in the treatment of infantile dysentery and non-dysenteric diarrhoea, and establishing, if possible, the drug of choice.

Sulphaguanidine has become well established in the treatment of bacillary dysentery and is recommended as the most suitable drug in tropical countries because there is little or no danger of crystalluria, and it has the advantage of rarely causing unfavourable side-effects (Boyd, 1951; Scadding, 1944). It is considered most effective in the early stages of an acute attack, but of least value when treatment is started late in the illness (Lyon, 1943; Brewer, 1943). This is of considerable practical importance in communities who do not seek medical advice until local remedies have failed and the disease is in an advanced or chronic stage. A further disadvantage so far as children are concerned is the high dosage of sulphaguanidine which is recommended. In an acutely ill and dehydrated child there is often difficulty in ensuring that the appropriate dose is swallowed.

Poth and Ross (1944) claim that phthalylsulphathiazole is highly specific in Flexner dysentery and have also proved it of value in the treatment of non-dysenteric diarrhoea. This, however, has not been borne out by Brodie *et al.* (1946), who found that it took longer to effect a cure with phthalylsulphathiazole than with either sulphaguanidine or controls, but that it reduced considerably the number of bacteriologically positive cases during convalescence. Both sulphaguanidine and phthalylsulphathiazole have the disadvantage of failing to control a parenteral or secondary infection which may complicate or perpetuate the state of diarrhoea.

Since it is known that the dysentery organisms inhabit the mucous membrane lining of the intestinal tract, the "absorbable" sulphonamides have the advantage of reaching the source of infection both through the lumen of the gut and via the blood stream (Hardy and Watt, 1944).

From previous experiments (Hardy, 1945) sulphadiazine has been recommended as the sulphonamide of choice in bacillary dysentery, with sulphadimidine of almost equal efficacy. Watt and Cummins (1945), however, place sulphadimidine in the undesirable class of sulphonamide owing to the greater percentage of toxic reactions observed in their series.

Although the possibility of renal complications with "absorbable" sulphonamides must always be borne in mind, particularly in hot climates, sulphadimidine is reported to be more highly soluble in all urines than sulphadiazine (M.R.C., 1945), and was therefore chosen for use in the present trial.

Realizing, therefore, the various advantages and disadvantages of the drugs employed, the experiment was designed as follows:

Selection of Cases.—All infants and children entering the medical wards of King George VI Hospital, Nairobi, with the main presenting symptom of diarrhoea, were admitted to the series and each succeeding case was treated with phthalylsulphathiazole, sulphadimidine, and sulphaguanidine respectively.

Clinical Assessment.—The severity of each case on admission was classified as follows: mild, moderate, severe, or moribund. As it was rarely possible to obtain an accurate history from the parents regarding the length of illness and the number or character of the stools passed daily, the clinical assessment was made on the general appearance, toxicity, and hydration of the patient. This assessment and the subsequent daily records of progress were made personally to ensure uniformity throughout the series. The groin temperature was recorded twice daily.

Dosage.—Although all children in the present series were weighed on admission, it was realized that this could not always be done in out-patient departments and the more isolated hospitals. The scheme of dosage was therefore assessed according to age (Table I) and appropriate adjust-

TABLE I

	Phthalylsulphathiazole and Sulphadimidine	Sulphaguanidine
Adults	4 g. daily	10 g. daily
8-12 years	3 g. "	8 " "
4-8 "	2.5 g. "	6 " "
2-4 "	2 g. "	4 " "
6 months-2 years	1.5 g. "	3 " "
0-6 months	1 g. "	2 " "

TABLE II

	Phthalylsulphathiazole	Sulphadimidine	Sulphaguanidine
No. of cases	107	107	103
Clinical condition on admission:			
Mild	16	26	21
Moderate	38	23	31
Severe	31	40	30
Moribund	22	18	21

ments were made for emaciated and undernourished children. Each dose was given in the form of a suspension and the appropriate dose administered at six-hourly intervals.

A total of 317 African children were treated, with an average age of 1 year and 8 months. Table II shows the distribution of cases and the clinical condition on admission.

Results

Treatment was limited to a seven-day period, and if there was no response at the end of this time the trial drug was discontinued and other therapy instituted.

The response to treatment is shown in Table III; although the total number of cases in the sulphaguanidine series fit for discharge within the trial period was fewer than in either the phthalylsulphathiazole or the sulphadimidine series the figure is not significant.

In an assessment of the bacteriological results (Table IV) phthalylsulphathiazole appeared less effective in the cases of proved bacillary dysentery, but gave a higher percentage

TABLE III

	Phthalylsulphathiazole	Sulphadimidine	Sulphaguanidine
No. fit for discharge between 3rd and 6th days	24	30	17
No. fit for discharge on 7th day	49	44	46
No. still febrile on 5th, 6th, or 7th day	26	26	35
Total No. discharged within trial period	73 (68.2%)	74 (69.1%)	63 (61.1%)

TABLE IV

	Phthalylsulphathiazole	Sulphadimidine	Sulphaguanidine
Total No. with proved shigellae	50 (46.7%)	48 (44.9%)	48 (46.6%)
Shigellae present Day 1	44	41	43
Negative culture Day 5	17 (38.6%)	21 (51.2%)	20 (46.5%)
No. pathogens Day 1 but shigellae isolated Day 5	6	7	5
Salmonellae, <i>B. proteus</i> , or <i>B. paracolon</i> isolated Day 1	18	22	19
Negative culture Day 5	10 (55.5%)	8 (35.4%)	9 (47.3%)
No pathogens throughout	39	37	36
Total No. deaths	15	16	13
No. showing shigellae	9	8	7

of negative cultures in the non-dysenteric group, whereas sulphadimidine showed a higher percentage of negative cultures in the Shigella group and less in the non-dysenteric series. The results with sulphaguanidine were similar in both groups. These figures, however, are not significant, and it can be said that the three drugs are of equal efficacy as regards both sterilization of stools and general clinical improvement.

Of the Shigella organisms isolated throughout the series, 70% were *S. flexneri*, 11% *S. schmitzi*, 4% *S. sonnei*, and 15% were classified as atypical Shigella organisms. No difference was noted in the efficacy of the three trial drugs against these different strains, and the few Sonne infections encountered were no more resistant to treatment than the Flexner or Schmitzi infections or the atypical organisms.

No oliguria, anuria, or other obvious toxic reactions were encountered with any of the drugs under trial, and the number of parenteral infusions required was the same for each group.

In the sulphadimidine series it was noted that other chemotherapy was required in a significantly smaller number of cases (Table V) than with either of the "non-absorbable" compounds, despite the fact that the incidence of parenteral complications was approximately the same in all groups.

TABLE V

	Phthalylsulphathiazole	Sulphadimidine	Sulphaguanidine
No. requiring infusions	35	32	35
"therapy" other chemo-	33	14	29

TABLE VI

Parenteral Infections	Phthalylsulphathiazole			Sulphadimidine			Sulphaguanidine		
	No. of Cases	No. Showing <i>B. proteus</i> , <i>B. paracolon</i> , or <i>Salmonellae</i>	No. Showing Shigellae	No. of Cases	No. Showing <i>B. proteus</i> , <i>B. paracolon</i> , or <i>Salmonellae</i>	No. Showing Shigellae	No. of Cases	No. Showing <i>B. proteus</i> , <i>B. paracolon</i> , or <i>Salmonellae</i>	No. Showing Shigellae
Pneumonia	13	1	7	16	1	10	11	1	5
Pulmonary tuberculosis	6	—	4	6	—	2	3	—	2
Bronchitis	5	—	2	5	—	2	1	—	1
Upper respiratory tract infection	3	1	—	—	—	—	3	1	2
Otitis media	1	1	—	—	—	—	2	—	2
Thrush	3	—	1	4	—	2	2	—	—
Conjunctivitis	2	1	—	—	—	—	—	—	—
Polio-myelitis	—	—	—	2	1	1	—	—	—
Laryngitis	—	—	—	1	—	1	—	—	—
Cellulitis	—	—	—	1	—	1	—	—	—
Pyelitis	—	—	—	1	—	1	—	—	—
Malaria	—	—	—	1	—	1	—	—	—
Encephalitis	—	—	—	—	—	—	1	—	1
Nephritis	—	—	—	—	—	—	—	—	—
Total	33	4	14	38	2	21	23	2	14

Table VI gives an indication of the variety of parenteral infections encountered among children presenting with diarrhoea and shows the incidence of dual infections among the cases of proved bacillary dysentery. From these figures it has been estimated that of the 146 cases of proved bacillary dysentery throughout the entire series 33.5% had a co-existing parenteral infection.

Summary and Conclusions

In tropical countries where diarrhoea is a common presenting symptom in children, and large numbers of cases are seen by a limited number of medical personnel, the problem of making a precise diagnosis can be very difficult, particularly if hospital and laboratory facilities are not immediately available.

Under these circumstances treatment must of necessity be simple, giving the optimum facilities to the greatest number of patients, whether treatment be undertaken in out-patient dispensaries, clinics, or district hospitals.

A survey was therefore made of 317 cases of diarrhoea in African children, each succeeding case being treated with phthalylsulphathiazole, sulphadimidine, and sulphaguanidine respectively, with the aim of establishing the relative merits of the "absorbable" and "non-absorbable" sulphonamides in the treatment of bacillary dysentery and non-dysenteric diarrhoea.

The average age group of the children in the series was 1 year and 8 months and the causes of the diarrhoea fell roughly into five groups: (1) proved bacillary dysentery; (2) enteric infections where salmonellae, *B. proteus*, or *B. paracolon* were isolated on stool culture; (3) enteric infections with no pathogenic organisms on stool culture and no obvious parenteral infections; (4) parenteral infections; (5) mixed enteral and parenteral infections.

It was found that all three drugs were equally effective in cases where *Shigella* organisms were isolated from the stools and gave similar results in the enteric infections of non-dysenteric origin.

If diarrhoea was found to be secondary to a parenteral infection or if mixed infections were present, sulphadimidine had a definite advantage in that, in many cases, it controlled both infections without additional chemotherapy.

Toxic reactions such as oliguria or anuria were not encountered with any of these drugs under trial, and no other undesirable side-effects were noticed.

The trial period for each drug was limited to seven days, by which time 68.2% of the cases on phthalylsulphathiazole, 69.1% on sulphadimidine, and 61.1% on sulphaguanidine were fit for discharge.

A point of considerable importance was the relatively high incidence of dual infections, showing that it was not enough to attribute the diarrhoea to an obvious parenteral infection or yet to conclude that the majority of cases would be dysenteric in origin, since the two might well coincide, with the symptoms of one sometimes overshadowing those of the other.

Therefore, in reviewing all aspects of the problem of diarrhoea in African children, and bearing in mind that not all cases are admitted to hospital or seen and treated by fully qualified medical personnel, it is essential to provide a regime of treatment which combines efficiency with ease of administration, simplicity, safety, and cheapness.

Since the "wide spectrum" antibiotics are not always available for routine use and the "non-absorbable" sulphonamides require the addition of penicillin or other antibiotics in the case of mixed infections, it is suggested that sulphadimidine could be used as a valuable general-purpose sulphonamide in the diarrhoeal diseases of African childhood.

My thanks are due to the Director of Medical Services, Kenya Colony, for permission to publish; to Dr. E. R. N. Cooke, Medical Research Laboratory, Nairobi, for the bacteriological work; and to the sisters and staff of King George VI Hospital, Nairobi, for their co-operation and help.

REFERENCES

- Boyd, J. S. K. (1951). *British Medical Journal*, **1**, 1440.
 Brewer, A. E. (1943). *Ibid.*, **1**, 36.
 Brodie, J., Cook, R. P., Drysdale, C. F., and McIntosh, D. G. (1946). *Ibid.*, **1**, 948.
 Hardy, A. V. (1945). *Publ. Hlth Rep. (Wash.)*, **60**, 1037.
 — and Watt, J. (1944). *J. Amer. med. Ass.*, **124**, 1173.
 Lyon, G. M. (1943). *J. Lab. clin. Med.*, **28**, 645.
 M.R.C. (1945). War Memorandum No. 10, p. 12. London.
 Poth, E. J., and Ross, C. A. (1944). *J. Lab. clin. Med.*, **29**, 785.
 Scadding, J. G. (1944). *Lancet*, **1**, 784.
 Watt, J., and Cummins, S. D. (1945). *Publ. Hlth Rep. (Wash.)*, **60**, 1355.

CHRONIC RECTAL BLEEDING DUE TO MILK

BY

F. P. ANTIA, M.D.Bom., M.S.Ill., M.R.C.P.Lond.

Associate Physician, B. D. Petit Hospital; Consulting Gastro-Enterologist, Tata Memorial Hospital and B. J. Wadia Hospital for Children, Bombay

AND

S. H. COOPER, M.B., B.S.

The following case of rectal bleeding probably due to an allergy to milk may be found of interest.

Case Report

A woman aged 38 was admitted to the B. D. Petit Hospital, Bombay, on November 15, 1953, with a history of bleeding per rectum for the past seven years. She had been operated on for both internal and external piles about six and a half years previously. She had been passing two stools a day, semi-solid, with no evidence of mucus. Blood was passed every day either mixed with stools or after the act of defaecation as frank blood or blood clots. The bleeding was not related to straining. She had been under observation in different hospitals for long periods, but bleeding per rectum persisted. There was no previous history of dysentery or diarrhoea. Her menstrual history was normal at first, but for the last three years she had a loss every three or four months for two or three days. Her father had severe asthma, and her son had allergic rhinitis. The patient had been married for 18 years and had twins, a boy and a girl, aged 17. Her husband was short-tempered, and at times used physical violence; consequently her married life was not happy.

Physical examination showed a well-built woman. Her blood pressure was 135/90 mm. Hg. No abnormality was detected in the cardiovascular, alimentary, or respiratory systems. The liver and spleen were not palpable. Vaginal examination showed no abnormality. A blood count showed: haemoglobin, 75%; red cells 3,100,000; white cells, 8,200 per c.mm. (polymorphs 82%, lymphocytes 18%). The bleeding time, coagulation time, platelet count, prothrombin time, and fragility tests were within normal limits. Seven years ago, when the patient was admitted to the same hospital, malingering was suspected because her husband was not treating her well at home, and traumatic bleeding from the rectum was supposed to be her device to stay in hospital. This time, however, every stool passed was semi-solid with mucus and frank blood not too well mixed. Microscopical examination showed many red blood cells. Urine analysis, gastric analysis and barium meal examination showed nothing abnormal. A barium enema suggested colitis of the descending and the sigmoid colon.

On November 18 a sigmoidoscope was passed 10 in. (25 cm.). At 2½ in. (6.3 cm.) an ulcer ¼ in. (1.9 cm.) in diameter was seen. The base was not raised. There were multiple punctate haemorrhagic areas ¼ to 1/6 in. (6 to 4 mm.) in diameter, the intervening mucosa showing only slight exudation of mucus throughout and no congestion. A smear from the mucous membrane did not show amoebae and the culture was negative for any pathogenic organism. Punch biopsy from the ulcerated area showed submucous infiltration with eosinophil and mononuclear cells.

Punctate haemorrhagic spots without evidence of inflammation of the colon suggested a diagnosis of allergy. Since the commonest allergen is milk (Antia, 1953), it was decided to exclude milk allergy. On November 20 the patient was put on fruit juice and water only. The bleeding per rectum stopped on November 22—according to the patient, for the first time in the last seven years. Two soft-boiled eggs were added on November 25 and biscuits on November 27,