The infants of mothers with skinfold thicknesses less than 7 mm (less than 25th percentile for the whole group) had significantly smaller anthropometric measurements than those of mothers with skinfold thicknesses greater than 12·1 mm (greater than 75th percentile) (see table II).

There were significant differences between the paying and non-paying groups in infant weight and length and maternal height and triceps skinfold thickness (see table III). Infants weighing under 2500 g constituted 24% of the whole group, 15% of the paying group, and 30% of the non-paying group.

TABLE III—*Infant anthropometric values in paying and non-paying groups. Values are means ± SD*

	Paying (150 cases)	Non-paying (172 cases)	Significance level (P)
Infant weight (g)	2904·0 ± 431·5	2697·7 ± 386·9	< 0·001
Infant length (cm)	47·931 ± 2·16	47·35 ± 2·19	< 0·05
Infant head circumference (cm)	33·38 ± 1·58	33·14 ± 1·50	NS
Infant triceps skinfold (mm)	3·65 ± 0·77	3·52 ± 0·65	< 0·1 (NS)
Infant subscapular skinfold (mm)	3·55 ± 0·82	3·41 ± 0·59	< 0·1 (NS)
Maternal height (cm)	153·1 ± 6·36	150·0 ± 5·27	< 0·001
Maternal skinfold thickness	11·64 ± 5·36	8·68 ± 4·09	< 0·001

Discussion

The positive correlation we found between maternal triceps skinfold thickness and infant anthropometric measurements is further evidence that the nutrition of the mother affects the nutrition of her baby. The social class differences in these measurements confirm this point, as many of our mothers were appreciably malnourished. Indeed, the mean maternal triceps skinfold thickness in our non-paying group was only 8·7 mm compared with the 16 mm found by Turner and Whitehouse[8] in British young women. Furthermore, the fetal growth retarding factor of maternal smoking was absent in our mothers.

Perinatal mortality in south India is as high as 68·8 per 1000 rural population and 62·8 per 1000 urban population.[10] This high rate is due partly to problems of intrauterine growth

retardation. Our results emphasise the need to pay attention to maternal nutrition in developing countries. Indeed, at least two studies[11][12] have shown that dietary supplementation during pregnancy benefits the growth of the infants.

In Britain Trussel[13] and Smalley and Bissenden[14] have also emphasised the importance of an adequate diet during pregnancy, particularly among immigrants. Furthermore, Davies et al[15] have suggested that the growth-retarding effect of maternal smoking is due to poor food intake during pregnancy. Our work has added to the evidence that an adequate maternal diet is necessary for adequate fetal growth—a fact that is important for the West as well as developing countries.

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(*Accepted 10 April 1978*)

Haemolytic-uraemic syndrome complicating shigella dysentery in south Indian children

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Summary and conclusions

Shigella dysentery caused 65% of all cases of acute renal failure (ARF) seen in children treated at the Christian Medical College Hospital, Vellore, during the 33 months ending September 1977. In the 40 children with ARF secondary to shigella dysentery, haematological findings suggested that they were suffering from the haemolytic-uraemic syndrome, and glomerular hypercellularity and fibrin deposition were present in all 12 patients whose renal histology could be studied. Peritoneal dialysis was the main element of treatment: 43% of children who underwent dialysis improved, compared with only 25% of those who did not undergo dialysis.

The haemolytic-uraemic syndrome precipitated by bacillary dysentery is therefore the most important cause of ARF in children aged under 5 years in Tamil Nadu and the adjoining area of Andhra Pradesh.

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Introduction

In Tamil Nadu and the adjoining area of Andhra Pradesh shigella dysentery is a common cause of acute renal failure

(ARF) in children aged under 5 years. This complication of dysentery was not noted in an earlier study[1] of bacillary dysentery from this hospital and it follows a change in the pattern of shigellosis; *Shigella dysenteriae* serotype I (*Sh shigae*) has replaced *Sh flexneri* as the most common isolate. We describe here our experience of ARF following shigella dysentery in children admitted from January 1975 to September 1977.

Patients and methods

Bacillary dysentery, characterised by the passage of frequent small stools mixed with blood and mucus and associated with tenesmus, was diagnosed clinically.[1] In many cases the diagnosis was confirmed by culture. ARF was diagnosed if there was anuria or prolonged oliguria (urinary output < 300 ml/m²/day) with a blood urea concentration of 16·6 mmol/l or more (⩾ 100 mg/100 ml).[2] Raised plasma creatinine and potassium and lowered bicarbonate concentrations were additional criteria. The haemolytic-uraemic syndrome was defined as the occurrence of acute nephropathy, haemolytic anaemia with fragmented cells (schistocytes), and thrombocytopenia.[3-5]

The duration of dysentery, the period of reduced urinary volume, any antibiotics received before admission, and the degree of dehydration were recorded.

The following haematological values were measured: haemoglobin, packed cell volume, total and differential peripheral leucocyte counts, and platelet and reticulocyte counts. Peripheral blood smears were examined for schistocytes, polychromasia, and nucleated red cells. In some patients plasma haemoglobin, plasma fibrinogen concentration, thrombin time, and partial thromboplastin time were also estimated. Microbiological investigations included rectal swab and blood cultures and antibiotic sensitivity tests on bacterial isolates. Renal function was monitored by serial measurements of blood urea, plasma creatinine, and electrolyte concentrations. Daily urinary output was also recorded.

Peritoneal dialysis was performed by the multiple puncture technique using the standard indications for starting dialysis.[2 4 5] Specific treatment with neomycin, nalidixic acid, or co-trimoxazole, and supportive measures such as blood transfusions were also used. Streptokinase and fibrinolytic agents were not used.

Renal biopsy was performed when the patient's condition permitted it and after informed consent had been obtained from the parents. Biopsy material was fixed in corrosive formol and necropsy material in 10% formalin; 3-μm sections of paraffin-embedded tissue were prepared and stained with haematoxylin and eosin, periodic acid Schiff, and Martius scarlet blue stains.

Results

Out of 320 children admitted with bacillary dysentery from January 1975 to September 1977, 40 had ARF. One child with bacillary dysentery and sulphonamide nephropathy was excluded from the study. These 40 children constituted 65% of all cases of childhood ARF treated in this hospital. Other cases of ARF occurred due to sulphonamide nephropathy (1 case), other diarrhoeas (12), glomerulonephritis (6), toxic tubular necrosis (2), and after operation (1).

The 40 children were from the northern districts of Tamil Nadu and adjacent areas of Andhra Pradesh. They were all aged under 5 years and had a mean age (±SD) of 16·5±14·04 months. All fulfilled the clinical criteria for the diagnosis of bacillary dysentery. Microscopical examination of the stools of every patient showed bacillary exudate. Cysts and trophozoites of *Entamoeba histolytica* were absent.

Rectal swab cultures were performed in 29 patients. *Sh dysenteriae* serotype I was isolated from 10 and *Sh flexneri* from one. Sixteen of the 18 patients whose rectal swab cultures gave negative results on culture had already received antibiotics before admission. Shigellae were grown in blood cultures from three patients, one of whom had a negative rectal swab culture, making a total of 12 bacteriologically confirmed cases (table I). All *Sh dysenteriae* isolates were resistant to chloramphenicol, streptomycin, tetracycline, and ampicillin and sensitive to neomycin, nalidixic acid, or co-trimoxazole.

In all patients dysentery preceded the onset of ARF by over 24 hours. There was no seasonal variation in the frequency of admissions and no family history of renal disease. Oliguria and anuria lasted

TABLE I—*Details of the 40 patients suffering from haemolytic-uraemic syndrome*

Case No	Age (months)	Sex	Platelet count (× 10⁹/l)	Plasma fibrinogen (g/l)	Shigella grown in culture* Rectal swab	Shigella grown in culture* Blood	Renal histology: fibrin deposits	No of peritoneal dialyses	Outcome
Patients with bacteriologically confirmed shigellosis									
1	8	M	10	3·40	Sh dysenteriae I	−		4	Improved
2	12	F	35	2·25	,, ,, ,,	−		1	Died
3	16	M	132	1·00	,, ,, ,,	−		3	Improved
4	9	M	230		,, ,, ,,	−		3	Died
5	12	F	420		,, ,, ,,	−		1	Died
6	18	M	75	1·40	,, ,, ,,			1	Improved
7	11	M	TOS		,, ,, ,,		+	0	Died
8	60	M	255		,, ,, ,,			0	Improved
9	8	F			,, ,, ,,			0	Died
10	48	M			,, ,, ,,	Sh dysenteriae I	+	0	Died
11	8	M			−*	,, ,,		2	Died
12	3	M	10	1·70	Sh flexneri III	Sh flexneri III		0	Died
Patients with clinical bacillary dysentery									
13	10	M	5	1·60	−*	−*	+	1	Improved
14	12	F	10	0·75	−*	−*		2	Improved
15	13	F	15	2·10	−*	−*	+	5	Improved
16	18	M	15	1·30	−*	−*		1	Died
17	11	F	28	1·87	−*	−*		5	Died
18	36	M	38		−*	−*	+	6	Improved
19	18	M	42	1·70	−*	−*		2	Died
20	8	F	50		−*	−*		0	Improved
21	11	F	90	1·50	−*	−*		2	Died
22	11	M	TOS		−*	−*	+	0	Died
23	6	M	TOS		−*	−*		0	Died
24	11	M	3	1·60	−	−		2	Improved
25	15	M	7		−			3	Died
26	23	M	18	2·65	−*			2	Improved
27	48	M	25		−*			1	Died
28	20	M	692	0·80	−*		+	6	Improved
29	36	M			−*		+	0	Died
30	24	M	42	1·10		−	+	3	Improved
31	6	M	74			−		0	Improved
32	11	F	110			−		3	Died
33	18	M	16				+	1	Died
34	5	M	32					1	Died
35	15	F	78				+	1	Died
36	6	F	TOS					1	Discharged
37	8	M	TOS					0	Discharged
38	8	F	405				+	2	Improved
39	1	M						0	Discharged
40	7	M						3	Discharged

*Minus signs indicate negative culture and asterisks indicate that antibiotics were given before admission.
TOS = Thrombocytopenia on peripheral blood smear.

from 1 to 25 days (mean 5·9 days). The mean blood urea value (±SD) was 25±8·2 mmol/l (150±49 mg/100 ml) and the mean plasma creatinine value 300±110 μmol/l (3·4±1·24 mg/100 ml).

Nutritional state was good in all but eight patients, four of whom had marasmic kwashiorkor (cases 10, 14, 23, and 25) and four of whom had marasmus (cases 3, 26, 30, and 39). Seven patients (cases 9, 20, 33, 36, 37, and 39) were severely dehydrated (over 10% loss of body weight). No patient had hypertension, cutaneous bleeding, or jaundice; 12 had haematemesis; seven had tarry stools as well as dysentery during their stay in hospital; and four had haemoglobinuria.

Leucocytosis (mean total leucocyte count (±SD) 33·5±17·6 × 10⁹/l) with a shift to the left and toxic granulation of the neutrophils
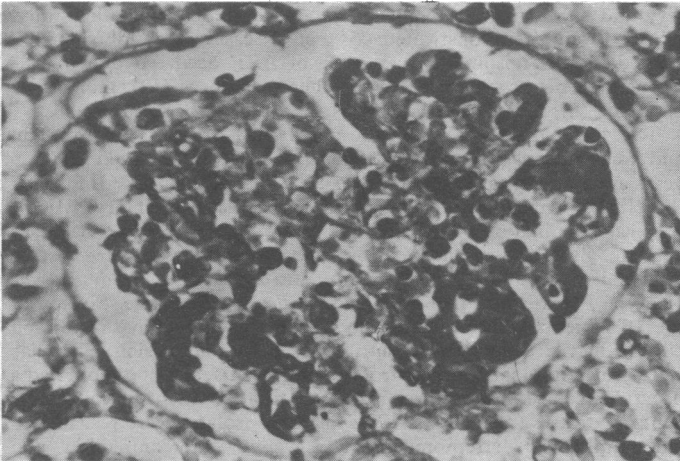

FIG 1—Case 35. A glomerulus with fibrin deposits and mild hypercellularity in necropsy material. (Martius scarlet blue stain. × 595.)
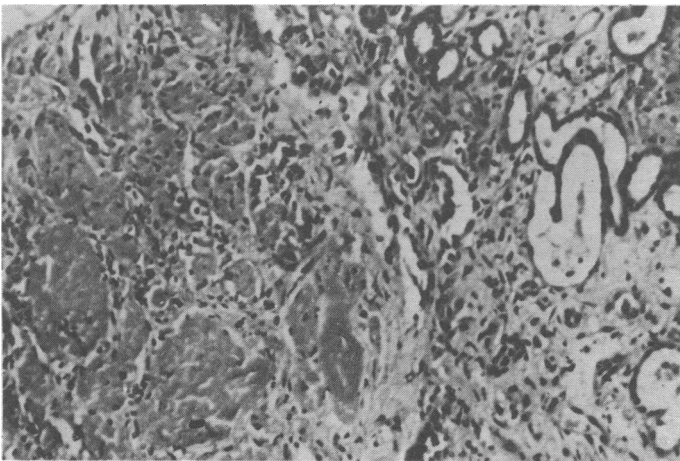

FIG 2—Case 28. Renal tissue showing focus of cortical necrosis. Other areas of this biopsy specimen showed viable glomeruli with fibrin deposits. (Haematoxylin and eosin. × 175.)
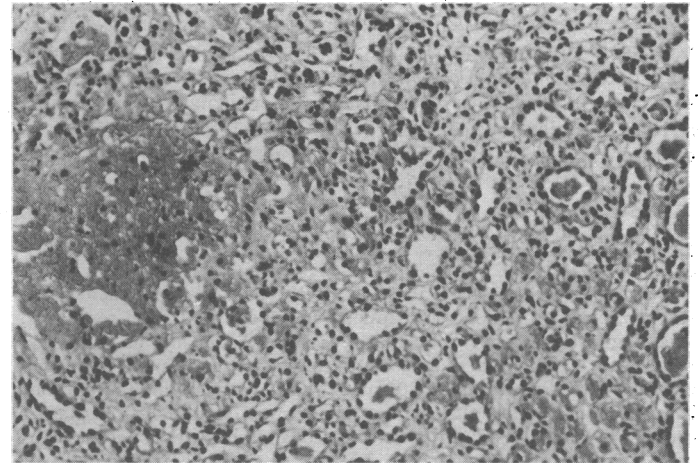

FIG 3—Case 33. Area of medullary necrosis in renal biopsy specimen. (Haematoxylin and eosin. × 175.)

was invariably present, as was anaemia with a mean packed cell volume of 0·20±0·14, schistocytes, and reticulocytosis. Twenty-seven patients had thrombocytopenia, four had normal platelet counts, and three had thrombocytosis (>300 ×10⁹/l). Platelet counts were not recorded in six patients because they died or were discharged soon after admission. Plasma haemoglobin was raised in six patients and normal in three; thrombin time was prolonged in seven and normal in four; and partial thromboplastin time was prolonged in four and normal in one.

Of the 28 patients who underwent peritoneal dialysis, 12 improved. Three of the remaining patients improved on conservative treatment, seven died before dialysis could be started, and two were discharged at the request of their parents (table I).

Renal histology was studied in 12 cases, in biopsy specimens in seven, and at necropsy in five (table II). All showed varying amounts of fibrin in the glomerular capillaries (fig 1) with or without fibrin in the walls of small blood vessels and accompanied by glomerular hypercellularity and focal glomerular capillary ectasia. The changes of acute tubular necrosis—tubular epithelial shedding and cast formation, interstitial oedema, interstitial inflammation at the corticomedullary junction, and mononuclear cells in the vasa rectae—were also seen. Patchy cortical necrosis (fig 2) was present in four cases and focal medullary necrosis in three (fig 3). Postmortem examination showed colitis with varying degrees of superficial necrosis and ulceration consistent with bacillary dysentery in three cases and pseudomembrane formation in the colon and terminal ileum in two cases. Fibrin deposits were not seen in other organs but in case 35 there was a small thrombus in the left atrium and an infarct in the spleen.

Discussion

During the period studied shigellosis was the most common cause of ARF in children admitted to this hospital. The uraemia complicating shigellosis can best be attributed to the haemolytic-uraemic syndrome, since dehydration and hypovolaemia were

TABLE II—Renal histopathology in 12 patients with haemolytic-uraemic syndrome after bacillary dysentery

Case No	Necropsy or biopsy	Location of fibrin deposits	Focal glomerular hypercellularity	Focal glomerular capillary ectasia	Acute tubular necrosis	Focal cortical necrosis	Focal medullary necrosis
7	Necropsy	Glomeruli	+	+	+	−	−
10	Necropsy	Glomeruli and arterioles	+	+	+	−	−
13	Biopsy	Glomeruli	+	+	−	−	−
15	Biopsy	Glomeruli	+	+	+	−	−
18	Biopsy	Glomeruli	+	+	+	−	−
22	Necropsy	Glomeruli	+	+	+	−	+
28	Biopsy	Glomeruli	+	+	+	+	−
29	Necropsy	Glomeruli and arterioles	+	+	+	+	−
30	Biopsy	Glomeruli	+	+	+	−	−
33	Biopsy	Glomeruli	+	+	+	+	+
35	Necropsy	Glomeruli and arterioles	+	+	+	+	+
38	Biopsy	Glomeruli	+	+	−	−	−

not important factors in these patients. Two-thirds of the children had thrombocytopenia and fulfilled all the criteria for classical haemolytic-uraemic syndrome. Some had decreased plasma fibrinogen and raised plasma haemoglobin concentrations; and the histological findings of glomerular hypercellularity and fibrin deposition with its sequelae, acute tubular necrosis and focal parenchymal necrosis, were also in keeping with a diagnosis of haemolytic-uraemic syndrome.[6] [7]

The seven patients with normal or raised platelet counts should also be considered as suffering from the haemolytic-uraemic syndrome, as such platelet values have been found in patients with this condition.[3] [5] [8-10] Of the six patients whose platelet counts were not recorded, two were shown at necropsy to have renal morphology typical of the syndrome.

In every patient the renal failure was preceded by a diarrhoeal illness typical of acute bacillary dysentery. This lasted a few days and was characterised by fever, abdominal pain, and frequent passage of stools with blood and mucus. The recovery of shigellae in 30% of these patients (from an area where the prevalence of shigella infection in preschool children is 3-6·7%[11] [12]) and the finding of superficial colonic ulceration at necropsy provide additional evidence that these patients had shigellosis and not merely the non-infective bloody diarrhoea described in the haemolytic-uraemic syndrome.[3] [4]

This syndrome can be precipitated by viral infections[13-16] and has followed infection with haemolytic streptococci[17] or salmonellae,[18] but its occurrence after shigellosis has only rarely been reported.[19-22] We have shown for the first time that infection with *Sh dysenteriae* serotype I is an important cause of the haemolytic-uraemic syndrome.

We are grateful to Mr V R Subramaniam of the department of biostatistics for his help. This paper was presented at the XV International Congress of Paediatrics, held at New Delhi, India, in October 1977.

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SIDE EFFECTS OF DRUGS

Adverse bronchial reactions to intravenous hydrocortisone in two aspirin-sensitive asthmatic patients

A leading article in the *BMJ*[1] in 1974 (based on a single case report published elsewhere[2]) drew attention to the possibility of allergic or idiosyncratic reactions to intravenous steroid preparations. We report two suspected adverse reactions to intravenous hydrocortisone, one of which was almost fatal. Both patients had longstanding asthma and were known to be sensitive to aspirin.

Case reports

Case 1—A 66-year-old housewife with a 32-year history of asthma had previously developed increased airflow obstruction after taking aspirin and also after a tartrazine-containing drink. She was receiving maintenance treatment with inhalational beclomethasone and salbutamol and, in addition, required prednisolone 15 mg weekly. On 16 December 1977 she was admitted electively for stabilisation after six weeks of increased wheezing. Her forced expiratory volume in one second was 0·7 l, compared with her best value of 1·5 l, and arterial blood gas estimations breathing air showed oxygen pressure 8·1 kPa (61 mm Hg) and carbon dioxide pressure 5·2 kPa (39 mm Hg). She was given nebulised salbutamol and her oral prednisolone was increased to 40 mg daily. Though she was comfortable at rest, a short course of parenteral steroids was thought to be advisable and she was given a loading dose of 200 mg hydrocortisone sodium phosphate by slow intravenous injection over two minutes. Within one minute after the injection she complained of severe breathlessness, and increased wheezing was obvious; within a further two minutes she became progressively cyanosed and suffered respiratory arrest. An endotracheal tube was inserted and she was mechanically ventilated for 11 hours. Subsequently she made a rapid recovery on increased oral steroids and is now well. The patient could recollect clearly a feeling of rapidly progressive dyspnoea from the moment of injection of the hydrocortisone.

Case 2—This 33-year-old woman had a 12-year history of asthma and had previously developed airflow obstruction after taking aspirin. She had received large doses of oral steroids elsewhere before attending this hospital, and after the introduction of inhalational beclomethasone these were being gradually reduced. Results of a short challenge test with Synacthen (tetracosactrin and mannitol) suggested impaired adrenal function, and when seen in the asthma clinic on 5 August 1977 she complained of tiredness and lethargy and had a blood pressure of 105/80 mm Hg. Because of suspected subacute adrenal insufficiency (later confirmed) she was given 100 mg hydrocortisone sodium succinate intravenously. She immediately vomited and within a few minutes developed a widespread urticarial eruption and increased wheezing. She was given chlorpheniramine and increased oral steroids and made an uneventful recovery.

Discussion

Of the recognised side effects of hydrocortisone salts, anorectal pruritus is commonly associated with intravenous hydrocortisone sodium phosphate[3] but the mechanism is not known. The patient in case 1 did not experience pruritus with this salt but developed severe airflow obstruction, which is unrecorded. Although there are several reports[4] of delayed adverse reactions to intra-articular steroids (of various types), airflow obstruction has not been a prominent feature. The report of Mendelson *et al*[2] of bronchospasm, urticaria, and angioedema occurring after intravenous methylprednisolone and hydrocortisone succinate in an asthmatic patient was the first to record an immediate anaphylactic reaction. Subsequently two more cases were reported,[4] both in patients with airflow obstruction who were given intravenous hydrocortisone sodium succinate. The mechanism of these reactions is not known, but results of separate challenges with the active steroid preparation and the diluent[2] suggest that preservatives or stabilisers are not responsible, and intradermal