HAEMOLYTIC URAEMIC SYNDROME IN CHILDREN

Sajid Maqbool, Mohammad Akbar, Tahir Shafi, Muhammad Walayat, Asif Javaid (Departments of Paediatrics and Nephrology, Shaikh Zayed Hospital, Lahore.)

ABSTRACT
Of the 4070 children admitted in the department of paediatrics, 830 (24%) presented with diarrhoea. Eleven of these had haemolytic ureamic syndrome (HUS) characterised by microangiopathic haemolytic anaemia, thrombocytopenia and acute renal failure. Only 3 had positive stool cultures (E.Coli 2, shigella dysenteriae 1). Two children expired while the rest recovered with conservative management and peritoneal dialysis. Thus HUS should be remembered as a complication of diarrhoea and a cause of acute renal failure in children (JPMA 41: 78, 1991).

INTRODUCTION
The triad of thrombocytopenia, microangiopathic haemolytic anaemia and acute nephropathy characterises the HUS. This represents the final common pathway for a number of pathogenic processes. The name HUS was given by Gasser and coworkers in 1955, with the belief that future studies would reveal a variety of causes, pathogenic mechanism and subsets of this syndrome. We present our experience with 11 patients admitted to our hospital with this diagnosis.

PATIENTS AND METHODS
All admitted patients suffering from gastrointestinal and respiratory problems were screened to rule out HUS. The diagnosis of HUS was established if evidence of acute renal failure, thrombocytopenia and fragmented RBCs were found on peripheral blood picture. Diagnostic workup included a complete blood picture with platelet count, evaluation of peripheral smear by a haematologist, complete urine analysis, blood urea (BUN), creatinine, serum electrolytes and fibrin degradation product estimation. Stool examination and cultures of stools and blood were also done. The management was mostly conservative, (correction and maintenance of fluid and electrolyte balance, blood transfusion, antibiotics as needed). Peritoneal dialysis was done when there was continued deterioration of clinical condition, rising BUN, creatinine, persistent anuria, oliguria and acidosis. These children were followed up till discharge and later as outpatients.

RESULTS
From January 1987 to June 1989 a total of 4070 children were admitted in the department of paediatrics, Shaikh Zayed Hospital, Lahore; of these 830 cases had diarrhoea. Eleven of these 830 cases met the diagnostic criteria of HUS. The majority (73%) were boys, the average age at presentation was 32 months. All children presented with loose stools while 9 (82%) had bloody diarrhoea. Ten (91%) were visibly pale, four (36%) had clinical evidence of purpura/ecchymoses. Three (27%) were in grade III coma and 3 (27%) were hypertensive on admission. Six (55%) were anuric of duration more than 5 days, three (27%) oliguric (duration more than 7 days) and only 2 (18%) had normal urine output. All patients were on antibiotics on arrival (more than half on Septran). Haemoglobin levels ranged from 4.5 g/dl to 12.6 1 g/dl (average 7.6g/dl) and platelet count varied from 28400 to 95000 (average 65,216). All patients had evidence of crenated RBCs, burr cells and helmet
cells on peripheral blood smear. Fibrin degradation products were within normal limits in 5 and raised in 6 cases. The average BUN was 100 mg/dl (range 28-210 mg/dl) and creatinine 5 mg/dl (range 1.6-9.6 mg/dl) on admission (Table).

Nine (82%) out of eleven cases recovered and 2 died despite peritoneal dialysis. Of the nine survivors, seven recovered completely with normal mental, haematological and renal functions (maximum follow up 1.5 years). Two showed normal mental function but evidence of residual renal damage.

**DISCUSSION**

In children, HUS is a well defined clinico-pathological entity whose etiology and pathogenesis is not yet known. Different agents have been implicated, and it does not seem unreasonable to invoke more than one cause for the syndrome. Amongst bacteria, shigella, salmonella, campylobacter enteritis, pseudomonas, have been considered in the etiology. Viruses (Coxsackie, ECHO, cytotoxic drugs and use of contraceptives may result in Adenoviruses, Influenza) may be responsible. Some HUS. A primary requisite for an inciting agent would seem to be the ability to injure epithelial cells. The organism most frequently involved has been verotoxin producing Escherichia coli (VTEC) or serologic evidence there of. The most widely held view about pathogenesis is that an agent induces endothelial injury mainly in the microvessels of the kidneys. This is followed by fibrin deposition and the development of a microangiopathic haemolytic anaemia whereby the RBCs and platelets are damaged mechanically by the fibrin strands as the cells attempt to pass through the narrowed vessels. Adherence of platelets to the altered capillary wall contributes to the formation of microthrombi and addition of toxic damage. The syndrome occurs mainly in infants and children and rarely in neonates with mean age of 3.6 years. This disorder is usually preceded by prodromal gastrointestinal (typical) or respiratory symptoms (atypical). In our study all patients present presented with gastrointestinal symptoms. Enterotoxigenic E. coli were isolated in two patients whereas in one patient shigella dysenteriae was cultured from stools. Physical examination of these patients reveals pallor, lethargy and irritability. Patients are usually dehydrated and may be mildly jaundiced. Hypertension, abdominal distension and hepatosplenomegaly may be found in some of the patients. Fluid overload with congestive heart failure may also be present. More severe neurological manifestations, including somnolence, disorientation, seizures and coma, have been observed in 30-50% of patients. In our patients 8(73%) had neurological manifestation. Anaemia is invariably present in these patients with haemoglobin levels between 2 and 10 g/dl. The peripheral smear shows fragmented erythrocytes, which are characteristic of microangiopathic haemolytic anaemia. Leukocytosis is a common finding, it was observed in all of our patients. Hypoalbuminemia which may reflect intestinal loss of albumin and hypocalcemia with hyperphosphatemia which are consequences of renal failure are found in some.
Platelet count is usually reduced but maybe normal or elevated at the time of diagnosis and does not correlate with the severity or duration of the disease. Thrombocytopenia is secondary to platelet consumption, since most patients have shortened platelet survival. External counting following administration of radio labelled platelets has demonstrated accumulation of radioactivity over spleen, liver and kidney suggesting that platelets are damaged in these organs. Renal involvement is always present but of variable severity. Elevated levels of blood urea nitrogen and serum creatinine are present reflecting a decrease in glomerular filtration rate. There is controversy with regard to the severity of renal involvement and its prognostic implication. Patients who ultimately recover have oliguria/anuria of less than two weeks duration but prolonged anuria does not necessarily mean irreversible renal and brain damage. Renal impairment was observed in all of our patients. About 85% of children with classic HUS experience a complete recovery with supportive care and peritoneal dialysis, specific therapy may be required only in certain subsets. Recurrence has been reported in 30% and in these about one third suffer progressive renal failure. In our patients recovery was seen in 82% but relapse was noted only in one patient. The follow up however has been of a short duration. Other electrolyte abnormalities in these patients are hypocalcemia, hyponatremia, hyperuricemia and metabolic acidosis. Oliguria has been reported from 2-100% of patients and anuria in 30-50%. Anuria and oliguria were observed in 6 (55%) and 3 (27%) of our patients respectively whereas two (18%) patients had normal urine output. So far there is no specific treatment for HUS, but several forms of therapy have been attempted in the past, including steroids, heparin, streptokinase and more recently antiplatelet drugs, exchange transfusions, prostacyclin (PGI\textsuperscript{2}) infusion, vitamin E and plasmapheresis have been tried. The benefits of newer therapies are questionable and clear superiority has yet to be shown. However, the mortality decreased only after the institution of better management of acute renal failure and use of dialysis. Dialysis should be continued until there is adequate return of renal functions.

REFERENCES