

Membranous and Necrotizing Pharyngitis in Childhood

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Summary

Aderele, W. I. and Antia, A. U. (1976) *Nigerian Journal of Paediatrics*, 3 (1), 15. **Membranous and Necrotizing Pharyngitis in Childhood.** Two distinct clinical varieties (the membranous and the necrotizing types) of severe pharyngitis in 56 children are described. While both varieties had many symptoms in common, the membranous variety was associated with pharyngeal membrane and signs of laryngeal obstruction, both of which were absent in the necrotizing variety, the distinctive features of which were necrosis and ulceration of the pharyngeal tissues. There was a high incidence of malnutrition among the two groups of patients.

The mortality was significantly higher in the necrotizing group than in the membranous variety. *C. diphtheriae* was the commonest organism isolated from patients with membranous pharyngitis, while *klebsiella* and a few other gram negative organisms were common isolates from the throat swabs of patients with the necrotizing variety. The aetiology and the pathogenesis of the necrotizing group are obscure and require further studies.

DURING the period, January to April 1972, four children with an unusual form of pharyngitis consisting of severe ulceration and necrosis of the pharyngeal tissues and bull-shaped neck were admitted to the Paediatric Department, University College Hospital (UCH), Ibadan. The unusual features and the uniformly poor prognosis in these four cases prompted us to undertake a retrospective review of similar cases admitted into the department between 1965 and 1973. The review also includes other cases of pharyngitis with membrane formation who were admitted during the same period.

Materials and Methods

The case-notes of children with throat infections and upper respiratory tract obstruction

during the nine-year period (January 1965 to December 1973), were reviewed. All the cases diagnosed as pharyngitis with membrane formation, ulceration or necrosis of the pharyngeal tissues, were included in the study. Cases of mild pharyngitis, simple follicular tonsillitis, herpetic stomatitis, retropharyngeal abscess and laryngotracheobronchitis were excluded. Data abstracted from the case-notes included the symptoms, signs, packed cell volume (PCV), total and differential white blood count (WBC), throat swab, blood culture, serum electrolytes and urea, urinalysis and reports of the chest and neck radiographs.

Results

During the period under review, there were 56 cases of severe pharyngitis which fulfilled

the above criteria. From the analysis of these cases, two distinct clinical groups emerged, namely: the membranous group, the essential feature of which was the presence of a membrane in the pharynx, and the necrotizing group, the main feature of which was necrosis of the pharynx.

Membranous Pharyngitis

Age and Sex Distribution

In this group, there were 42 cases (24 males and 18 females). Figure 1 shows the number of cases admitted per year during the period, 1965-1973. There were more cases in 1970, than in any other year. The age distribution (Fig. 2) of the 42 cases shows that 40 (95 per cent) were under the age of five years.

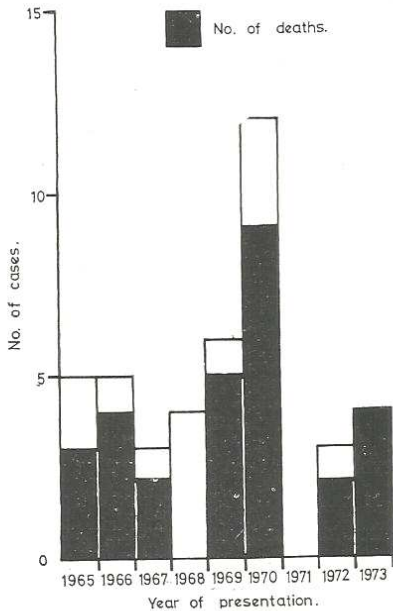


Fig. 1. No. of cases of membranous pharyngitis per year during the period, 1965-1973.

Monthly Admissions

The number of admissions per month is shown in Figure 3. It will be seen that, although cases occurred throughout the year, a majority, 25 (60 per cent), of the 42 cases were admitted during the dry months of October to March, thus suggesting that this type of pharyngitis is an airborne infection.

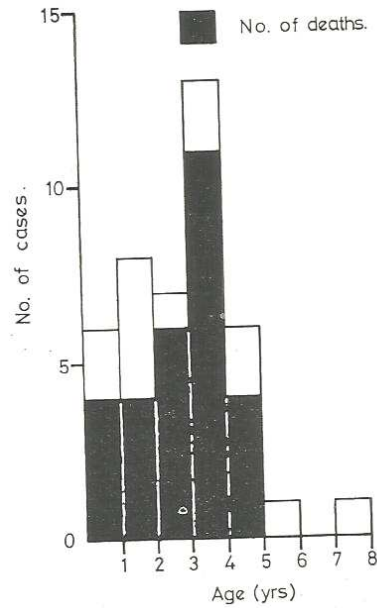


Fig. 2. Age distribution in 42 children with membranous pharyngitis

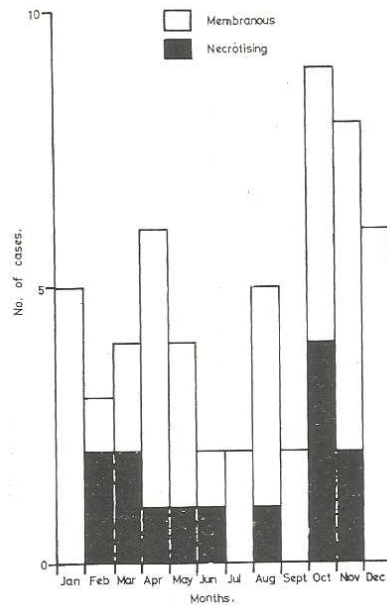


Fig. 3. No. of cases of membranous and necrotizing pharyngitis per month.

Symptoms

The major presenting symptoms are shown in Table 1. They included cough (24 cases)

TABLE I

Relative frequency of major Symptoms in 56 Nigerian Children with Membranous and Necrotizing Pharyngitis

<i>Symptoms</i>	<i>Type of Pharyngitis</i>			
	<i>Membranous (42)</i>		<i>Necrotizing (14)</i>	
	<i>No. of Cases</i>	<i>Per cent</i>	<i>No. of Cases</i>	<i>Per cent</i>
Cough	24	57	7	50
Difficulty in breathing	23	55	8	57
Fever	21	50	10	71
Swelling of the neck	16	38	12	86
Inability to swallow	9	21	6	43
Sorethroat	5	12	2	14
Bloody nasal discharge	5	12	7	50
Inability to speak	3	2	-	-

and fever (21 cases), both of which were of an average duration of 4 days; difficulty in breathing (23 cases; average duration of 1 day) and swelling of the neck (16 cases; average duration of 3 days). Other symptoms were inability to swallow, sorethroat, bloody nasal discharge, inability to speak, vomiting and diarrhoea.

Signs

Table II summarizes the signs in the 42 patients. Adherent membranes primarily involving the tonsils, were present in all the children. In 12 of the cases, the membrane extended to the posterior pharyngeal wall and the larynx. There was also purulent material in four cases, haemorrhage in the oropharynx in six, and mild ulceration of the pharynx in two others. Submandibular swelling (Fig. 4), due to enlargement of the lymph nodes, occurred bilaterally in 15 cases, and unilaterally in five others. There was stridor in 12 children, and cyanosis in three others. Clinically and radiologically, there was bronchopneumonia in two cases and lobar pneumonia in one other case. Prexiya (average temperature of 38.9°C;

range, 37.2-40.5°C), and tachycardia (average pulse rate of 146/minutes; range 120-208/minute) were present in all cases. None of the cases had overt signs of heart failure.

Thirty (71 per cent) of the 42 children were poorly nourished (average weight, 11.1 kg.; range, 5.4 Kg.-20.0 Kg.) Figure 5 illustrates the weight distribution of these patients compared with the weight distribution of two groups of Nigerian children, the elite and the low socio-economic groups (Janes, 1970).

Laboratory Findings

Bacteriological reports on the throat swabs were available in 33 cases. Pathogens were isolated from 18, while the remaining 15 were sterile. The isolated pathogens included corynebacterium diphtheriae (8), klebsiella (2), staphylococcus pyogenes (1), pseudomonas (1), proteus (1), streptococcus faecalis (1), E. coli (1), coliforms and klebsiella (1), coliforms and staphylococcus pyogenes (1), and Vincent's organisms (1). No organism was isolated from the blood cultures done in 15 cases. Urinalysis revealed moderate albuminuria in three patients, but the urine was albumin-free in ten. The average PCV was 33 per cent (range,

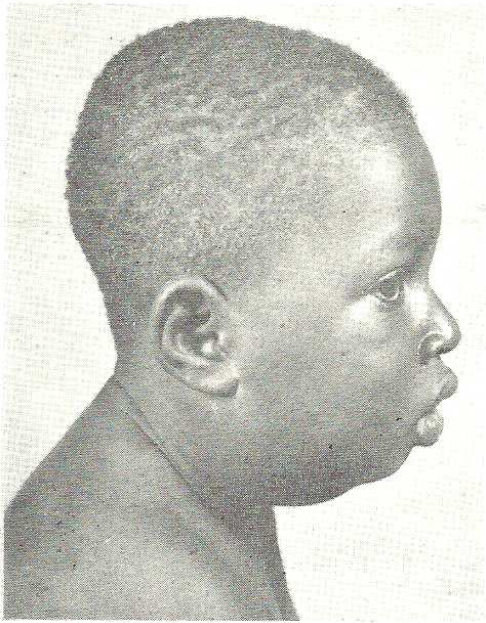


Fig. 4. A patient with membranous pharyngitis, showing submandibular swelling.

TABLE II
Relative frequency of major Signs in 56 Children with Membranous and Necrotizing Pharyngitis

Signs	Type of Pharyngitis			
	Membranous (42)	Necrotizing (14)	No. of Cases	Per cent
Membrane in the throat	42	—	—	—
Pyrexia	42	13	13	93
Tachycardia	42	13	13	93
Poor Nutrition	31	10	10	71
Submandibular swelling	20	12	12	86
Stridor	12	—	—	—
Haemorrhage from nose and pharynx	6	12	12	86
Cyanosis	3	—	—	—
Pharyngeal necrosis/severe ulceration	—	14	14	100

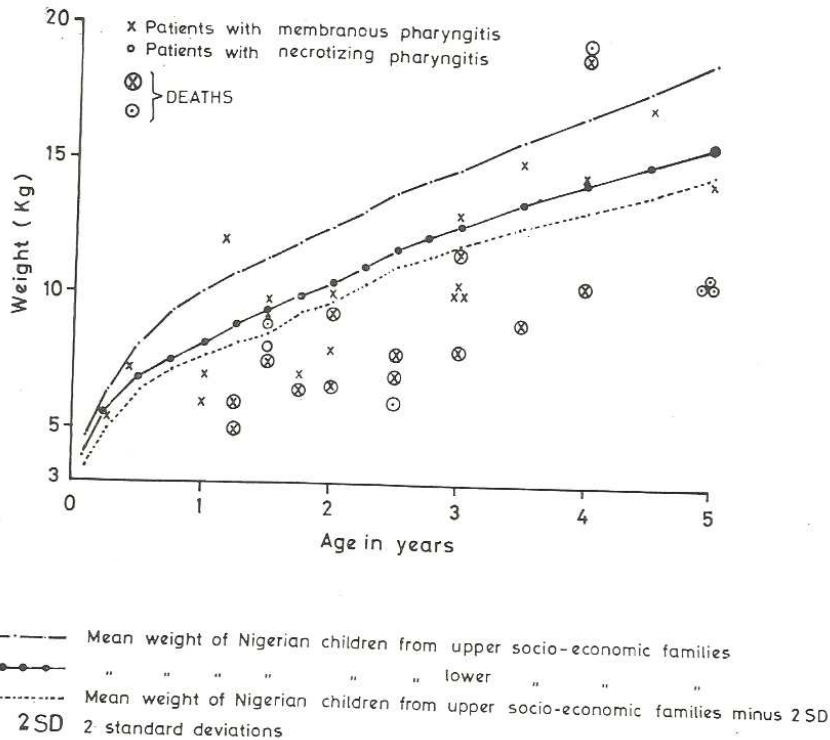


Fig. 5. Admission weights of children with membranous and necrotizing pharyngitis compared with normal weights of Nigerian children.

27-39 per cent), and the average total WBC was 14,000/c.mm. There was a preponderance of polymorphs in most cases. Serum electrolytes and urea levels were determined in seven patients, but disturbances were revealed in only one. This child was clinically dehydrated, and had electrolyte values of sodium, 120 mEq/L; potassium, 3.8 mEq/L; chloride, 92 mEq/L; bicarbonate, 19 mEq/L, and urea, 111 mg/100 ml). He died within 24 hours of admission, in spite of satisfactory rehydration.

Management

Diphtheria antitoxin was administered either intravenously or intramuscularly to 33 of the 42 children. All received antibiotics consisting of penicillin, erythromycin, chloramphenicol and streptomycin, used either singly or in combinations. Eleven children received hydrocortisone in addition. Supportive measures included administration of humidified oxygen and intravenous fluids. Tracheostomy was performed on 19 children.

Outcome

Twenty-nine (69 per cent) of the 42 patients died. Twenty (69 per cent) of the 29 died within 24 hours of admission. Among the dead were five of the eight from whose throats, *C. diphtheriae* was isolated, and seven of the 19 who had tracheostomy. All the seven cases who did not receive diphtheria antitoxin, died. Seven of the 29 patients who died, and four of the thirteen survivors, had received hydrocortisone. The average period of hospitalisation among the survivors was 20 days (range, 7 days to 3 months).

Necropsy Findings

Necropsy was performed on fourteen (48 per cent) of the 29 patients who died. The significant finding in all the fourteen cases was the presence of a tough, grey, tenacious and homogenous pseudomembrane in the pharynx, extending as far down as the interlobar bronchi in some cases. Histological changes of the

pharyngeal tissues in all the cases consisted of necrosis, haemorrhage, inflammatory exudate, and in some cases, diphtheritic organisms. In five of the fourteen necropsy cases, *C. diphtheriae* was isolated during life.

Necrotizing Pharyngitis

Age and Sex Distribution

There were 14 patients (8 males and 6 females) in this group. The ages ranged between 1 year and 9 years (Fig. 6).

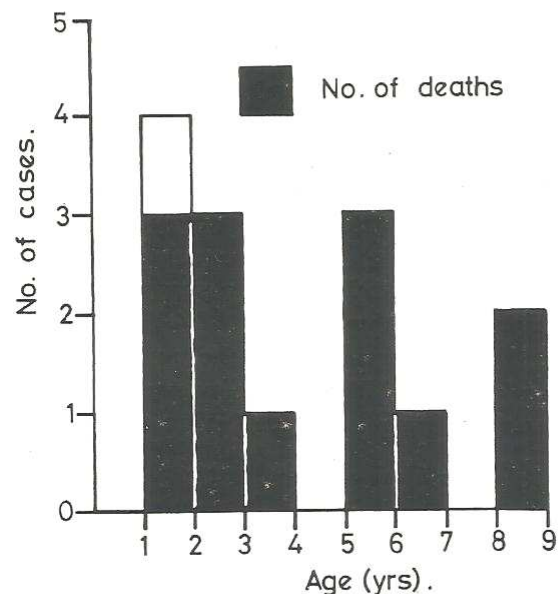


Fig. 6. No. of cases of necrotizing pharyngitis per year during the period, 1955-1973.

Monthly Admissions

The number of cases admitted per month (Fig. 3) shows that 10 (71 per cent) of the 14 patients were admitted during the period, October to March.

Symptoms

The major presenting symptoms are summarized in Table 1. Commonest were swelling of the neck and fever, which occurred in 12 and 10 cases respectively. Others were difficulty in breathing, cough, bloody nasal discharge and inability to swallow. The duration of symptoms

before hospitalization was generally short, being usually under 4 days. Less frequent symptoms included anorexia (2 cases), sorethroat (2 cases), vomiting and diarrhoea. There was no history of recent trauma to the throat in any of the cases.

Signs

In 12 of the children, there were ulceration, necrosis and oedema of the pharynx, and in the remaining two children, the tonsils and uvula were gangrenous. Haemorrhage from the nose and pharynx was observed in 12 cases and in a similar number, there were diffuse, brawny, bilateral submandibular swellings (Table 2). Pyrexia, (average temperature of 38.9°C; range, 36.9-40.0°C) and tachycardia (average pulse rate of 130/minute; range, 110-152/minute) were present in 13 out of the 14 cases. None of the cases had frank heart failure but one child had an unspecified terminal cardiac arrhythmia.

Ten (71 per cent) of the 14 children were malnourished (Fig. 5), the average weight being 11.7Kg. (range, 5.0-24.0Kg).

Laboratory Findings

Bacteriological reports on the throat swabs and pharyngeal sloughs were available in 10 cases. Of these, organisms were isolated from 8 patients (Klebsiella, 4; Klebsiella and coliforms, 1; staphylococcus pyogenes, 1; staphylococcus pyogenes and streptococcus faecalis, 1; staphylococcus pyogenes and beta-haemolytic streptococcus, 1). The average PCV was 35 per cent (range, 27-43 per cent); the average WBC was 18,000/c.mm (range, 11,000-22,000/c.mm) with a preponderance of polymorphs in most cases. A platelet count of 14,000/c.mm was found in one patient with nasal and pharyngeal bleeding. Serum electrolytes and urea were normal in two children, but in five others there were hyponatraemia, hypochloraemia, normokalaemia, metabolic acidosis and uraemia (serum urea levels, 73, 105, 105, 115 and 185mg/100ml, respectively). These five children died

in spite of adequate intravenous fluids consisting of normal saline, followed by dextrose-saline. Blood glucose levels were normal in 6 cases in whom this was estimated.

Management

Antibiotics, (penicillin, streptomycin, erythromycin, chloramphenicol, ampicillin, cloxacillin, singly or in various combinations) humidified oxygen and diphtheria antitoxin were administered to all but one of the 14 patients; in addition, six patients received intravenous or intramuscular hydrocortisone, 50-100mg, six-hourly. Tracheostomy was performed on two children.

Prognosis

Thirteen (93 per cent) of the 14 children died, (four within 24 hours, and the remaining nine between two and six days of admission). Both of the children who had tracheostomy died. The only survivor, a male child, aged one and a half years, presented with a 3-day history of fever, epistaxis and swelling of the neck. Examination showed a malnourished child (weight 9 Kg.), with signs of necrotizing pharyngitis. The laboratory investigations revealed a mixture of klebsiella and coliform organisms isolated from the throat swab; PCV, 35 per cent; WBC, 19,900/c.mm with 72 per cent neutrophils, 25 per cent lymphocytes and 3 per cent monocytes; normal serum electrolytes and urea. Treatment consisted of intramuscular hydrocortisone (50mg, six-hourly for 3 days), followed by oral prednisolone (20mg daily initially; and this dose was reduced after a few days), intramuscular penicillin and streptomycin followed by intramuscular erythromycin. This patient also received intravenous fluids and was hospitalised for seventeen days.

Necropsy Findings

Necropsy was carried out on five of the thirteen patients who died. In all the five, there were necrosis and ulceration of the pharyngeal tissue. In addition, two of the patients had

swellings of, and haemorrhage into the uvula, and another patient had a haemorrhagic exudate in the larynx, pleural cavity and in the lungs. Histological changes of the pharyngeal tissues in all the cases consisted of necrosis, haemorrhage and inflammation. The kidneys were pale in three, and normal in the remaining two of the five patients with high blood urea. Histology of the kidneys did not reveal any gross abnormality.

Discussion

This review has revealed the existence, in childhood, of two clinical types of frequently fatal pharyngitis, namely: the membranous and the necrotizing types. The short incubation period of four days associated with both varieties, suggests that they are droplet infections. Despite the similarity in symptomatology, there are certain physical signs which distinguish the two types. Pharyngeal membrane which was present in all the cases of membranous type was noticeably absent in the necrotizing group. Similarly, laryngeal obstruction and stridor, were significant features of membranous pharyngitis while necrosis of the pharyngeal tissues was the characteristic feature of the necrotizing form.

The commonest organism associated with membranous pharyngitis was *C. diphtheriae* which was isolated from the throat swabs of 8 out of the 42 cases. Other organisms isolated included coliforms, klebsiella and staphylococcus aureus. Although no causative organism was isolated in at least nine other children in this group, it is presumed that they had diphtheria infection since necropsy findings were consistent with the diagnosis of pharyngeal diphtheria. Failure to isolate *C. diphtheriae* from cases of diphtheria is not uncommon. Groarke *et. al.*, (1960), reported that out of 159 documented cases of diphtheria in England and Wales in 1954, 28 cases (18 per cent), were diagnosed on clinical grounds only. In contrast to the specific *C. diphtheriae* organism associated with a majority of the cases with the membranous

variety, the predominant organism isolated from the throats of most patients with the necrotizing pharyngitis was klebsiella.

Although the prognosis was generally poor in both groups, the mortality of 93 per cent was significantly higher among those with the necrotizing type than among those with the membranous variety (69 per cent). The survival of only one out of the fourteen cases with necrotizing pharyngitis appears to have been fortuitous, since similar management was carried out on all the cases in this group. There can be no doubt that an important contributory factor to the high mortality in both groups was malnutrition which was evident in most of the patients (Fig. 5). Renal dysfunction as evidenced by raised urea, which occurred in five of the fourteen patients with necrotizing pharyngitis was perhaps, an additional contributory factor to the higher mortality in this group of patients. Any explanation for the uraemia in the five cases in this group is speculative. The accompanying hypoelectrolytaemia in these five cases suggested severe dehydration. However, in spite of apparently satisfactory rehydration, the serum urea level continued to rise in three of the five cases. It may however, be argued that the persistent rise in the serum urea was due to inadequate replacement of the fluid deficit. Since this explanation seems to be unlikely, it may be speculated that the infection in these patients directly or indirectly caused irreversible damage to the kidneys notwithstanding the absence of gross renal abnormality at necropsy.

While it is reasonable to conclude that most of the cases of membranous pharyngitis were caused by *C. diphtheriae*, the specific causative organism(s) in cases with the necrotizing pharyngitis remains undetermined. It is tenuous to ascribe any aetiological role to the Gram negative organisms isolated from the throat swabs of a majority of the children with this type of pharyngitis. It is known that various organisms, including Gram negative ones, may

temporarily colonize the throats of newborn infants within the first 24 hours of birth (Torrey and Reese, 1945; Mathur *et al.*, 1970). Gracey *et al.*, (1973), have also reported colonization by streptococcus faecalis, *E. coli*, klebsiella, pseudomonas and proteus of throats of malnourished, but otherwise well, Australian children. It seems therefore, that isolation of Gram negative organisms from the throats of most of our cases, who were indeed, malnourished, does not necessarily establish a causative role of these organisms in this type of pharyngitis. Alternatively, two possible explanations may be suggested. First, the pharyngeal necrosis may be an abnormal reaction to the Gram negative organisms. Secondly, since there were certain similarities between the two conditions in the symptomatology and physical signs such as bull-shaped neck and epistaxis, it is possible that a highly lethal variant of diphtheria was the causative organism. Indeed, one child with necrotizing pharyngitis developed a terminal arrhythmia, a complication which may occur as a manifestation of toxic myocarditis due to diphtheria infection (Warin and Ironside, 1969). Serious renal damage which occurred in a few of the cases in this group is also known to complicate diphtheria infection. It must however be admitted that, to our knowledge, absence of pharyngeal membrane in pharyngeal diphtheria has never been reported. It should be pointed out that although no history of trauma to the throat was obtained from any of the patients, uvulectomies and other forms of throat 'operations' are sometimes carried out on children by local traditional healers for various reasons. It is therefore possible that in some of the cases with necrotizing pharyngitis such operative procedures might have been carried out prior to presentation at the hospital.

Other conditions which are associated with severe and often fatal pharyngitis which should be considered in the differential diagnosis include agranulocytosis, infectious mononucleosis, and Ludwig's angina. There was neither clinical nor laboratory evidence that any of the

14 patients had any of these conditions. The involvement of the kidneys in some of the patients and thrombocytopenia in one of the cases would suggest a disseminated disorder, which may be caused by viruses, especially, the adenoviruses. Further studies, particularly on the role of viruses in the aetiology and pathogenesis of this highly fatal type of pharyngitis, is required. Until the aetiology and pathogenesis of this necrotizing variety of pharyngitis are determined, it is suggested that any child presenting with an unusual form of pharyngitis, especially if accompanied by necrosis or severe ulceration should undergo thorough investigations including throat swabs and blood specimens for virology and bacteriology (preferably undertaken by the Resident soon after admission). Other essential investigations are serum electrolytes, urea and glucose estimations. It is recommended that such a child should be given intramuscular diphtheria antitoxin (20,000-40,000 units), intravenous wide spectrum antibiotics and adequate intravenous fluids, the amount and nature of which would depend on the clinical and biochemical status of the child. In addition, he should receive intravenous infusions of hydrocortisone (50-100mg four to six-hourly). Additionally, evidence of shock should be looked for and treated urgently.

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