the addition of dehydroemetine, and the remaining patient died. These results equal those from previous trials of combined therapy. Surgical drainage plays a greater role in management in children than in adults, because of the frequency of multiple abscesses that are inaccessible to needle aspiration. In such instances dehydroemetine is also given during the postoperative period.

We thank Dr. H. Wannenburg, Medical Superintendent, King Edward VIII Hospital, for facilities. The Amoebiasis Research Unit (Director, R. Elsdon-Dew) is sponsored by the South African Medical Research Council, the Natal Provincial Administration, the University of Natal, and the United States Public Health Service.

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†We report with regret the death of Professor S. J. Powell on 2 June 1973.

Laryngotracheo-oesophageal cleft

Congenital abnormalities of the larynx are not uncommon. Holinger and Brown (1967) collected a series of 866 cases in Chicago that included only 2 cases of laryngotracheo-oesophageal cleft.

We describe a case of this malformation which has received little attention in the British literature.

Case report

A primigravida developed hydramnios during the 33rd week of pregnancy. At 37 weeks in another hospital she was delivered spontaneously of a female infant weighing 1840 g. The Apgar score was 8 at one minute. Oxygen was administered by face mask until regular respirations were established.

The baby regurgitated her first three feeds and at the age of 8 hours had a respiratory rate of 72, with marked sternal indrawing. Dextrostix at this time recorded less than 25 mg/100 ml and intravenous dextrose was given. She was transferred to Oxford. The clinical findings were confirmed and no malformations were detected.

The initial diagnosis of aspiration pneumonia due to regurgitation of feeds was confirmed radiologically. Blood gas analysis at this time showed a mild metabolic acidosis that was corrected with intravenous bicarbonate. Cultures were taken and antibiotics started.

Tube feeding was resumed at age 36 hours, but the baby became cyanosed shortly afterwards. Stridor and coarse crepitations throughout the lungs were heard.

FIG. 1.—Oblique x-ray showing barium flowing from oesophagus anteriorly into the trachea.
Direct laryngoscopy revealed what was interpreted as the nasogastric tube in the trachea, but re-examination suggested that the tube was bowed forward from the oesophagus through a cleft in the posterior laryngeal wall. The extent of the cleft was shown radiologically by injecting Gastrografin under low pressure through the nasogastric tube, while withdrawing it steadily up the oesophagus. The dye was seen suddenly to flow through the cleft into the trachea (Fig. 1). Tube feeding was again stopped, and intravenous 10% dextrose restarted.

She became severely jaundiced, and between 90 and 114 hours of age required three exchange transfusions. No blood group incompatibility was shown, and the hyperbilirubinaemia was attributed to infection in a premature infant.

The long-term aim was to allow the baby to grow to approximately 3-0 kg to facilitate surgery. She was nursed sitting up and given thickened feeds through a nasogastric tube situated in the duodenum. The upper airway was continuously aspirated through a Replogle tube. There were, nevertheless, continuous problems with recurrent aspiration, attacks of cyanosis, and even respiratory arrest. On these occasions the endotracheal tube required for resuscitation often had to be left in situ for several days. Chest x-rays showed recurrent patchy infiltrates. Pseudomonas aeruginosa, cultured from peripheral sites and tracheal aspirate but never from blood culture, was treated successfully with gentamicin and carbenicillin on several occasions.

Her condition again deteriorated 3½ weeks after birth. She had a fever, tachypnoea, tachycardia, and signs of heart failure with a triple rhythm and hepatomegaly. Despite treatment with digoxin, diuretics, and antibiotics, she died aged 26 days.

Necropsy showed a linear defect measuring 1·2 cm in the posterior wall of the larynx. The defect was in the midline extending from the interarytenoid fold to below the cricoid cartilage (Fig. 2a). The oesophageal stratified squamous epithelium encroached on the laryngeal pseudostratified ciliated columnar epithelium (Fig. 2b). The mucosa of the larynx and trachea adjacent to the cleft was oedematous and moderately congested with focal erosions and patches of squamous metaplasia. Confluent bronchopneumonic changes were seen in the lungs. Terminal aspiration of gastric contents had occurred, but the characteristic changes of an established aspiration pneumonia were not seen. A feature of interest was the marked hyperplasia of bronchial mucous glands affecting both the serous and mucus secreting components.

No other congenital abnormalities were seen. A smooth depression on the surface of the liver corresponded to the distribution of a lobular branch of the hepatic artery which contained an old thrombus.

**Discussion**

Laryngotracheo-oesophageal cleft is due to a failure of dorsal fusion of the cartilage centres on
each side of the glottis, which normally fuse to form the cricoid cartilage by the 45th day of gestation. This may be combined in the more severe forms of the defect with abnormal development of the tracheo-oesophageal septum extending the cleft caudally to the carina. Maternal hydramnios, premature delivery, and associated malformations are often present. The anomaly presents in the early neonatal period with stridor, feeding difficulties, and recurrent aspiration, but correct early diagnosis is rare. This may be due to the edges of the cleft closing completely during phonation (Blumberg et al., 1965). Many cases have been recognized only at necropsy, despite frequent laryngoscopy or even surgical exploration of the neck and mediastinum. Our patient was typical, with premature delivery after hydramnios, stridor, an abnormal cry, and aspiration of feeds during the first 2 days.

The condition is rare, and of approximately 35 cases (Blumberg et al., 1965; Griscom, 1966; Felman and Talbert, 1972) only 4 survivors were reported until recently when Phelan et al. (1973) described an extraordinary sibship in which certainly 3, and probably 5, cases survived childhood without operation. Of the 4 previously described survivors, 2 lived for one month (Felman and Talbert, 1972; Geiger et al., 1970), and another for 8 months (Shapiro and Falla, 1966) before diagnosis and operation. Only Pettersson's (1955) case survived operation during the first week. A familial incidence of the defect has now been reported three times (Crooks, 1954; Zachary and Emery, 1961; Phelan et al., 1973) and may be associated with congenital subglottic stenosis in other sibs.

Our patient had recurrent problems with aspiration, and we planned correction by operation when her weight had increased to approximately 3·0 kg. We therefore sat her upright and gave thickened feeds through a nasogastric tube situated in the duodenum. This was preferred to a gastrostomy, which has its own hazards and which would not reduce significantly the risk of regurgitation through the cleft. However, the nasogastric tube probably aggravated pharyngeal secretions and by curving forward through the cleft, partially obstructed the airway. Even using continuous upper airway suction through a Reploge tube we were unable to prevent aspiration of secretions or regurgitation of stomach contents through the cleft. We could have started intravenous feeding once the failure of nasogastric feeding, as assessed by poor weight gain and recurrent aspiration, became apparent. Removal of the nasogastric tube would also have decreased the pharyngeal secretions. Intravenous feeding was not used at any stage as we were achieving an excellent caloric intake and we have little experience with the techniques. Even in units with considerable expertise in its use in the newborn there is a high incidence of serious complications.

We knew the cleft was comparatively short from our x-ray evidence and from the fact that endotracheal intubation when needed for resuscitation secured an airtight seal without inflating the gastrointestinal tract. The lungs could therefore have been protected by tracheostomy, an operation we are normally very unwilling to perform on the newborn, but one that is nevertheless an integral part of the operative closure of this defect. With a tracheostomy in situ the airway would have been protected and the Reploge tube, which probably provoked as much secretion as it aspirated as well as being a convenient reservoir for the pseudomonas, could have been removed. Oral feeding could then have been given safely.

Early tracheostomy followed by oral feeding seems to us the logical management of low birth-weight babies with laryngotracheo-oesophageal cleft who are symptomatic and require closure of the defect, and in whom some weight gain before the operation is required.

Summary

A fatal case of laryngotracheo-oesophageal cleft is described. We discuss the management of this condition in which only 4 cases are reported to have survived correction by operation.

We thank Professor J. P. M. Tizard for permission to report a case under his care, and Dr. F. H. Kemp for the x-ray report.

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Short reports

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Anuria due to sulphadiazine

While acute oliguria due to precipitation of sulphonamide crystals in the urinary tract is well recognized it is now uncommon, and standard textbooks give little detailed information on its treatment. We report the case of a child who became anuric while being treated with sulphadiazine for purulent meningitis.

Case report

History. A previously healthy boy weighing 17 kg, aged 3 years, was admitted with purulent meningitis. There was a purpuric eruption and Neisseria meningitidis was considered to be the likely pathogen, though cultures of his blood, CSF, urine, and throat swab were subsequently reported to be sterile. He appeared moderately dehydrated but blood urea level was 35 mg/100 ml and serum electrolytes were normal. His urine contained no cells or protein. He was treated with intravenous fluids, benzyl penicillin 1 megaunit, chloramphenicol 250 mg, sulphadiazine 750 mg, and hydrocortisone, all given 6-hourly intravenously, and oral phenytoin. He responded well, and 24 hours later the intravenous therapy and phenytoin were stopped. Treatment was continued with oral sulphadiazine 750 mg 6-hourly and intramuscular penicillin and chloramphenicol.

On the fourth day he developed a mild facial and oral herpes simplex eruption accompanied by occasional vomiting. On the sixth day of therapy he was noted to have frequency of micturition but there was no fever, pain, or dysuria. The following morning he passed 20 ml of heavily blood-stained urine containing protein and a few white cells, but no casts or crystals. His blood urea had risen to 98 mg/100 ml. There was no haematological evidence of intravascular coagulation. The sulphadiazine was stopped, but in spite of an intravenous infusion of 32 mEq sodium bicarbonate in 660 ml of 5% dextrose, and 1150 ml oral fluids over the next 12 hours, he remained totally anuric. There was no response to 60 ml of 20% mannitol intravenously, frusemide 50 mg intravenously, or to a bladder washout with warm 0-5% sodium bicarbonate. He was transferred to this hospital for management of his renal failure.

On admission he was clinically well with no oedema, blood pressure 120/80 mmHg, no enlargement or tenderness of his kidneys, and no abnormal neurological signs despite 24-hour anuria.

Investigations. Hb was 11 g/100 ml, platelets 208,000/mm³, urea 120 mg/100 ml, sodium 129 mmol/l, potassium 4-9 mmol/l, uric acid 5-2 mg/100 ml, calcium 9-2 mg/100 ml, phosphate 6-7 mg/100 ml, albumin 3-5 g/100 ml, antistreptolysin O titre <20 Todd units/ml, antinuclear factor negative, serum β₂ globulin 80 mg/100 ml. Analysis of the last urine specimen passed before the child became completely anuric revealed numerous red cells, sodium 66 mmol/l, potassium 6 mmol/l, urea 82 mg/100 ml, albumin 100 mg/100 ml, proteinuria poorly selective (θ = 34°). The urine-plasma urea ratio was 0-86 (normally >5 in children with physiological oliguria).

Cystoscopy showed an oedematous left ureteric orifice with cellular debris but no crystals in the bladder. On bilateral retrograde pyelography using sodium diatrizoate 25% w/v solution (Hypaque) there was dilatation and inactivity of both ureters, renal pelves, and minor calyces (Fig. 1) but no organic obstruction could be shown. A needle renal biopsy (Fig. 2) was obtained which contained 24 normal glomeruli and showed fairly uniform tubular dilatation and epithelial degeneration with moderate interstitial oedema and two small foci of interstitial mononuclear cells. There was no arterial abnormality, and crystals were not seen.

Six hours after ureteric catheterization the child passed 150 ml blood-stained urine and thereafter maintained an adequate urine flow rate. The following day, after having received no sulphadiazine for 48 hours, his urine contained crystals with the characteristic 'wheatsheaf' appearance of acetylsulphadiazine. This specimen also gave a positive Bratton-Marshall (Varley, 1967) test for sulphonamides. 7 days after onset of anuria his creatinine clearance was 71 ml/min per 1·73 m² (plasma creatinine 0·6 mg/100 ml), and the haematuria and proteinuria had ceased. Intravenous pyelography on the tenth day showed normal kidneys and ureters.

Discussion

Sulphonamides may cause renal damage by crystallization and obstruction in the urinary tract or more rarely by toxic acute tubular necrosis, acute interstitial nephritis, or a generalized necrotizing angiitis (More, McMillan, and Duff, 1946). In our patient the renal biopsy appearances were similar to those described in necropsy material from patients dying of obstructive uropathy due to sulphonamide crystallization (Murphy et al., 1944).

The sudden onset of frequent or painful micturition in a patient receiving sulphonamides should arouse the suspicion of crystalluria. Characteristically these symptoms are followed within 24 hours by oliguria with crystalluria, heavy proteinuria, and haematuria. However, the urine at this stage may contain no crystals (Murphy et al.,