

their excretion could be provoked later by leucine loading tests. After 6 months without biotin therapy, excretion of the abnormal metabolites recurred, but again stopped within 48 hours after biotin therapy.

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Diaphragmatic paralysis in the newborn

Paralysis of the hemidiaphragm resulting from injury of the phrenic nerve is considered to be a rarity in the newborn infant (Schaffer and Avery, 1971), though 3 such cases were found among 1671 consecutive deliveries (Cavrot and Richard, 1957), and an earlier search of published reports provided another 74 cases (Richard *et al.*, 1957). It seems likely that diaphragmatic paralysis occurs with greater frequency than is reported, partly because symptoms vary so much in severity. Thus mild transient cases may not attract attention as in the case reported by Smith (1972). On the other hand, in severer cases other diagnoses such as congenital heart disease are incorrectly made, as in the case reported by Adams and Gyepes (1971) where severe cyanosis led to heart catheterization and angiography being performed because the newborn

was erroneously thought to have severe cyanotic congenital heart disease.

The 3 cases of unilateral paralysis of the diaphragm described here illustrate the wide spectrum of the clinical manifestations. The first baby had only mild respiratory distress and the diagnosis was only made at age 3 months; the second presented with the classical clinical picture of this condition; in the third baby cyanosis was sufficiently severe to mimic congenital heart disease.

Case reports

Case 1. A 3-month-old male was admitted because of mild respiratory difficulty. He was born at another hospital to a 37-year-old primipara primigravida. The infant was a breech presentation and at 36 weeks a forceps extraction was reported to have been 'difficult'. Birthweight was 2910 g. Immediately after birth the infant was tachypnoeic and cyanotic and he failed to use his left arm. He was placed in an incubator and was given oxygen. At 36 hours a chest x-ray showed nothing abnormal. Thereafter he improved and, in spite of slight persisting tachypnoea, he was discharged at 15 days. From then until the day he was admitted to our department he had mild respiratory difficulty and two episodes of 'bronchopneumonia'.

On admission at the age of 3 months the baby was slightly tachypnoeic but otherwise comfortable. The Erb's palsy had disappeared completely. Breath sounds were absent over the lower half of the left chest. Chest x-ray showed elevation of the left hemidiaphragm (Fig.).

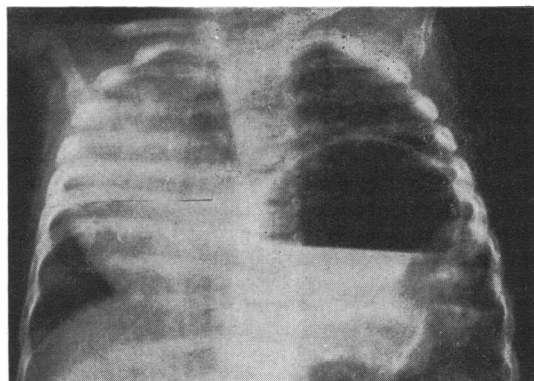


FIG.—Case 1. Elevation of the left hemidiaphragm and mediastinal shift to the right.

Fluoroscopy showed paradoxical movement of the left side of the diaphragm and exaggeration of the mediastinal shift to the right on expiration.

The baby was observed for several days; symptoms other than mild tachypnoea were absent, so he was discharged. He was readmitted at 5 months because he was still tachypnoeic. Chest x-ray was almost identical to that taken 2 months previously. Surgical plication

of the paralysed diaphragm was then considered, but the parents refused permission. The infant was discharged and has not been seen since.

Case 2. A 20-day-old male was admitted to hospital because he was thought to have bronchopneumonia. He had been delivered by breech extraction weighing 3100 g. A right Erb's paralysis was noted and he was permanently tachypnoeic. Tachypnoea became more marked and later cyanosis occurred. On admission he looked acutely ill with slight cyanosis; he still had Erb's palsy of the right arm. Examination of the chest showed dullness and crackling rales over the right chest anteriorly. Chest x-ray showed elevation of the right hemidiaphragm and an area of density in the upper right lobe. Paradoxical movement of the raised right diaphragm was seen on fluoroscopy. He was given oxygen (45%), penicillin, and kanamycin. His condition gradually improved and he was discharged at the age of 7 weeks. At 4 months he was doing well, x-ray of the chest was normal, and normal movement of the diaphragm was seen on fluoroscopy.

Case 3. An 8-day-old female was referred because of suspected congenital heart disease. She was born to a 33-year-old primipara at the end of a normal pregnancy, weighing 3600 g. Delivery had been 'very difficult' and the baby at birth had been lethargic and cyanosed. At 5 days her condition deteriorated with tachypnoea and fever. Chest x-ray taken at that time suggested that the heart was enlarged.

On admission she was critically ill, cyanosed, and tachypnoeic; she also had Erb's palsy of the right arm. Rales were heard over the lungs bilaterally; a soft systolic murmur was heard at the apex. Chest x-ray showed mild cardiomegaly and a fracture of the left clavicle. ECG was interpreted as having right axis deviation and right ventricular hypertrophy with right atrial enlargement. A diagnosis of bronchopneumonia in an infant with cyanotic heart disease was made. Oxygen (45%), penicillin, and kanamycin were given. Over the next 5 days her general condition showed little improvement and further investigation of the suspected heart disease was planned, until it became clear that pulmonary rather than cardiac dysfunction was present. At 16 days chest x-ray showed elevation of the right hemidiaphragm and mediastinal shift to the left, and paradoxical movement of the raised right hemidiaphragm was present on fluoroscopy.

A few days later the baby's condition deteriorated; tachypnoea and cyanosis became more intense. She contracted *Esch. coli* gastroenteritis and died a few days later. Permission for necropsy was refused.

Discussion

It seems likely that unilateral diaphragmatic paralysis due to injury of the phrenic nerve is more common than published reports suggest, with mild cases often overlooked because they cause minor or no respiratory disturbance. On the other hand

fluoroscopy, which usually is the procedure that clinches the diagnosis, is not carried out in all dyspnoeic newborns.

In Case 1 the diagnosis was made at the age of 3 months, though the baby was in hospital for the first 15 days of life and an x-ray of the chest was taken. In Case 2 the condition was diagnosed because the baby was admitted to hospital for bronchopneumonia, and little attention would probably have been paid to the baby's mild transient respiratory difficulty, if the acute episode did not occur.

Some cases are erroneously thought to have congenital heart disease and/or intracranial injury, as in Case 3 where the diagnosis of heart disease was supported by the cyanosis, the absence in the initial chest x-ray of findings suggesting lung disorder, and some EEG abnormalities. The correct diagnosis was not made until the 16th day of life.

Unilateral paralysis of the diaphragm should be considered in cases of respiratory distress during the neonatal period, particularly in babies born after difficult delivery by breech presentation and/or forceps extraction. The presence of Erb's palsy in these babies increases the probability of diaphragmatic paralysis and, since x-ray of the chest is not necessarily diagnostic, such babies should be examined by fluoroscopy. The final outcome of diaphragmatic paralysis depends upon the severity of the damage to the phrenic nerve. When this is mild, recovery occurs usually within the first 2 to 3 months. With more severe damage, paralysis may persist and after 4 to 5 months surgical treatment must be considered.

Summary

Three cases of unilateral diaphragmatic paralysis caused by injury to the phrenic nerve are presented. The first showed only minor respiratory difficulty and the diagnosis was not made until 3 months. The second presented the classical clinical picture of this condition. In the third, cyanosis led to an erroneous diagnosis of congenital heart disease. Phrenic nerve palsy should be considered in any newborn with respiratory distress, particularly if occurring after a difficult delivery, a breech presentation, and/or forceps extraction. In such cases fluoroscopy of the chest is mandatory.

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Treatment with new synthetic analogue of vasopressin in diabetes insipidus

The aims of treatment of diabetes insipidus are replacement therapy with a vasopressin preparation, ancillary use of chlorpropamide or thiazide diuretics in some cases, and eradication of the underlying cause of the condition where appropriate. Replacement therapy only will be considered in this communication. This poses several problems. Pitressin snuff may cause local complications such as chronic rhinitis as well as pulmonary problems, for example bronchospasm and pulmonary fibrosis; lysine vasopressin nasal snuff has the disadvantage of a short duration of action. Injections of pitressin may result in physical pain and psychological upset, as exemplified in this case; also, preparation of the solution is crucial in order to prevent administration of the inert vehicle in the absence of the active pitressin.

DDAVP (1-deamino-8-D-arginine vasopressin) has been claimed to possess a higher antidiuretic potency and a longer duration of action than the vasopressin preparations currently in use. Andersson and Arner (1972) reported success with DDAVP in the management of 10 adult patients with cranial diabetes insipidus of various aetiologies, but no similar experience has been reported in children.

Case report

A previously very healthy girl, now aged 10½ years, presented in 1969 with a 3-month history of polyuria and polydipsia. She had sustained no obvious head injury and she did not complain of headache, vomiting, or convulsions; there were no other urinary tract symptoms. There was a negative family history of diabetes mellitus and polyuria and/or polydipsia.

On examination she appeared a normal, well looking

girl with satisfactory hydration. The fundi and visual fields were normal, as was the remainder of the CNS, and the respiratory, cardiovascular, and gastrointestinal systems.

There was no glycosuria. Repeated examinations of the urine failed to reveal any evidence of urinary tract infection. An accurate fluid balance showed that her average fluid intake was 2–2½ l. daily and that her urinary output was 2–3 l./day. A fluid deprivation test was carried out lasting 15 hours; her urinary output continued at a high level. The highest urinary specific gravity during the test was 1008 and she lost 1·8 kg in weight. She was then given an intravenous infusion of hypertonic (2·5%) saline over 45 minutes; there was no significant change in urinary output or in urinary specific gravity. Pitressin 0·1 unit was injected intravenously and the urinary flow fell from a pre-injection level of 3·8 ml/minute to 1·0 ml/minute; the highest specific gravity obtained was 1011. Full blood count, blood urea, serum electrolytes, calcium, inorganic phosphorus, alkaline phosphatase, proteins, and electrophoresis were all normal. Skull x-ray, CSF, EEG, and air encephalography detected no abnormality.

It was concluded, therefore, that this girl was suffering from idiopathic pituitary diabetes insipidus.

Therapy was started with injections of pitressin tannate in oil, as well as lysine vasopressin nasal spray four times daily. The patient refused to administer the spray a short time after its introduction. Initially she required one injection every 3 or 4 days, her symptoms being well controlled on such a regimen. It soon became obvious that injections were required more frequently, i.e. on a daily basis. With this came many psychological problems which were extremely difficult to overcome.

A supply of DDAVP was obtained and the patient was readmitted for a trial of therapy. The last dose of pitressin tannate in oil was injected the day before admission (point A in Fig.) A fluid balance chart was constructed; simultaneous serum and urine specimens were obtained on several occasions for estimation of osmolality; the specific gravity of all urine specimens was measured. Three doses of 7·5 µg DDAVP were administered on day 4 (point B in Fig.) and no further drug was given until day 8 (point C in Fig.).

Results

The results are set out in the Fig. On days 1 and 2 it was noted that the patient was concentrating her urine satisfactorily, presumably as a result of the pitressin given before admission. On day 3 the urine osmolality fell below that of the serum, indicating that she had little circulating antidiuretic hormone. On day 4 the patient was given three doses of DDAVP and urine osmolality (and specific gravity) increased with a corresponding decrease in her fluid intake and output. This effect was noted also on day 5, indicating that the DDAVP was still operating up to 24 hours after the previous dose.