Corynebacterium lysis, and urease were negative. On tellurite medium the colonies were medium in size, convex, rough, and dark grey. The toxigenicity test using an Elek plate was negative. The organism was identified as a nontoxigenic Corynebacterium diphtheriae, gravis type. Dr. R. E. Weaver, Communicable Disease Centre, Atlanta, U.S.A., confirmed the identification. Sensitivity test results in minimum inhibitory concentrations (µg/ml) were as follows: gentamicin 0-01, penicillin 1-0, tetracycline 0-5, cephalothin 0-5, chloramphenicol 1-0, erythromycin 0-01, clindamycin 0-06, and lincomycin 0-25.

**Discussion**

Corynebacterial endocarditis is rare. In most reports the organisms are described as 'diphtheroid' without detailed identification (Merzbach et al., 1965; Reid and Greenwood, 1967; Davis et al., 1963; Dismukes et al., 1973; Manhas et al., 1972; Stein, Harken, and Dexter, 1966). In most cases the organisms have been isolated from blood cultures in living patients, but in many of these cases other organisms were isolated in addition to the corynebacteria (Reid and Greenwood, 1967; Stein et al., 1966). 'Diphtheroids' have also been isolated from blood cultures after cardiopulmonary bypass surgery for the repair of cardiac valvular defects (Davis et al., 1963) and from infected prosthetic valves (Dismukes et al., 1973; Manhas et al., 1972; Stein et al., 1966). The latter may present either early or late in the postoperative period.

Pike (1951) reported a case of endocarditis due to toxigenic C. diphtheriae and referred to earlier reports of cases in which nontoxigenic organisms were isolated. Facial, nasal, or cutaneous diphtheritic lesions may or may not be present in such cases. Corynebacterial species are widely distributed, being found in the soil and atmosphere and as contaminants in blood cultures. Certain strains, including C. hofmanni, C. xerosis, and nontoxigenic C. diphtheriae, are saprophytes in man. They are therefore potential causes of endocarditis.

Bacterial endocarditis in most cases affects valves deformed by acquired or congenital heart disease. Our patient had no congenital heart lesion and the macroscopical and microscopical appearances of the chordae tendinae and myocardium seemed to exclude antecedent rheumatic carditis. Normal valves may occasionally be the seat of endocarditis, particularly when caused by virulent organisms. The implication of our case is that any organism isolated from a patient with a clinical diagnosis of infective endocarditis should be regarded as the possible pathogen and not dismissed as a contaminant. Organisms should be identified fully and not reported in vague terms such as 'diphtheroid', so that a more accurate idea of the source and nature of the organism may be obtained.

**Summary**

Fulminant endocarditis affecting the mitral valve in an 11-year-old boy was caused by a nontoxigenic strain of Corynebacterium diphtheriae.

We thank Professor John Wainwright for the necropsy findings.

**References**


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**Peritoneal dialysis and exchange transfusion in a neonate with argininosuccinic aciduria**

Peritoneal dialysis has been used in conditions such as renal, cardiac, and hepatic failure. Although it has been used in the management of coma in urea cycle deficiency states (Siegel and Brown, 1973), its effectiveness in controlling ammonia intoxication has been questioned (Siegel and Brown, 1973; Saudubray et al., 1973). In a patient with
hyperammonaemia secondary to arginosuccinic aciduria we found peritoneal dialysis of considerable value in reducing blood ammonia levels, in contrast to the limited success of exchange transfusion in the same patient.

**Case report**

A male infant, weighing 3·35 kg at birth, was admitted at 60 hours of age because of poor sucking, groaning, vomiting, and increasing respiratory distress during the previous few hours. The pregnancy and delivery had been uneventful. The infant, normal at birth, was breast fed at 36 hours. He became drowsy, hypotonic, and vomited the next feed. A sib of the patient had died soon after birth of a similar condition. Though no diagnosis has been made biochemically this led us to suspect an inborn error of metabolism.

On admission the blood pH was 7·41, Pco2 15 mm, base excess—11 mEq/l, and serum bicarbonate 9·9 mEq/l. The arterial concentration of ammonia was 535 µg/100 ml and a large amount of arginosuccinic acid (ASA) was found in the urine and cerebrospinal fluid (CSF) by high voltage electrophoresis screening. A diagnosis of arginosuccinic aciduria was made within a few hours of admission. The patient was fed exclusively by intravenous fluids (dextrose 20%, 1500 ml/24 h per m²) through a superior vena caval catheter; sodium bicarbonate was added to correct the metabolic acidosis. An exchange transfusion, using citrate as an anticoagulant, was carried out to try to decrease the ammonia levels. However, the ammonia concentration increased to 850 µg/100 ml. Another exchange transfusion, with fresh heparinized blood, was no more successful (Fig.). On the fourth day of life peritoneal dialysis was started in a final attempt to control hyperammonaemia. At the end of the same day a cardiorespiratory arrest necessitated intubation and artificial ventilation. The patient's condition deteriorated gradually, despite continuing the dialysis, and he died on the seventh day.

**Methods and results**

Ammonia levels in plasma samples and peritoneal dialysate fluid samples were determined by the Fenton (1962) method. In children and adults the normal values remain below 100 µg/100 ml, but may increase up to 150 µg/100 ml during the first 72 hours of life. A summary of ammonia concentrations in plasma is shown in the Fig. along with the treatment. Routine screening of the patient's urine and CSF by high voltage electrophoresis (Whatman 3M filter paper 40×20 cm, pyridine buffer pH 5·3, 80 V/cm for 30 min) showed a large amount of the free form as well as the two anhydrides of ASA. Quantitative amino acid analysis, performed by ion exchange chromatography by the method of Cusworth and Westall (1961), confirmed the high urinary excretion of ASA, which was 6·5 g/24 h on the fourth day (undetectable in normal newborns). The urea cycle enzyme activities, arginosuccinic lyase and arginase, in liver obtained half an hour after death were determined on a frozen aliquot within 3 weeks by the method of Brown and Cohen (1959). The arginosuccinic acid cleavage enzyme activity was less than 0·5% of control values but the arginase activity was within the normal range (Table).

**TABLE**

*Activities of urea cycle enzymes in liver (µmol/min per g wet weight of tissue)*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argininosuccinate lyase</td>
<td>0·03</td>
</tr>
<tr>
<td>Arginase</td>
<td>4·7</td>
</tr>
</tbody>
</table>

**Exchange transfusion.** The first exchange was with 250 ml of 24-hour-old citrated blood: 10 ml was exchanged over a period of 8 min. The second exchange was with 300 ml of fresh heparinized blood with the same procedure. Despite these exchange transfusions there was a gradual increase in plasma ammonia concentration up to 850 µg/100 ml during the first exchange, which was not significantly reduced by the second exchange (Fig.).

**Peritoneal dialysis.** Dialysis, through a left flank incision, was with warmed commercial dialysate (Dianeal G 174) to which 5 mEq/l of KCl and 250 mg/l of ampicillin were added. Exchanges of 40 ml/kg were performed in a 60-min cycle; the fluid was infused over a period of 15 min. After an equilibration period of 25 min the dialysate was allowed to drain up to 20 min. Since the child developed renal failure after the cardiac arrest a hypertonic dialysate (Dianeal G 184) was used in one out of every three cycles. During the 20-min period when peritoneal dialysate was being drained 150 ml of 20% lactulose was given rectally in order to trap the gut ammonia. Immediately before dialysis the arterial ammonia concentration was 735 µg/100 ml and 15 hours after the procedure it had fallen to 300 µg/100 ml.
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ml; analysis of dialysate confirmed that the fall in ammonia concentration was due to dialysis. A total of 5 mg of ammonia was removed in the dialysate during the first 6-hour period (Fig.).

Discussion

The clinical outcome in hyperammonaemia secondary to a urea cycle enzyme defect seems to be related to the plasma and/or CSF ammonia concentration. Neonatal death tends to occur when this concentration exceeds 300 μg/100 ml. However, patients detected in later childhood seem to have increased ammonia tolerance, perhaps as a function of brain maturation. Peritoneal dialysis has had variable success in reducing ammonia levels in congenital ammonia intoxication. A transient lowering was observed in the case of Saudubray et al. (1973) and no significant reduction was achieved in the case reported by Siegel and Brown (1973).

Peritoneal dialysis was performed in our case because of the failure of the two exchange transfusions to decrease the ammonia levels. Neither the use of citrated blood to increase the activity of the tricarboxylic acid cycle nor fresh blood which minimized the transfused blood ammonia content helped the patient. Unfortunately no ammonia determination was performed on the stored blood used for the exchange transfusion to estimate the ammonia load during this procedure. In addition, the secondary effects of the exchange transfusion on the liver blood flow remain obscure. Haemoglobin may be specifically toxic to the liver by producing more ammonia and/or by increasing portosystemic shunting (Bessman, 1967).

Our data confirm that peritoneal dialysis is more efficient in decreasing blood ammonia levels when there is a high concentration gradient but, after an initial fall, it fails to lower the plasma ammonia concentration below 300 μg/100 ml (Saudubray et al., 1973). Since the amount of ammonia cleared during the dialysis seems to be constant the lack of a further decrease in plasma suggests a persistent high rate of endogenous production of ammonia compared to the clearing rate of the dialysis. A major stress such as an intercurrent infection or surgery is known to provoke metabolic decompensation through an increase in catabolism. The peritoneal dialysis itself may act as a stress and thus help to maintain a metabolic disturbance.

The question of the inexorable course in our patient may now be considered. Despite the dramatic decrease in plasma ammonia concentration to 300 μg/100 ml this level may still be toxic to the immature brain, which seems to be more vulner-
soun for the ammonia assay; and Dr. J. Dochain for giving us the opportunity to examine this patient.

REFERENCES


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**Decreased antihaemophilic globulin and leucocyte response to epinephrine in preterm infants**

The ability of the reticuloendothelial system (RES) and the spleen to respond quickly and efficiently to challenge is thought to be an important factor in the prevention of acute fulminant infections. The increased susceptibility of preterm infants to infections cannot be explained by the deficiencies in their immune system, and the importance of the RES has therefore recently received attention (Gotoff, 1974). Measurement of RES and splenic activity is difficult, especially in preterm neonates, and the idea of splenic hypofunction in preterm infants comes from indirect evidence.

Holroyde, Oski, and Gardner (1969) observed a high percentage of 'pocked' erythrocytes in the blood of preterm infants, similar to those seen in patients after splenectomy, which they thought was due to the immaturity of the RES, mainly of the spleen. Others (Casper, Rodey, and Thatcher, 1974) noted their presence in patients with a nonfunctional spleen. Acevedo and Maurer (1963) showed that preterm newborns do not remove erythrocytes containing Heinz bodies as efficiently as normal babies, therein resembling splenectomized individuals.

Epinephrine injections (or infusions) have well-known, if not well-understood, effects upon the RES and the spleen, and two of them are easily investigated. They are (1) the rise in the number of formed elements such as leucocytes in the circulating blood (Chatterjee, Dameshek, and Stefanini, 1953), and (2) the rise in the level of plasma antihaemophilic activity (Ingram, 1961). Information about these effects of epinephrine in neonates is lacking, so we investigated them.

**Subjects and methods**

Two groups of neonates (groups 1 and 2) between the ages of 2 and 4 days and two groups of older children (groups 3 and 4) were studied.

*Group 1.* Comprised 21 preterm infants (15 males, 6 females) with a gestational age of about 30-38 weeks and a birthweight of 1100–2400 g.

*Group 2.* Comprised 23 term infants (12 males, 11 females) whose birthweight was between 2900 and 3440 g.

*Group 3.* Comprised 20 children aged 3 months to 6 years (10 males and 10 females) who served as a control group. All were apparently healthy and had no haematological disorder.

*Group 4.* Comprised 13 children who had had splenectomy (12 because of trauma, 1 for spherocytosis) and 1 with congenital asplenia syndrome.

With written parental permission, blood was drawn from a vein before and 30 minutes after a subcutaneous injection of epinephrine 0·01 mg/kg. A leucocyte count was made simultaneously, on capillary blood. The antihaemophilic activity of the plasma was estimated by the one-stage PTT test (Rodman, Barrow, and Graham, 1958), using a commercial antihaemophilic globulin-deficient serum (Dade Laboratory).

**Results**

Tables I and II summarize our findings. Before the injection there was not much difference between the four groups either in antihaemophilic activity or leucocyte count. But the differences in the response to epinephrine were highly significant. While the term infants reacted similarly to the controls the response of the preterm neonates was negligible, as was that of the splenectomized group. No differences were observed between males and females in any of the four groups.

**Discussion**

Our data suggest that preterm neonates fail to react normally to epinephrine injections, so far as
Peritoneal dialysis and exchange transfusion in a neonate with argininosuccinic aciduria.

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