

are being made for emergency delivery. If resuscitation occurs within five minutes delivery may be undertaken with reasonable confidence.

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- <sup>1</sup> D'Souza SW. Neurodevelopmental outcome after birth asphyxia. In: Chiswick ML, ed. *Recent advances in perinatal medicine*. Edinburgh: Churchill Livingstone, 1983:137-52.
- <sup>2</sup> Rodeck CH, Holman CA, Karnicki J, et al. Direct intravascular fetal blood transfusion by fetoscopy in severe rhesus isoimmunisations. *Lancet* 1981; i:625-7.
- <sup>3</sup> Liley AW. Liquor amnii analysis in the management of the pregnancy complicated by rhesus serialisation. *Am J Obstet Gynecol* 1961;82:1359-70.
- <sup>4</sup> Campbell S, Pearce JM. Ultrasound visualisation of congenital malformations. *Br Med Bull* 1983;39:322-31.
- <sup>5</sup> Rodeck CH, Nicolaides KH, Warsof SC, et al. The management of severe rhesus isoimmunisation by fetoscopic intravascular transfusion. *Am J Obstet Gynecol* (in press).

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## Dicyclomine: worrying symptoms associated with its use in some small babies

Dicyclomine is a smooth muscle antispasmodic frequently prescribed during infancy for alleged "colic." We report two cases in which dramatic respiratory events were associated with ingestion of the drug.

### Case reports

*Case 1*—A 6 week old girl was given a very small amount of Merbentyl (Merrell Pharmaceuticals) on a spoon. She became transiently apnoeic and pale but recovered quickly. The next day the full prescribed dose of 5 ml was administered. She again became apnoeic and subsequently cyanosed. She recovered during the ambulance journey to hospital while receiving mouth to mouth resuscitation. Subsequent examination showed no abnormality. The electrocardiogram was normal.

*Case 2*—A 5 week old girl was given the prescribed dose of Merbentyl and immediately became pale, rigid, and apnoeic. She recovered quickly without resuscitation. An identical though more dramatic and prolonged symptom complex occurred after the next dose and the medication was discontinued by the mother. No abnormalities were subsequently identified on examination.

### Comment

The explanation for these apparent side effects of dicyclomine is obscure. The immediacy of effect suggests an idiosyncratic local action, perhaps at laryngeal level. It was not possible to exclude inhalation but there was no clinical evidence to support this. Both children had previously taken other medications from a spoon without difficulty.

The product manufacturers' data sheet specifies that this preparation should be used with caution in infants of under 6 weeks of age and lists breathing difficulties including breathlessness, respiratory collapse and apnoea, seizures, syncope, asphyxia, muscular hypotonia, and coma as possible though rare complications in this age group. This information is based on four cases reported to the manufacturer in the past 10 years. All four infants were 3 weeks of age and all had dramatic respiratory symptoms immediately after ingestion of a dicyclomine preparation. The symptoms lasted up to 30 minutes in two of the children. All recovered normally (Merrell Pharmaceuticals Ltd, personal communication). Four notifications of a similar pattern of events have been made to the Committee on the Safety of Medicines (personal communication). All four children were under 7 weeks of age and all recovered normally.

These potential side effects do not appear to be widely recognised and are not noted in the current edition of the *British National Formulary*. Underreporting may therefore be common. It seems prudent to review carefully any infant with reported respiratory problems temporally associated with the administration of dicyclomine and specifically discourage its use in infants under 6 weeks of age. In older infants a maximum dose of 5 mg is recommended with a daily limit of 20 mg. Any potential local irritating effect may be reduced by dilution with syrup BP. The indiscriminate use of this drug for all manner of feeding problems is to be deprecated.

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## Clostridium welchii infection after amniocentesis

Postabortal sepsis due to *Clostridium welchii* has been reported with an incidence of 0.5-1.0%.<sup>1</sup> The overall mortality ranges from 50% to 85%, and when haemolysis, disseminated intravascular coagulation, and renal failure are present the death rate is 70% despite adequate medical management.<sup>2,3</sup> Amniocentesis is a safe procedure with a slight increase of 1.0-1.5% in the rate of fetal loss.<sup>4</sup> Amnionitis after amniocentesis has been reported but at a rate of less than 0.1%.<sup>5</sup>

We report a case of *Cl welchii* infection in a patient who aborted after amniocentesis.

### Case report

A 39 year old woman (gravida 3, para 0) booked at a district general hospital in June 1983. Amniocentesis was performed under ultrasound control at 16 weeks for chromosomal analysis. Two attempts to obtain liquor were unsuccessful and the fetal heart was observed before and after the procedure by ultrasound. The patient was admitted to hospital within 12 hours with an inevitable abortion and aborted a macerated, infected fetus.

Erythromycin and metronidazole were administered intravenously. Over the next few hours the patient's condition deteriorated. She became jaundiced, hypotensive, and hypoxic. She was intubated and intermittent positive pressure ventilation instituted. She rapidly became oliguric, passing small quantities of dark urine only. Exchange blood transfusion was followed by evacuation of retained products of conception. There was no improvement, however, and she was transferred to the intensive care unit at this hospital 24 hours after admission.

Initial assessment confirmed disseminated intravascular coagulation, renal failure, haemolytic anaemia, shock lung, and Gram positive septicaemia. Cultures of blood and placental tissue subsequently confirmed infection by *Cl welchii* sensitive to erythromycin and metronidazole. A high vaginal swab taken before she aborted did not grow *Cl welchii*. Intermittent positive pressure ventilation was continued and haemodialysis performed. She was transfused with packed cells and fresh frozen plasma. Total abdominal hysterectomy and bilateral salpingectomy were performed six hours after admission because of continuing haemolysis and severe hypotension. The uterus appeared macroscopically intact but *Cl welchii* was cultured from the uterine cavity and myometrium. She gradually improved: the haemolysis stopped and her fever disappeared after 48 hours. She remained in renal failure, however, for which she required haemodialysis over the next four weeks. Five months after aborting her renal function was still impaired, though she did not require dialysis.

### Comment

*Cl welchii* is a Gram positive, anaerobic, non-motile, spore forming organism which is often encapsulated and capable of producing exotoxins. Among these are  $\alpha$  toxin (lecithinase C), which acts on the surfaces of red and white cells and is responsible for the intravascular haemolysis which causes anaemia and jaundice. It may also produce haemorrhage as a result of its necrotising action on capillaries and arteriolar walls.

*Cl welchii* may be recovered from the vagina and cervix in 1-9% of healthy pregnant women, but only a small proportion are virulent.<sup>1</sup> Septic abortion due to *Cl welchii* rarely occurs in clinical practice

unless certain conditions prevail. The organism must be introduced into the uterus, dead tissue must be present at the time, and the injured tissue must remain in the uterus for long enough to permit incubation. In our patient probably the organism was introduced into the uterus from bowel during the unsuccessful attempt at amniocentesis, because the high vaginal swab taken before the abortion was negative for clostridia.

*Cl welchii* septicaemia, especially when haemolysis is present, is regarded as an indication for total abdominal hysterectomy. The improved survival rates of the early 1970s were attributed to this aggressive surgical approach.<sup>2</sup> In the absence of haemolysis, however, prompt and adequate antibiotic treatment with immediate curettage will often effect a cure if coupled with good supportive care.<sup>3</sup>

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<sup>1</sup> Douglas GW. Toxic effects of *Welch* bacillus in post abortal infection. *NY State J Med* 1956;**56**:3673-7.

<sup>2</sup> Decker WH, Hall W. Treatment of abortion infected with *Clostridium welchii*. *Am J Obstet Gynecol* 1966;**95**:394-9.

<sup>3</sup> Pritchard JA, Whalley PJ. Abortion complicated by *Clostridium perfringens* infection. *Am J Obstet Gynecol* 1971;**111**:484-92.

<sup>4</sup> Medical Research Council Working Party on Amniocentesis. Assessment of the hazards of amniocentesis. *Br J Obstet Gynaecol* 1978;**85**:suppl 2.

<sup>5</sup> United States National Institute of Child Health and Human Development Study Group. Mid-trimester amniocentesis for prenatal diagnosis. Safety and accuracy. *JAMA* 1976;**236**:1471-6.

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## Diagnosis of encephalitozoonosis in man by serological tests

*Encephalitozoon cuniculi* causes lesions in the central nervous system and the kidneys in small mammals.<sup>1</sup> Few cases have been reported in man, and most have been in patients with immunosuppression.<sup>2</sup> Serological testing for encephalitozoonosis has not previously been attempted in man but is used in veterinary practice. We used indirect immunofluorescence to examine 22 serum samples from patients with disorders of the central nervous system of uncertain origin. One sample gave clearly positive results for *E cuniculi*, and we report on the patient.

### Case report

A boy born in Colombia, probably early in 1980, was taken to an orphanage and in 1981 adopted by a Swedish family. Earlier health records were not available, but he was healthy on arrival in Sweden and growth and development progressed normally.

In May 1982 he was admitted to hospital when generalised convulsive seizures with left sided predominance developed after light facial trauma. His temperature was normal. Examination showed slight liver enlargement. Serum alanine and aspartate transaminase activities were 1.45 and 1.74 mmol/l (87 and 104 IU/l). Further laboratory tests did not indicate any acquired or congenital infection. Lumbar puncture, a skull x ray film, and repeated electroencephalograms did not show any abnormality. Five weeks later a further left sided seizure occurred. On one occasion a right sided brain focus was recorded on electroencephalography, but this could not later be verified. Computed tomography of the brain gave normal results. Serological tests performed in July showed antibodies to *E cuniculi*, and as animals infected with this organism excrete spores in the urine<sup>1</sup> urological analysis was performed. Intravenous pyelography yielded normal results, and blood urea concentration and urine osmolality were normal; there was no proteinuria or glucosuria. Gram positive organisms, however, with nuclei that stained blue with Giemsa, were seen twice in sediments. The organisms, lying free or in aggregates, measured 1.5×2.5 μm and reacted with a fluorescent anti-*E cuniculi* conjugate. Intraperitoneal injection of urine samples into mice free of encephalitozoonosis resulted, after three weeks, in growth of organisms indistinguishable from *E cuniculi* in two of five animals. Ascitic fluid from the mice induced growth of the parasite after three weeks when added to dog

kidney cell cultures. Later attempts to culture the organism from urine samples were unsuccessful. He was given carbamazepine 90 mg twice daily as a prophylactic anticonvulsive and discharged from hospital.

In late August he was readmitted because of respiratory tract infection, raised temperature, and a swollen left knee. Aspirated joint fluid was aseptic, containing mononuclear cells but no antibodies to *E cuniculi*. In September stiffness of the shoulders and vertebral joints supervened, and the right knee became swollen. Indomethacin 20 mg daily and chloroquine 125 mg daily were started but he did not begin to recover until intra-articular knee injections of dexamethasone 40 mg were given in December. His health remained excellent after his discharge from hospital in February 1983. Indomethacin was stopped in December and chloroquine in May, but he continued to take carbamazepine 90 mg twice daily.

All serum samples showed high IgG titres against *E cuniculi* (>1/2560). One sample taken in 1981 also showed IgM antibodies (1/160). Serum alanine and aspartate transaminase activities increased during October 1982 to 5.62 and 3.32 mmol/l (337 and 199 IU/l) but returned to normal (0.59 and 0.41 mmol/l (35 and 25 IU/l)) in December. His erythrocyte sedimentation rate increased to 59 mm in the first hour before becoming normal in February 1983. Lymphocyte examinations performed in October 1982 and June 1983 showed normal B cell counts and low (1.0) ratios of helper to suppressor T cells, but suppressor T cells were never increased.

### Comment

This patient was clearly infected by a microsporidian, presumably *E cuniculi*, and IgM antibodies suggest that he was infected before his arrival in Sweden. The seizures probably reflected infection in the brain, and the arthritic symptoms may have been sequelae of infection, but neither can be attributed with certainty to the parasite. There was, however, a striking similarity to another case of encephalitozoonosis, in which spores of *E cuniculi* were found in the cerebrospinal fluid and urine of a boy who had seizures and later recovered.<sup>3</sup> Little is known about the pathology of encephalitozoonosis in man, but an intact immune system seems to arrest the infection as most cases have occurred in immunocompromised patients.<sup>2</sup> Furthermore, animal studies show that functioning T cells are necessary to prevent infection with *E cuniculi*.<sup>4</sup> Depression of immunity dependent on T cells has been observed in several parasitoses, and an increased prevalence of antibody to *E cuniculi* has been detected in patients with parasitoses, particularly malaria.<sup>5</sup> Although our patient had no sign of any other parasitic disease, there was a lymphocyte abnormality, but its relation to *E cuniculi* remains obscure.

We believe that this is the first reported case in which specific antibodies as well as the parasite have been found in man. Currently available data suggest that encephalitozoonosis is more common than has been thought. The difficulty of finding the parasite, because it lives in internal organs and only briefly appears in body fluids, may explain the few cases reported in man.

<sup>1</sup> Shaddock JA, Pakes SP. Encephalitozoonosis (nosematosis) and toxoplasmosis. *Am J Pathol* 1971;**64**:657-71.

<sup>2</sup> Bywater JEC. Is encephalitozoonosis a zoonosis? *Laboratory Animals* 1979;**13**:149-51.

<sup>3</sup> Matsubayashi H, Koike T, Mikata T, Hagiwara S. A case of Encephalitozoon-like body infection in man. *AMA Arch Pathol* 1959;**67**:181-7.

<sup>4</sup> Niederkorn JY, Shaddock JA, Schmidt ES. Susceptibility of selected inbred strains of mice to Encephalitozoon cuniculi. *J Infect Dis* 1981;**144**:249-53.

<sup>5</sup> Singh M, Kane GJ, Mackinlay L, et al. Detection of antibodies to Nosema cuniculi (protozoa: microsporidia) in human and animal sera by the indirect fluorescent antibody technique. *Southeast Asian J Trop Med Public Health* 1982;**13**:110-3.

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