One gram ethamsylate or placebo was injected intravenously at the time of induction of anaesthesia and 500 mg intramuscularly every six hours for 48 hours postoperatively. Prerandomised coded ampoules were used in a double blind manner and the code was not broken until the study was completed. None of the patients received prophylactic antibiotics or any prophylactic measures against venous thrombosis. All the operations were carried out by me, and blood loss was measured by laboratory estimation of the haemoglobin content of swabs used at operation.

None of the patients received epidural anaesthesia or vasoconstrictive drugs, nor did any patient receive dextran for fluid replacement. All the patients were accommodated on the same postoperative ward and fully mobilised by the third postoperative day. Deep vein thrombosis was diagnosed using ^{125}I labelled fibrinogen, as described by Negus *et al.*⁴ Measurements of radioactivity were taken at 10 cm intervals along the medial surface of the thigh and calf of each leg on postoperative days 1, 3, and 6. A difference of 15% or more between adjacent sites, or at identical sites between limbs, was regarded as a positive result.

Fourteen patients showed increases greater than 15% at one of the measured sites during the postoperative period. Five of these (21%) occurred in the ethamsylate group and nine (33%) in the placebo group. This difference was not statistically significant ($p > 0.05$; Fisher's exact test). None of the patients showed clinical signs of thrombosis. The table lists the postoperative morbidity of the patients.

Postoperative morbidity

Morbidity	Ethamsylate Group (n = 24)	Placebo Group (n = 27)
Mean (SD) surgical blood loss in ml	162.8 (99.3)	168.2 (93.8)
Mean (SD) No of postoperative days with maximum temperature $> 37.2^\circ\text{C}$	2.42 (1.56)	2.44 (1.60)
Vaginal haematoma (day 5 clinical assessment)	0	0
Deep vein thrombosis (^{125}I -fibrinogen method)	5	9

Since the data for blood loss showed some departure from normal they were log transformed before comparison using Student's *t* test ($t = 0.36$; $df = 49$; $p > 0.05$). There was no significant difference between the two groups in terms of surgical blood loss or postoperative fever (table), and no case of vaginal haematoma occurred in either group.

Comment

Attempts at explaining the haemostatic mechanism of ethamsylate are as yet hypothetical. It seems likely that ethamsylate encourages the formation of long chain mucopolysaccharides in the capillary wall, thereby increasing capillary strength and reducing the bleeding time. There is no effect on cell counts or on fibrinogen or prothrombin concentrations and therefore no theoretical reason for any increased tendency to thrombosis with administration of ethamsylate.

This study showed no evidence of any increase in the incidence of postoperative deep vein thrombosis with ethamsylate. This conclusion corroborates the results of a clinical trial using ethamsylate in post-partum patients,³ which showed that the drug had no thrombogenic effects. The present study failed to show a reduction in blood loss or postoperative morbidity in ethamsylate treated patients undergoing major vaginal surgery, probably because the large vessels concerned are not affected by a drug acting at capillary level.

I am very grateful to Mrs M Dove, of St Mary's Hospital, Portsmouth, for the blood loss estimations and to Mr C A R Lamont, St Mary's Hospital, Portsmouth, for allowing me to study his patients.

¹ Symes JM, Offen DN, Lyttle JA, Blandy JP, Chaput de Saintogne DM. The effect of Dicynene on blood loss during and after transurethral resection of the prostate. *Br J Urology* 1975;47:203-7.

² Vere MF, Sellers SM, Joyce DN, Staddon GE. Use of ethamsylate in vaginal surgery and deep-vein thrombosis. *Br Med J* 1979;iii:528.

³ Harrison RF, Ennis J, Brennan M. Crying wolf on drug safety. *Br Med J* 1982;284:901.

⁴ Negus D, Pinto DJ, Le Quesne LP, Brown N, Chapman M. ^{125}I -labelled fibrinogen in the diagnosis of deep-vein thrombosis and its correlation with phlebography. *Br J Surg* 1968;55:835-9.

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In utero resuscitation after cardiac arrest in a fetus

Although birth asphyxia is an important aetiological factor leading to neonatal death and perinatal brain haemorrhage, several studies on the resuscitation of babies with perinatal cardiac arrest have shown that the outcome is generally good when the heart beat returns within five minutes after birth.¹ We report on a hydropic fetus with severe rhesus isoimmunisation that was successfully resuscitated in utero by external cardiac massage, after cardiac arrest for three minutes during fetoscopic intravascular blood transfusion at 19 weeks' gestation.² Real time ultrasonography ruled out cerebral oedema and periventricular or intraventricular haemorrhage, and the baby was delivered in good condition several weeks later.

Case report

A 28 year old woman, whose blood group was A Rh negative, was in her ninth pregnancy. The first four had been uneventful and had resulted in normal deliveries at term. After the fourth delivery, however, she was found to have anti-D antibodies. In the subsequent four pregnancies the fetuses had severe rhesus isoimmunisation, which resulted in two neonatal deaths at 36 and 33 weeks' gestation followed by two intrauterine deaths at 30 and 26 weeks' gestation.

In this pregnancy the maternal antibody concentration was 17 IU/ml at 14 weeks and 213 IU/ml at 18 weeks despite thrice weekly plasmapheresis. Spectrophotometric measurements of amniotic fluid (change in optical density at 450 nm) at 17 and 18 weeks were 0.116 and 0.127 respectively ("mildly affected" zone of an extrapolated Liley's chart³). She was referred to this unit at 18 weeks after ultrasound examination showed a fetus with scalp oedema associated with large pericardial, pleural, and ascitic effusions.

At 18, 19, 23, 26, and 29 weeks fresh packed (packed cell volume 0.6-0.8) group O Rh negative blood was infused into an umbilical cord artery under direct fetoscopic vision. The figure shows the fetal packed cell volume before and after each transfusion. After the first transfusion the fetal oedema and pleural and pericardial effusions resolved rapidly but there was some residual ascites. During an otherwise uneventful second transfusion sudden, severe fetal bradycardia culminating in cardiac asystole within two minutes was seen on real time ultrasound scanning. She was turned into the left lateral position, and, under continuous ultrasound guidance, the fetal heart was massaged at 40 compressions a minute by digital pressure through the maternal abdomen, the fetal chest being compressed against the posterior uterine wall. Spontaneous cardiac activity resumed in three minutes.

The rest of the pregnancy and subsequent intravascular transfusions were uneventful. Serial real time ultrasound scans of the fetal brain and measurement of the anterior and posterior horns of the lateral ventricles⁴ ruled out cerebral oedema and periventricular or intraventricular haemorrhage and their sequelae of hydrocephaly and porencephalic cysts. Fetal growth was normal, and the ascites resolved. At 32 weeks a 1932 g non-hydropic boy was delivered by elective caesarean section. His Apgar score was three at one minute and nine at five minutes. His cord blood haemoglobin concentration was 6.1 g/dl and plasma bilirubin concentration 60 $\mu\text{mol/l}$ (3.5 mg/100 ml). He required three exchange transfusions, but there were no neonatal complications. Subsequent growth and neurodevelopment were normal.

Fetal packed cell volumes before (□) and after (▲) five successive intravascular transfusions and at delivery (○).

Comment

This case shows how the advent of fetoscopic intravascular transfusions has greatly improved the outlook for fetuses with severe rhesus isoimmunisation that develop hydrops at an early gestational age.⁵ Furthermore, the successful outcome of antepartum cardiac massage in utero suggests that this technique might be incorporated in the management of intrapartum fetal death. As cardiotocography is used to monitor most women in labour fetal cardiac arrest can now be recognised immediately. External cardiac massage may therefore be performed under real time ultrasound guidance while arrangements

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

We thank Dr J R Kemp and the staff of the rhesus isoimmunisation centre at Lewisham Hospital for referring the patient and providing us with donor blood; and Drs H R Gamsu and W J Fysh, who managed the neonate at the neonatal unit at King's College Hospital.

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- ² Rodeck CH, Holman CA, Karnicki J, et al. Direct intravascular fetal blood transfusion by fetoscopy in severe rhesus isoimmunisations. *Lancet* 1981; i:625-7.
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- ⁴ Campbell S, Pearce JM. Ultrasound visualisation of congenital malformations. *Br Med Bull* 1983;39:322-31.
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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%.¹ 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.^{2,3} Amniocentesis is a safe procedure with a slight increase of 1.0-1.5% in the rate of fetal loss.⁴ Amnionitis after amniocentesis has been reported but at a rate of less than 0.1%.⁵

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 α 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.¹ Septic abortion due to *Cl welchii* rarely occurs in clinical practice