CURRENT TOPIC

Vascular compromise in newborn infants

D T Gault

With improved neonatal resuscitation techniques a number of infants are now surviving only to develop vascular problems secondary to intravascular catheterisation, repeated venepuncture, or arterial blood sampling. Spontaneous thromboses are also more common in early life than in later childhood.^{1 2} Guidelines for the prevention, diagnosis, and treatment of blocked vessels in adult patients are not automatically applicable to the newborn. The size of the delicate vessels, the immature haemostatic mechanism, and the background of relative polycythaemia pose special problems.

Thromboembolic vessel obstruction may result in death or irreversible damage to an organ or limb. In addition to blockage of peripheral vessels,^{3 4} thrombosis of the cerebral,⁵ pulmonary,^{6 7} coronary,^{8 9} renal,¹⁰ and mesenteric arteries,¹¹ is reported in the neonate. Peripheral artery occlusion usually presents with a cold, pulseless, mottled, and discoloured limb. Obstruction of the central veins or arteries may be more difficult to recognise. Renal vein thrombosis, for example, does not always present with haematuria and an enlarged kidney, and thrombosis of the aorta may not disclose itself with congestive cardiac failure and ischaemia of the lower limbs.¹

Incidence

The incidence of thrombosis in the newborn appears to be increasing.¹² This may be due to more widespread use of intravascular catheters, prolongation of life in very ill infants, or a more careful analysis of necropsy material where previously the diagnosis of vessel thrombosis was missed.

Cannulation of the umbilical vein is particularly associated with thrombosis. Postmortem examination of infants revealed thrombotic complications of umbilical vein catheterisation in between 20 and 61% of cases, although in some of them the infusion of a hyperosmolar solution may have been a factor.^{13 14} Umbilical artery cannulae have also been shown frequently to cause thrombosis both on necropsy studies^{15 16} and on aortography.¹⁷ Of course, not all the reported thromboses would have led to ischaemic damage. In some cases the vessel is only partially occluded and in others an adequate collateral circulation exists. In a large series of 4000 patients with umbilical artery catheters, only 1% developed actual clinical symptoms of thrombosis.¹⁸

The placement of vascular catheters carries a potential risk no matter which vessel is involved. Neonatal thrombosis has been described in

association with radial,¹⁹ femoral,²⁰ pulmonary,²¹ and temporal artery²² lines, as well as with catheters into the jugular^{7 23} or femoral²⁴ veins. Thrombi are also found when catheters are not used. A review of consecutive necropsies revealed a 4.5% incidence of thrombosis in uncatheterised cases, and an 11% incidence when intravascular catheters were used.²⁵ Even temporary catheterisation can cause problems. In a prospective study of children undergoing cardiac catheterisation, 3.6% developed clinical symptoms of femoral artery thrombosis.²⁶ An extensive literature review of 1045 cannulations of the radial artery in newborn infants showed that 6% of cases suffered transient ischaemia and 0.5% had permanent ischaemic damage.²⁷ Even hand amputation after radial artery cannulation has been reported.²⁸ The incidence of vessel occlusion without ischaemic changes, however, is as high as 63%,²⁹ and in such cases, an adequate collateral circulation exists. Flow in the blocked vessel is often restored several days after catheter removal.

The propensity to develop thrombosis is related to size of the infant. The risk of vessel obstruction after cardiac catheterisation is highest in infants of less than 10 kg.^{27 30 31}

Aetiology

The cause of thrombosis in the neonatal period is often uncertain but some key factors bear special mention. It is mainly sick children who are affected. In one early series, 80% of cases were associated with infection. One factor here may be the growth of small endocardial vegetations which dislodge to occlude distant vessels.⁴ Emboli may also derive from cardiac thrombi secondary to fibrillation and anomalous valves.⁴

Some maternal factors are important. Both venous thrombosis and peripheral gangrene have been reported in the infants of diabetic mothers.^{32–34} Venous emboli may pass through the foramen ovale to enter the arterial circulation.³⁴

Thrombus formation in fetal placental veins is unusual in a normal pregnancy, but occurs quite often in maternal hypertension.³⁵ Chorionic thrombi may embolise to fetal vessels and have been linked to the presence of pulmonary and portal venous emboli.³⁵ In cases of initial twin pregnancy with subsequent fetus papyraceous of one, fragments of thromboplastic material may pass through vascular shunts to the circulation of the live fetus,³⁶ to present as local ischaemic damage due to thrombosis.^{36–38} It is estimated that 32% of pregnancies which

Department of Plastic Surgery,
Mount Vernon Hospital,
Rickmansworth Road,
Northwood, Middlesex
HA6 2RN

Correspondence to:
Mr Gault.

are twin at 10 weeks lead to singleton deliveries.³⁹ Thrombi may also form within a patent ductus, particularly when there is an aneurysmal dilatation,⁴⁰ and resulting emboli can cause peripheral vessel occlusion.⁴

Virchow postulated three major factors contributing to the formation of thrombi: abnormalities of the vessel wall, disturbances of blood flow, and changes in blood coagulability.⁴¹ This provides a convenient framework within which to examine how neonatal thrombi may form.

(1) ABNORMALITIES OF THE VESSEL WALL

If during birth a limb is trapped between the fetal head and the maternal pelvis, damage to the intima of a major vessel sufficient to precipitate thrombosis may occur.⁴² Birth trauma may explain some cases of limb ischaemia but thrombosis has also been seen after caesarean section,⁴³ in association, for example, with amniotic construction bands⁴³ and entrapment by the umbilical cord.⁴²

External pressure on the vessel wall due to a compartment syndrome has been reported to cause vessel obstruction and digital ischaemia; fasciotomy was beneficial.⁴⁴ Even drugs extravasated into the subcutaneous tissues during emergency neonatal reconstruction can obstruct the venous return of an upper limb, and removal of the offending material by aspiration using blunt cannulae can restore the circulation (D T Gault, personal observation).

Thrombosis of femoral vessels leading to amputation after venepuncture has been reported.⁴⁵ Intentional and inadvertent arterial puncture is also known to cause arterial thrombosis,⁴⁶ especially if a substance which irritates the vessel intima is infused.⁴⁷ Even a vasculitis in a newborn infant has presented with peripheral gangrene.⁴⁸

Intravascular catheters can act as a nidus for fibrin and platelets, may damage the endothelium of the vessel wall, may partially occlude a vessel, and may precipitate vasospasm. Neonatal monitoring with umbilical artery catheters, introduced in 1962,⁴⁹ is now commonplace and is associated with the majority of catheter related thrombosis. The risk is greatest when hyperosmolar solutions are infused.²⁶

(2) FLOW

Hyperviscosity of the blood is reported in 1–5% of neonates.^{50–52} Blood viscosity is a function of plasma viscosity and packed cell volume. In newborn infants, a venous packed cell volume greater than 0.65 is considered to be indicative of hyperviscosity; a small rise in packed cell volume above 0.70 results in a considerable increase in blood viscosity.⁵² Delayed cord clamping can increase packed cell volume by permitting extra placental blood to be transferred to the infant. Hyperviscosity is also related to the deformability and aggregability of the red blood cells—those of a newborn infant are larger and less deformable than in older children and are associated with increased platelet adhesion.⁵³

Increased blood viscosity is noted in the

infants of smokers⁵⁴ and diabetic mothers⁵⁵ where sluggish maternal circulation may cause compensatory polycythaemia in the fetal blood. Small for dates babies are also prone to polycythaemia and in them this may be a response to chronic hypoxia as a result of placental insufficiency.⁵⁰ Hyperviscosity adversely affects blood flow leading to a relative local hypoxia and acidosis which may prematurely trigger the coagulation system.⁵⁶ Peripheral gangrene in a term infant with polycythaemia has been reported.⁵⁷

The risk of arterial and venous thrombosis is high in dehydrated infants, usually those with neonatal diarrhoea.^{4 33 57–61} The newborn have little reserve to cope with dehydration, and an extracellular fluid volume deficit rapidly leads to a low flow state that could aggravate a tendency to thrombosis.⁴⁶

(3) COAGULATION

It is currently thought that damage to the vessel wall and disturbances of blood flow are more directly implicated in neonatal thrombosis than the peculiarities of neonatal haemostasis and fibrinolysis.¹ In a healthy infant both the coagulation and fibrinolytic systems are immature but in balance. Inherited deficiencies of antithrombin III⁶² and protein C⁶³ have been reported in neonates and were associated with fatal thrombosis.

Treatment

Neonatal intensive care units are likely to encounter vascular compromise and should formulate a treatment policy. Even when arterial occlusion does not cause irreversible ischaemia, the affected extremities may suffer retarded growth.^{64–66} The small calibre of the vessels, their tendency to spasm, and reports of re-thrombosis after surgery have in the past curbed enthusiasm for a surgical solution. However, with recent advances in microsurgical techniques, some success has been recorded.

HEPARIN

The newborn infant appears to require a proportionally larger amount of heparin than an adult to achieve an adequate therapeutic effect and as the half life is short, continuous infusion is the best method of treatment.⁶⁷ A 50 unit/kg bolus followed by 20 units/kg/hour has been shown to resolve femoral artery thrombosis after cardiac catheterisation in 43% to 80% of cases.^{67–69} McDonald and Hathaway showed that a mean dose of 27 units/kg/hour was required to give plasma heparin concentrations in the therapeutic range (0.3–0.5 units/ml) and they reported good results in 14 out of 15 babies studied.⁶⁷

THROMBOLYSIS

Thrombolytic treatment has been shown to be effective and safe in a paediatric population.^{26 68 70} Two thrombolytic agents, streptokinase and urokinase, are widely used to activate plasminogen which is converted to the

proteolytic enzyme plasmin, capable of dissolving fibrin clots. Administered systematically, these drugs can treat both arterial and venous thromboses, but there is a risk of haemorrhage, especially in preterm babies who already run a high risk of intracranial haemorrhage.⁷¹ Clots less than five days old are more susceptible to thrombolysis,⁷⁰ but chronic obstructions have also been treated.⁷²⁻⁷³ A loading dose of 10 000 units/kg of streptokinase and then 1000 units/kg/hour is recommended.⁶⁸ The treatment is then adjusted to reduce fibrinogen concentrations to between 1.0 and 1.4 g/l. If little response is noted, streptokinase can be increased to 2000 units/kg/hour. Streptokinase is made from the streptococcus, and may be affected by the presence of antistreptococcal antibodies; urokinase is considered by some to be preferable as it is non-antigenic. A loading dose of 4000 units/kg of urokinase followed by 4000 units/kg/hour⁶⁸⁻⁷⁴ has been commonly used but some authors have doubled the loading dose⁷⁵ or the hourly infusion rate.⁷⁶

The fibrinolytic mechanism is not fully developed at birth, and a bias of the haemostatic mechanism towards fibrin formation has been reported.⁷⁷ Like heparin, a higher concentration of the plasminogen activator may be required for successful thrombolysis in the newborn and premature infant relative to older children and adults.⁷⁸⁻⁷⁹ Corrigan *et al* showed that 11 times the amount of urokinase was required to achieve levels of activity seen in adults.⁷⁹

Many authors have reported success with thrombolytic treatment. In heparin resistant femoral thrombosis, thrombolysis was successful in excess of 85% of cases.²⁶⁻⁶⁸⁻⁷⁸ Thrombolysis has been recommended as the first line treatment for thrombosis, with thrombectomy reserved for those that do not respond.⁸⁰ Local administration at the site of the blockage using a catheter permits lower doses to be used.⁸¹ Selective treatment with 50 units/kg/hour of streptokinase has shown good results in children.⁷⁰⁻⁸²

SURGERY

Thrombectomy in very young infants is prone to re clotting⁸³ but despite this, useful limb salvage is often achieved.⁸³⁻⁸⁶ The passage of a Fogarty catheter down a small vessel may fissure the intima,⁸⁶ and even mobilising a vessel has been reported to cause thrombosis in this age group.⁸⁷ Flanigan *et al* noted that very small (2–3 French gauge) Fogarty catheters could not enter the femoral arteries of a neonate.⁸⁸ Clots may, however, be removed by aspiration using a small plastic catheter with a blunt end.⁴⁶⁻⁸⁷ Both success³⁻⁴⁶⁻⁶⁹⁻⁸⁶⁻⁸⁹⁻⁹¹ and failure⁹² of thrombectomy is recorded.

The femoral and brachial arteries in neonates are of a similar size to the digital vessels in adults where microsurgical replantation surgery is now routine. Even when thrombectomy from such vessels does not restore all pulses, the limb is often salvaged and the surgery may well improve access to the collateral circulation. In one recent case where persistent rethrombosis beset a surgical reconstruction in a preterm

infant, the limb was salvaged using postoperative thrombolytic treatment.⁸⁵ Surgery to salvage a failed trial of thrombolysis, and thrombolysis to improve the results of surgery may yet provide the most comprehensive treatment option. Even when a limb is viable after a thrombosis, there may be later growth discrepancy. Surgery, when the child is older, has been described to improve limb blood flow and equalise limb length.⁶⁵⁻⁶⁹

Complications

Vascular occlusion can precipitate distal ischaemic damage and necrosis, but even when an adequate collateral circulation develops, a variety of late complications can occur. In the upper limb, contractures and stunted forearm bone growth have been reported.⁹³ Damage to the femoral artery after cardiac catheterisation has also caused reduced leg growth⁶⁴⁻⁶⁶⁻⁸⁸ and some children have even gone on to develop claudication.⁸³

Prevention

Catheter related vascular occlusion is likely to be influenced by the type of catheter, its placement, and the concomitant use of heparin. The use of smaller catheters for cardiac catheterisation has decreased the incidence of femoral artery thrombosis.²⁶ Heparin as a 100 unit/kg bolus at the time of catheterisation has also reduced the incidence of thrombosis in these children.⁹⁴ Low dose heparin (1–2 units/ml in infusions) has been shown to prolong umbilical artery catheter patency,⁹⁵ but may not affect the thrombosis rate.

Silastic catheters are less thrombogenic than standard polyvinyl chloride catheters⁹⁶ and end hole catheters are less thrombogenic than side hole catheters.⁹⁷ The use of thromboresistant umbilical artery catheters (heparin bonded to the surface polyurethane) failed to reduce the incidence of complications significantly.⁹⁸ The thrombosis rate is not affected by a change in the placement of the catheter tip, either at the seventh thoracic or fourth lumbar segment.⁹⁹

Conclusion

Vascular compromise in a neonate was first described in 1828 and of the first 52 cases of ischaemic extremities, 17 died and 17 lost limbs.⁴³ Much better results are now obtained. Early recognition of the problem with prompt instigation of thrombolytic treatment has become the mainstay of treatment. Good results of surgical thrombectomy are also now recorded, and once again, early referral is essential. While rethrombosis after surgery may occur, the unconventional combination of surgery and subsequent thrombolytic treatment has salvaged limbs in very difficult circumstances.⁸⁵

1 Schmidt B, Zipursky A. Thrombotic disease in newborn infants. *Clin Perinatol* 1984;11:461–88.

2 Morison JE. *Foetal and neonatal pathology*. London: Butterworth, 1970:323–8.

3 Braly BD. Neonatal arterial thrombosis and embolism. *Surgery* 1965;58:869–73.

- 4 Gross RE. Arterial embolism and thrombosis in infancy. *Am J Dis Child* 1945;70:61-73.
- 5 Barmada MA, Moosy J, Shuman RM. Cerebral infarcts with arterial occlusion in neonates. *Ann Neurol* 1979;6:495-502.
- 6 Burrows PE, Leahy FA, Reed MH. Neonatal pulmonary infarction. *Am J Dis Child* 1983;137:61-4.
- 7 Wesley JR, Keens TG, Miller SW, Platzer ACG. Pulmonary embolism in the neonate. *J Pediatr* 1978;93:113-5.
- 8 Gault MH, Usher R. Coronary thrombosis with myocardial infarction in a newborn infant. *N Engl J Med* 1960;263:379-82.
- 9 Sapire DW, Markowitz R, Valdes-Dapena M, Engel S. Thrombosis of the left coronary artery in a newborn infant. *J Pediatr* 1977;90:957-9.
- 10 Durante D, Jones D, Spitzer R. Neonatal renal arterial embolism syndrome. *J Pediatr* 1976;89:978-81.
- 11 DeSa DJ. The spectrum of ischemic bowel disease in the newborn. *Perspect Pediatr Pathol* 1976;3:273-309.
- 12 Oski FA, Naiman JL. *Hematologic problems in the newborn*. Philadelphia: WB Saunders, 1982.
- 13 Scott JM. Iatrogenic lesions in babies following umbilical vein catheterization. *Arch Dis Child* 1965;40:426-9.
- 14 Symansky MR, Fox HA. Umbilical vessel catheterization: Indications, management and evaluation of the technique. *J Pediatr* 1972;80:820-6.
- 15 Tyson JE, DeSa DJ, Moore S. Thromboatheromatous complications of umbilical arterial catheterization in the newborn period. Clinicopathological study. *Arch Dis Child* 1976;51:744-54.
- 16 Gupta JM, Robertson NRC, Wigglesworth JS. Umbilical artery catheterization in the newborn. *Arch Dis Child* 1968;43:382-7.
- 17 Neal WA, Reynolds JW, Jarvis CW, et al. Umbilical artery catheterization: demonstration of arterial thrombus by aortography. *Pediatrics* 1972;50:6-13.
- 18 O'Neill JA, Neblett WW, Born ML. Management of major thromboembolic complications of umbilical artery catheters. *J Pediatr Surg* 1981;16:972-8.
- 19 Cartwright GW, Schreiner RL. Major complication secondary to percutaneous radial artery catheterization in the neonate. *Pediatrics* 1980;65:139-41.
- 20 Stanger P, Heymann MA, Tarnhoff H, et al. Complications of cardiac catheterization of neonates, infants and children. *Circulation* 1974;50:595-608.
- 21 Pokora TJ, Boros SJ, Brennom WS, et al. Fatal neonatal thrombosis associated with a pulmonary artery catheter. *Crit Care Med* 1981;9:618-9.
- 22 Prian GW, Wright GB, Rumack CM, et al. Apparent cerebral embolization after temporal artery catheterization. *J Pediatr* 1978;93:115-8.
- 23 Plam MB, McGough EC, Nixon GW, et al. Right atrial ball valve thrombus: a complication of central venous alimentation in an infant. *J Thorac Cardiovasc Surg* 1979;78:579-82.
- 24 Hawker RE, Celermajer JM, Cartmill TB, et al. Thrombosis of the inferior vena cava following balloon septostomy in transposition of the great arteries. *Am Heart J* 1971;82:593-5.
- 25 Wigger HJ, Bransilver BR, Blanc WA. Thromboses due to catheterization in infants and children. *J Pediatr* 1970;76:1-11.
- 26 Wessel DL, Keane JF, Fellows KE, Robichaud H, Lock JE. Fibrinolytic therapy for femoral arterial thrombosis after cardiac catheterization in infants and children. *Am J Cardiol* 1986;58:347-51.
- 27 Hack WWM, Vos A, Okken A. Incidence of forearm and hand ischaemia related to radial artery cannulation in newborn infants. *Intensive Care Medicine* 1990;16:50-3.
- 28 Samaan HA. The hazards of radial artery pressure monitoring. *J Cardiovasc Surg (Torino)* 1971;12:342-7.
- 29 Hack WWM, Vos A, van der Lei J, Okken A. Incidence and duration of total occlusion of the radial artery in newborn infants after catheter removal. *Eur J Pediatr* 1990;149:275-7.
- 30 Sunderland CO, Nichols GM, Henken DP, et al. Percutaneous cardiac catheterization and atrial balloon septostomy in pediatrics. *J Pediatr* 1976;89:584-7.
- 31 Mortenson W, Hallböök T, Lundstrom NR. Percutaneous catheterization of the femoral vessels in children. II. Thrombotic occlusion of the catheterized artery: frequency and causes. *Pediatr Radiol* 1975;4:1-9.
- 32 Ward TF. Multiple thromboses in an infant of a diabetic mother. *J Pediatr* 1977;90:982-4.
- 33 Oppenheimer EH, Esterley JR. Thrombosis in the newborn: comparison between infants of diabetic and non diabetic mothers. *J Pediatr* 1965;67:549-56.
- 34 Valderama E, Gribetz I, Strauss L. Peripheral gangrene in a newborn infant associated with renal and adrenal vein thrombosis. *J Pediatr* 1972;80:101.
- 35 DeSa DJ. Intimal cushions in foetal placental veins. *J Pathol* 1973;110:347-52.
- 36 Wagner DS, Klein RL, Robinson HB, Novak RW. Placental emboli from a fetus papyraceous. *J Pediatr Surg* 1990;25:538-42.
- 37 Rayner CR, Lloyd DJ, Ward K. Neonatal upper limb ischaemia. The case for conservative management. *J Hand Surg [Br]* 1984;9:57-8.
- 38 Gilbert EF, Hogan GR, Stevenson MM, Suzuki H. Gangrene of an extremity in the newborn. *Pediatrics* 1970;45:469-72.
- 39 Benirschke K, Driscoll SG. *The pathology of the human placenta*. New York: Springer Verlag, 1967:91-179.
- 40 Falcone MW, Perloff JK, Roberts WC. Aneurysm of the non-patent ductus arteriosus. *Am J Cardiol* 1972;29:422-6.
- 41 Virchow R. Phlogose und Thrombose im Gefässsystem. In: Virchow R, ed. *Gesammelte Abhandlungen zur Wissenschaftlichen Medizin*. Frankfurt a/m: Meidinger Sohn, 1856:458.
- 42 Steiner MD. Gangrene of an extremity in a newborn child. *Am J Obstet Gynecol* 1945;49:686-90.
- 43 Askue WE, Wong R. Gangrene of the extremities in the newborn infant. *J Pediatr* 1952;40:588-98.
- 44 Christiansen SD, Desai NS, Pulito AR, Slack MR. Ischemic extremities due to compartment syndromes in a septic neonate. *J Pediatr Surg* 1983;18:641-3.
- 45 Nasbeth DC, Jones JE. Gangrene of the lower extremities of infants after femoral venipuncture. *N Engl J Med* 1963;268:1003-5.
- 46 Perry MO. Iatrogenic injuries of arteries in infants. *Surg Gynecol Obstet* 1983;157:415-8.
- 47 Wehbe MA, Moore JH. Digital ischemia in the neonate following intravenous therapy. *Pediatrics* 1985;76:99-103.
- 48 Miller JJ, Fries JF. Simultaneous vasculitis in a mother and newborn infant. *J Pediatr* 1975;87:443-5.
- 49 Nelson NM, Prodhom LS, Cherry RB, et al. Pulmonary function in the newborn infant. *Pediatrics* 1962;30:975-89.
- 50 Linderkamp O. Blood rheology in the newborn infant. *Bailliere's Clinical Haematology* 1987;1:801-26.
- 51 Brooks GI, Backes CR. Hyperviscosity secondary to polycythemia in appropriate for gestational age neonate. *Journal of the American Obstetric Association* 1981;80:415-8.
- 52 Black VD, Lubchenco LO. Neonatal polycythemia and hyperviscosity. *Pediatr Clin North Am* 1982;29:1137-48.
- 53 Aarts PAMM, Bolhuis PA, Sakariassen KS, Heethaar R, Sixma JJ. Red blood cell size is important for adherence of blood platelets to artery subendothelium. *Blood* 1983;62:214-7.
- 54 Buchan P. Fetal intrauterine growth retardation and hyperviscosity. In: Heilmann L, Buchan P, eds. *Hemorheological disorders in obstetrics and neonatology*. Stuttgart: Schattauer, 1984:7-20.
- 55 Violaris K, Bitzios E, Rudolph N. Increased blood viscosity and tachypnea in infants of diabetic mothers. *Arch Dis Child* 1986;61:910-2.
- 56 Peters M, ten Cate JW, Koo LH, Breederveld C. Persistent antithrombin III deficiency: risk factor for thromboembolic complications in neonates small for gestational age. *J Pediatr* 1984;105:310-4.
- 57 Papageorgiou A, Stern L. Polycythemia and gangrene of an extremity in a newborn infant. *J Pediatr* 1972;81:985-7.
- 58 Mehta MG, Betkerur UN. Peripheral gangrene in infancy. Report of 3 cases. *Indian J Pediatr* 1973;40:154-5.
- 59 Heller G, Alvari G. Gangrene of the extremities of the newborn. Occurrence of functional recovery. *Am J Dis Child* 1941;62:133-40.
- 60 Belman AB. Renal vein thrombosis in infancy and childhood—a contemporary survey. *Clin Pediatr (Phila)* 1976;15:1033-44.
- 61 Renfield ML, Kraybill EN. Consumption coagulopathy with renal vein thrombosis. *J Pediatr* 1973;82:1054-6.
- 62 Bjarke B, Herin P, Blomback M. Neonatal aortic thrombosis. A possible clinical manifestation of congenital antithrombin III deficiency. *Acta Paediatr Scand* 1974;63:297-301.
- 63 Seligsohn U, Berger A, Abend M, et al. Homozygous protein C deficiency manifested by massive venous thrombosis in the newborn. *N Engl J Med* 1984;310:559-62.
- 64 Bassett FH, Lincoln CR, King TD, Canent RV. Inequality in the size of the lower extremity following cardiac catheterization. *South Med J* 1968;61:1013-7.
- 65 Bloom JD, Mozersky DJ, Buckley CJ, Hagood CO. Defective limb growth as a complication of catheterization of the femoral artery. *Surg Gynecol Obstet* 1974;138:524-6.
- 66 Whitehouse WM, Coran AG, Stanley JC, et al. Pediatric vascular trauma. Manifestations, management and sequelae of extremity arterial injury in patients undergoing surgical treatment. *Arch Surg* 1976;111:1269-75.
- 67 McDonald MM, Hathaway WE. Anticoagulant therapy by continuous heparinization in newborn and older infants. *J Pediatr* 1982;101:451-7.
- 68 Ino T, Benson LN, Freedom RM, Barker GA, Aipursky A, Rowe RD. Thrombolytic therapy for femoral artery thrombosis after pediatric cardiac catheterization. *Am Heart J* 1988;115:633-9.
- 69 Klein MD, Coran AG, Whitehouse WM, Stanley JC, Wesley JR, Lebowitz EA. Management of iatrogenic arterial injuries in infants and children. *J Pediatr Surg* 1982;17:933-9.
- 70 Pritchard SL, Culham JAG, Rogers PCJ. Low dose fibrinolytic therapy in infants. *J Pediatr* 1985;106:594-8.
- 71 Volpe J. Intracranial hemorrhage; periventricular in intraventricular hemorrhage of the premature infant. In: Volpe JJ, ed. *Neurology of the newborn*. Philadelphia: WB Saunders, 1987:311-61.
- 72 Hess H, Ingrisch H, Mietaschk A, Rath H. Local low dose thrombolytic therapy of peripheral arterial occlusions. *N Engl J Med* 1982;307:1627-30.
- 73 Becker GJ, Rabe FE, Richmond BD, et al. Low dose fibrinolytic therapy. *Radiology* 1983;148:663-70.
- 74 Delaplane D, Scott JP, Riggs TW, Silverman BL, Hunt CE. Urokinase therapy for a catheter related right arterial thrombus. *J Pediatr* 1982;100:149-52.
- 75 Husted VA, Wicklund BM. Treatment of neonatal aortic thrombosis with urokinase. *Am J Pediatr Hematol Oncol* 1990;12:336-9.
- 76 Schmidt B, Wais U, Furste HO, Pringsheim W. Arterial occlusion in a preterm infant; successful non surgical treatment with urokinase and low dose heparin. *Helvetica Paediatrica Acta* 1982;37:483-8.
- 77 Suarez CR, Walenga J, Mangogna LC, Fareed J. Neonatal and maternal fibrinolysis. Activation at time of birth. *Am J Hematol* 1985;19:365-72.
- 78 Brus F, Witsenberg M, Hofhuis WJD, Hazelzet JA, Hess J. Streptokinase treatment for femoral artery thrombosis after

- arterial cardiac catheterization in infants and children. *Br Heart J* 1990;63:291-4.
- 79 Corrigan JJ, Sleeth JJ, Jeter M, Lox CD. Newborns fibrinolytic mechanism; components and plasmin generation. *Am J Hematol* 1989;32:273-8.
 - 80 Kirk CR, Qureshi SA. Microvascular surgery to preserve a preterm infants ischaemic arm. *BMJ* 1988;297:1198.
 - 81 Dotter CT, Rosch J, Seaman AJ. Selective clot lysis with low dose streptokinase. *Radiology* 1974;111:131.
 - 82 Abejo R, John EG, Spigos DG. Low dose streptokinase-induced clot lysis of an occluded arteriovenous fistula. *J Pediatr* 1985;106:321-3.
 - 83 Smith C, Green RM. Pediatric vascular injuries. *Surgery* 1981;90:20-31.
 - 84 Davison PM, Sully L. Microvascular surgery to preserve a preterm infants ischaemic arm. *BMJ* 1988;297:788.
 - 85 Kay S, Gilpin DJ. Combined microsurgical and thrombolytic salvage of an ischaemic lower limb in a 1079 gram preterm neonate. *Br J Plast Surg* 1991;44:310-1.
 - 86 Stavorovsky M, Iellin A, Spirir Z. Acute ischemia of the limb in a newborn treated successfully by thrombectomy. *Am J Surg* 1975;129:337-40.
 - 87 Cahill JL, Talbert JL, Ottesen OE, et al. Arterial complications following cardiac catheterization in infants and children. *J Pediatr Surg* 1967;2:134-43.
 - 88 Flanagan DP, Stolar CJH, Pringle KC, Schuler JJ, Fisher E, Vidyasager D. Aortic thrombosis after umbilical artery catheterization. Successful surgical management. *Arch Surg* 1982;117:371-4.
 - 89 Henry W, Johnson BB, Petersen AL. Left common iliac arterial embolectomy in the newborn. *Western Journal of Surgery* 1960;68:352-3.
 - 90 Hatch EI, Burrington JD. Neonatal aortic occlusion with successful embolectomy. *J Pediatr Surg* 1971;6:665.
 - 91 Fee HJ, McAvoy JM, Dainko EA. Neonatal arterial occlusion. *J Pediatr Surg* 1977;12:711-3.
 - 92 Wiseman NE, Briggs JN, Bolton VS. Neonatal arterial occlusion with ischemic limb gangrene. *J Pediatr Surg* 1977;12:707-10.
 - 93 Engel J, Heim M, Tsur H. Late complications of neonatal volkmans ischaemia. *The Hand* 1982;14:162-3.
 - 94 Girod DA, Hurwitz RA, Caldwell RL. Heparinization for prevention of thrombosis following pediatric percutaneous arterial catheterization. *Pediatr Cardiol* 1982;3:175-80.
 - 95 Rajani K, Goetzman BW, Wennberg RP, et al. Effect of heparinization of fluids infused through an umbilical artery catheter on catheter patency and frequency of complications. *Pediatrics* 1979;63:552-6.
 - 96 Boros SJ, Thompson TR, Reynolds JW, et al. Reduced thrombus formation with silicone elastomer (Silastic) umbilical artery catheters. *Pediatrics* 1975;56:981-6.
 - 97 Westrom G, Finnstrom O, Stenport G. Umbilical artery catheterization in newborns. I. Thrombosis related to catheter type and position. *Acta Paediatr Scand* 1979;68:575-81.
 - 98 Jackson JC, Truog WE, Watchko JF, Mack LA, Cyr DR, van Belle G. Efficacy of thromboresistant umbilical artery catheters in reducing aortic thrombosis and related complications. *J Pediatr* 1987;110:102-5.
 - 99 Mokrohsisky ST, Levine RL, Blumhagen JD, Wesenberg RL, Simmons MA. Low positioning of umbilical artery catheters increases associated complications in newborn infants. *N Engl J Med* 1978;299:561-4.

Commentary

Severe examples of ischaemic limb damage, especially those culminating in amputation, have probably become less common as a result of increased vigilance for early signs of ischaemia, better catheters and related equipment, and improved skills of the operators. None the less, the rising population of extremely preterm babies are a vulnerable group and fear of retinopathy may lead to determined attempts at arterial oxygen monitoring by sampling through an arterial catheter or by repeated arterial puncture.

A range of physical signs may be observed which suggest limb ischaemia including mottling, blue discoloration, blanching, poor capillary refilling, coolness, and poor pulses. Often these signs are transient but sometimes they progress to frank gangrene with a demarcation line.

Mr Gault's informative and well referenced paper indicates the spectrum of treatments available, including the scope for surgery. A

major difficulty for paediatricians is that there is still insufficient information derived from clinical studies to decide the appropriate management in individual circumstances, especially in extremely small babies. When signs of limb ischaemia are first observed we usually do not know whether they are due to reversible arterial 'spasm', thrombosis, or embolism. Dextran, heparin, streptokinase, and urokinase have risks in very small ill babies. Neonatal care is about balancing risks but we are hampered if neither the risks nor the benefits are understood. Finally, most paediatricians won't have ready access to a surgeon with experience in micro-surgery—such experience that there is being embodied in single case reports.

Faced with these uncertainties the best approach is firstly to avoid unnecessary harm. A perceived risk of retinopathy is no reason to strive for arterial access *at all costs*. When invasion of arterial territory is contemplated there is always room for considering the alternative monitoring strategies. It would seem sensible to correct polycythaemia, hypovolaemia, and hypotension before arterial catheterisation, bearing in mind that these factors predispose to vascular compromise. Hyperosmolar solutions should not be infused through arterial catheters, and increased vigilance is required in babies receiving vasopressor drugs. The catheter should be promptly removed if signs of ischaemia, including early blanching, develop. It should not be replaced at the same site even if the signs regress.

The litigation implications of vascular compromise should be acknowledged. Medical and nursing staff must be protected from blame when there was no negligence; but we must also protect a patient's right to compensation where the standard of care was unreasonable. Accurate documentation in the medical and nursing records of events in relation to arterial catheterisation is a basis for the fair assessment of claims.

Arterial catheterisation, including unsuccessful attempts, should be noted and the time recorded. The same applies to arterial punctures—timed information on the blood gas chart is acceptable provided the site of the arterial sample is given. When an arterial catheter is in use a measurement of the adequacy of the circulation in the appropriate limb should be recorded at hourly intervals in the intensive care chart—for example, 'warm and pink'. Signs consistent with ischaemia should be recorded and timed. If, as a result, a catheter is removed then the time of removal must be noted. The progression or regression of ischaemic signs should be recorded along with the timing of any treatments.

In practice, a careful attitude towards documentation usually goes hand in hand with clinical vigilance and against this background avoidable vascular compromise is less likely to occur.

M. L. CHISWICK
North West Regional Perinatal Centre,
St Mary's Hospital, Whitworth Park,
Manchester M13 0JH