Discussion

The safe adult dosage of eucalyptus oil as an internal medicine is quoted as 0.06 to 0.2 ml.¹ Death in adults has occurred after 4 or 5 ml, and is usual after 30 ml.² Recovery however, has been reported after the ingestion of 120 to 220 ml.³ The toxic effects of ingestion of this toxic, volatile hydrocarbon are rapid in onset and extensive. They include a burning sensation in the mouth and throat, abdominal pain, and spontaneous vomiting which may be delayed up to 4 hours after ingestion.⁴ Respiratory problems include bronchospasm and tachypnoea, with dangerous respiratory depression following severe intoxication. Central nervous system involvement includes diminution or loss of reflexes, and depression of consciousness which may progress to coma. Convulsions are rare in the adult but may be prominent in the child.⁵ Direct nephrotoxicity may follow the ingestion of large volumes and cutaneous manifestations have been described.⁶

The management of eucalyptus oil poisoning³ is mainly supportive. Attempts to induce vomiting in the child should be avoided and the possibility of vomiting and aspiration of oil implies that gastric lavage should be performed with great care, a cuffed endotracheal tube being inserted in the presence of central nervous system depression. Urinary output should be carefully monitored, particularly when hypotension is present or if large volumes of oil have been ingested. In severe poisoning, peritoneal or

haemodialysis is of value.³ The role of catharsis has not been adequately assessed.

Although the use of eucalyptus oil is becoming less fashionable, the hazards of its ingestion remain, particularly in the child. Our case serves as a reminder of the severe toxicity of this substance, illustrating the rapid onset of its severe respiratory and central nervous system effects.

We thank Dr M H Winterborn for permission to report this patient.

References

- 1 Martindale W. *The extra pharmacopoeia*. 27th ed. London: Pharmaceutical Press, 1977.
- 2 MacPherson J. The toxicology of eucalyptus oil. *Med J Aust* 1925; ii: 108-10.
- 3 Gurr F W, Scroggie J G. Eucalyptus oil poisoning treated by dialysis and mannitol infusion with an appendix on the analysis of biological fluids for alcohol and eucalyptol. *Australas Ann Med* 1965; 14: 238-49.
- 4 Foggies W. Eucalyptus oil poisoning. *Br Med J* 1911; i: 359-60.
- 5 Chun L T. Accidental poisoning in children, with special reference to kerosene poisoning. *Hawaii Med J* 1951; 11: 83-7.
- 6 Kirkness W R. Poisoning by oil of eucalyptus. *Br Med J* 1910; i: 261.

Correspondence to Dr M H Winterborn, Department of Paediatrics, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST.

Factor X deficiency in the neonatal period

S J MACHIN, M R WINTER, S C DAVIES, AND I J MACKIE

Department of Haematology, Middlesex Hospital, and Department of Haematology, Central Middlesex Hospital, London

SUMMARY An infant with a severe deficiency of factor X presented in the neonatal period with uncontrollable bleeding from heel prick sites, spontaneous bruising, and haematoma. The deficiency was controlled by infusions of dried human factors II, IX, and X concentrate; the half-life of the infused factor X material is only 18 hours. Despite prophylactic weekly infusions of factor X concentrate, the child developed a fatal intracerebral haemorrhage when only 4 months old. Coagulation studies on both parents and the elder sister showed no obvious coagulation abnormality.

Factor X deficiency is a rare bleeding disorder inherited as an autosomal incompletely recessive trait. Usually the deficient state is clinically relatively slight, and for effective haemostasis a factor X level >10% is thought to be adequate.¹

Case report

An Indian girl was born after an uneventful pregnancy which had progressed to term. She was clinically well and delivery had been normal. A prophylactic intramuscular injection of 1 mg vitamin K₁ was given one hour after birth into the

right thigh. On day 1 jaundice was noted; the serum bilirubin was 260 $\mu\text{mol/l}$ (16.3 mg/100 ml) and the haematocrit 0.55 from a heel prick sample. The infection screen was negative and there was no evidence of intravascular haemolysis. On day 2 the baby appeared less jaundiced and the bilirubin was 190 $\mu\text{mol/l}$ (11.9 mg/100 ml) with a haematocrit 0.40. However, that evening an enlarging thigh haematoma appeared at the site of the injection, the heel prick sites started to rebleed, and spontaneous ecchymosis and purpura developed over the left shoulder and the lower abdomen. A blood count showed Hb 13.1 g/dl, haematocrit 0.39, white blood count $12.1 \times 10^9/\text{l}$, and platelets $152 \times 10^9/\text{l}$. Early the next morning the baby was covered in generalised bruising and purpura, with enlarging haematoma in the left shoulder and right thigh, and continuous uncontrollable oozing of blood from the heel prick sites. The results of the patient's coagulation studies are shown in the Table. These were characteristic of severe factor X deficiency with prolonged prothrombin time, kaolin partial thromboplastin time, and stypven time. These abnormalities were corrected by the addition of normal citrated plasma, normal serum, and factor V-deficient plasma, but not by the addition of aluminium hydroxide-absorbed normal plasma. Specific assays for factor X using the stypven time system showed less than 1% coagulant activity. Assays for clotting factors II, V, VII, VIII, IX, and XII were within normal limits, excluding the possibility of multiple combined deficiencies.

The baby was given an infusion of 10 ml Oxford factor II, IX, and X type DE (1) concentrate containing 250 units factor X activity, and 75 ml compatible packed red cells. Almost immediately the continuous bleeding from the heels ceased, and during the next few hours no fresh bruises appeared and the haematoma regressed. After the initial infusion, factor X assays during the next 40 hours determined the half-life of the infused factor X as approximately 18 hours. Regular infusions of

factors II, IX, and X concentrate were then given during the next 6 days to maintain a factor X level $>30\%$. During this period there was no spontaneous bleeding, no fresh purpuric lesions appeared, and the cord separated without blood loss.

The baby was discharged home when 12 days old and regular prophylactic infusions of 10 ml factor II, IX, and X concentrate were given at approximately weekly intervals. However, on four occasions the baby developed spontaneous bruising on the arms and trunk during the next 3 months which required further infusions of concentrate. Despite regular prophylactic infusion, she developed a fatal cerebral haemorrhage when 4 months old.

The family

Both parents were Indian. There was no history of consanguinity but both parents had come from the same village in India. They had one other child, a healthy girl, 1½ years old. There was no family history of any excessive bleeding tendency. Coagulation studies performed on the parents and sister were within normal limits. The factor X level in the father was 95%, the mother 77%, and the sister 80%.

Discussion

Congenital deficiency of factor X was first described in 1956.² Since then about 25 cases have been recorded, including 3 other cases of factor X deficiency in an Indian family.³ Several forms of the defect have been described including patients with an abnormal factor X molecule and decreased coagulant activity.⁴ In another variant the factor X assay is low only when tissue thromboplastin instead of the stypven time system is used.

Our patient had a severe clinical bleeding disorder with $<1\%$ factor X procoagulant activity and a prolonged bleeding time. The abnormal bleeding time with normal platelet aggregation studies is unexplained, but a prolonged bleeding time has been reported in severe factor X deficiency.⁵

Spontaneous bleeding episodes in the neonatal period and a fatal brain haemorrhage when 4 months old reflect the severity of the deficiency. Intracerebral haemorrhages have been described in 2 other patients with severe factor X deficiency.⁶

Bleeding was arrested after the infusion of 250 units factor X concentrate. The effective half-life of the infused factor X material was approximately 18 hours. This is at variance with previous estimates of the half-life of infused factor X, which have ranged from 32 to 48 hours.⁷ It is important to establish the half-life of infused coagulant material

Table Coagulation screen on the child

	Patient	Normal range
Platelet count ($\times 10^9/\text{l}$)	117	150–400
Duke bleeding time (min)	>15	1–5
Kaolin PTT (seconds)	120	32–38
Prothrombin time (seconds)	180	12–14
Thrombin time (seconds)	17	10–12
Stypven time (seconds)	120	15–18
Factor X assay (%)	<1	60–170
<i>Prothrombin time corrections</i>		<i>Seconds</i>
80% patient's plasma + 20% normal plasma		20
80% patient's plasma + 20% absorbed plasma		86
80% patient's plasma + 20% factor V-deficient plasma		23
80% patient's plasma + 20% normal serum		18

in patients with severe clotting factor deficiencies, especially when they are actively bleeding, as the half-life may vary considerably from patient to patient. The bleeding in our patient during the neonatal period was controlled by daily infusions of factor X concentrate to maintain a level of factor X coagulant activity >30% for 6 days.

Previously, family studies have reported factor X activity in heterozygotes ranging from 30 to 70% and normal homozygous factor X activity ranging from 70 to 170%.⁸ Both our patient's parents and elder sister had factor X activity within the lower normal range. However, in all congenital coagulation factor deficiencies, there is considerable overlap between the range of coagulant activity in obligate carriers and the normal population, and the possibility of a spontaneous genetic mutation cannot be excluded.

References

- ¹ Rizza C R. The management of patients with coagulation factor deficiencies. In: Biggs R, ed. *Human blood coagulation, haemostasis, and thrombosis*. Oxford: Blackwell, 1976: 210-24.

- ² Telfer T P, Denson K W, Wright D R. A new coagulation defect. *Br J Haematol* 1956; **2**: 308-16.
- ³ Sarup B M, Perkash A, Aikat B K. Congenital Stuart-Prower factor (factor X) deficiency. *J Indian Med Assoc* 1972; **59**: 110-4.
- ⁴ Denson K W E, Lurie A, De Cataldo F, Mannucci P M. The factor X defect: recognition of abnormal forms of factor X. *Br J Haematol* 1970; **18**: 317-27.
- ⁵ Bounameaux Y. Coagulopathies avec temps de saignement prolong. *Thromb Diathes Haemorrhagica* 1963; **9**: 417-26.
- ⁶ Girolami A, Molaro G, Calligaris A, De Luca G. Severe congenital factor X deficiency in a 5 month old child. *Thromb Diathes Haemorrhagica* 1970; **24**: 175-84.
- ⁷ O'Leary D S, Ruymann F B, Conrad M E. Therapeutic approaches to factor X deficiency with emphasis on the use of a new clotting factor concentrate (Konyne). *J Lab Clin Med* 1971; **77**: 23-32.
- ⁸ Lechler E, Webster W P, Roberts H R, Penick G D. The inheritance of Stuart disease. *Am J Med Sci* 1965; **249**: 291-4.

Correspondence to Dr S J Machin, Department of Haematology, The Middlesex Hospital, Mortimer Street, London W1N 8AA.