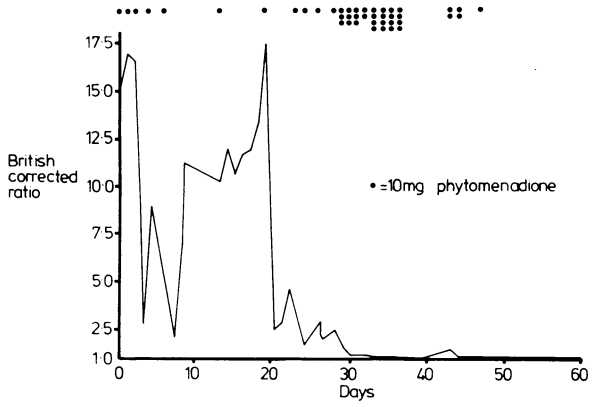
# SHORT REPORTS

## Difenacoum (Neosorexa) poisoning

Difenacoum is a coumarin anticoagulant developed as a rodenticide[1] that is freely available from supermarkets, chemists, and hardware stores. Accidental or criminal poisoning or self-poisoning is a hazard, and the effect on the anticoagulant mechanism is considerably more prolonged than that of warfarin. The following case history and details of animal experiments indicate the danger associated with this and related compounds.

### Case report

A 17-year-old girl had made several suicide attempts since 1978, mostly by drug overdoses. On 7 May 1981 she was admitted having consumed 500 g rat poison (Neosorexa) and swallowed broken razor blades and pins. Coagulation tests gave an initial British corrected ratio of 15·0. Phytomenadione (vitamin $K_1$; Konakion) was given both by mouth and intravenously at intervals from 7 May to 23 June (figure) before the ingested poison appeared to have been cleared from the system.




Effect of phytomenadione (vitamin $K_1$) on clotting activity after ingestion of difenacoum.

After a prolonged stay in hospital for psychiatric treatment she was allowed home but required readmission having consumed approximately 1800 g rat bait between 23 November and 6 December together with 40 map pins. She was anaemic (haemoglobin concentration 7·0 g/dl) with a British corrected ratio of 23·0 and required blood transfusion (two units) together with two units of fresh-frozen plasma, which rapidly reduced the British corrected ratio to 5·0. Phytomenadione 10 mg by mouth four times daily resulted in a normal British corrected ratio within 42 days. She subsequently passed 39 pins per rectum; the 40th was removed at gastroscopy.

### Animal experiments

The duration of action of difenacoum and its ability to antagonise vitamin $K_1$ in vivo were investigated in male New Zealand White rabbits (2·5-3·0 kg); measurement of clotting activity and drug administration were as previously described.[2] In the first experiment prothrombin complex activity was measured at intervals after a single dose of difenacoum (0·85 mg/kg). For the first 21 days vitamin $K_1$ (2 mg/kg) was administered intraperitoneally every two days to prevent death from haemorrhage; during this period prothrombin complex activity was determined immediately before administration of the vitamin.

In the second experiment the effect of a single intravenous injection of vitamin $K_1$ (0·5 mg/kg) on clotting activity in rabbits anticoagulated (prothrombin complex activity $< 30\%$) with either warfarin 63 mg/kg or difenacoum (0·85 mg/kg) was determined.

### Comment

Coumarin anticoagulants such as warfarin are thought to interfere with synthesis of clotting factor by inhibiting the regeneration of vitamin $K_1$ from its biologically inactive metabolite vitamin $K_1$ 2,3-epoxide.[3] Warfarin and difenacoum produce an accumulation of tritium-labelled vitamin $K_1$ 2,3-epoxide in rabbits after administration of tritium-labelled vitamin $K_1$,[2] which is consistent with this hypothesis. The duration of anticoagulation produced by difenacoum in the rabbit, however, is much longer than that produced by warfarin.[2,4] Prothrombin complex activity below 50% was recorded 45 days after a single dose of difenacoum (0·85 mg/kg). Furthermore, difenacoum is a more effective antagonist of vitamin $K_1$ than warfarin in the rabbit. Thus 18 hours after administration of vitamin $K_1$ prothrombin complex activity was significantly lower ($p < 0{\cdot}001$) in animals pretreated with 0·85 mg difenacoum/kg than in animals pretreated with 63 mg warfarin/kg ($11 \pm 2\%$ *v* $50 \pm 3\%$) even though warfarin was administered in a dose 100 times greater on a molar basis.

The clinical effect of ingestion of difenacoum in man is similar to that observed in animal experiments. These findings indicate that difenacoum is a much more persistent and potent antagonist of vitamin $K_1$ than warfarin. In cases of poisoning with rodenticides containing difenacoum, which are freely available to the general public, vitamin $K_1$ should be administered at frequent intervals until the British corrected ratio returns to normal. Thereafter, we suggest that the ratio should be monitored for several weeks to ensure that the pharmacological effect of the drug has stopped.


1 Hadler MR, Shadbolt RS. Novel 4-hydroxycoumarin anticoagulants active against resistant rats. *Nature* 1975;**253**:275-6.

2 Park BK, Leck JB, Wilson AC, Serlin MJ, Breckenridge AM. A study of the effect of anticoagulants on ($^3$H) vitamin K metabolism and prothrombin complex activity in the rabbit. *Biochem Pharmacol* 1979;**28**: 1323-9.

3 Bell RG. Metabolism of vitamin K and prothrombin synthesis; anticoagulants and the vitamin K-epoxide cycle. *Fed Proc* 1978;**37**:2599-604.

4 Park BK, Leck JB, Breckenridge AM. The dose dependent effect of warfarin on vitamin $K_1$ metabolism and clotting factor synthesis in the rabbit. *Biochem Pharmacol* 1980;**29**:1601-2.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## Treatment of vitamin $D_2$ poisoning by induction of hepatic enzymes

Drugs that induce synthesis of hepatic microsomal enzymes may, by interference with vitamin D metabolism in the liver, produce hypocalcaemia and osteomalacia.[1] Glutethimide is such a compound,[1] and we used it to treat a patient with vitamin $D_2$ poisoning who exhibited persistent hypercalcaemia since we thought that its administration would deplete the excess vitamin D from the body stores at a quicker than natural rate, thereby shortening the duration of toxic effects. We report the case here.

### Case report

A 77-year-old woman was admitted as an emergency in a confused state. A clear history was unobtainable. On examination she was obese; no other abnormal findings were noted. Investigations showed calcium concentration 3·52 mmol/l (14·1 mg/100 ml) (normal 2·20-2·70 mmol/l; 8·8-10·8 mg/100 ml); phosphate 0·97 mmol/l (3·0 mg/100 ml) (normal 0·80-1·40 mmol/l; 2·5-4·3 mg/100 ml); alkaline phosphatase 128 U/l (normal 35-130); albumin 41 g/l (normal 30-50); globulin 37 g/l (normal 23-35); total bilirubin 7 μmol/l (409 μg/100 ml) (normal 2-17 μmol/l; 117-994 μg/100 ml); creatinine 229 μmol/l (2·6 mg/100 ml) (normal 40-110 μmol/l; 0·5-1·2 mg/100 ml); alanine aminotransferase 23 U/l (normal 7-45); γ-glutamyl transferase 44 U/l (normal 0-65); IgG 10·0 g/l (normal 5·0-16); IgA 3·34 g/l (normal 0·5-