Current Practice

TODAY'S DRUGS

With the help of expert contributors we print in this section notes on drugs in common use.

Vitamin K

The metabolic production by the liver of various coagulation factors (prothrombin, and factors VII, IX, and X) is dependent on a vitamin which Dam called K (*Koagulation* vitamin). To this day the mechanism by which vitamin K promotes formation of these clotting factors is unknown. The vitamin was originally found in the unsaponifiable non-sterol fraction of pig-liver fat and in alfalfa, but it is also present in the photosynthetic portions of plants and in many vegetable oils. The faeces of most animals contain large amounts of the vitamin, produced by the intestinal bacteria. Putrefied protein such as fish-meal and casein are also rich in the vitamin. Chemically, vitamin K occurs naturally in at least two forms, which are known as vitamins K_1 and K_2. Both are derivatives of naphthoquinone. The structurally related synthetic compound menaphthone or vitamin K_3 has an activity equal to the naturally occurring compounds. Apart from their action in increasing the plasma concentrations of various coagulation factors, they are pharmacologically inert. Vitamin K_1 and K_2 are non-toxic even when given in huge doses. Menaphthone and its water-soluble analogues, on the other hand, are capable of inducing haemolysis in persons who are deficient in the red-cell enzyme glucose-6-phosphate dehydrogenase, as well as in non-deficient subjects when large doses are used.

Preparations of Vitamin K

Approved Name	Synonyms	Proprietary Names
Phytomenadione (B.P.)	Vitamin K_1 Phytonadione (U.S.P.)	Mephyton Aquamephyton Konakion Mono-Kay (U.S.A.)
Menaphthone (B.P.)	Vitamin K3 Menadione (U.S.P.)	
Menaphthone sodium bisulphite (B.P.)	Menadione sodium bisulphite (U.S.P.)	Vitavel K (for injection) Hykinone (U.S.A.)
Menadiol sodium diphosphate (U.S.P.)		Synkavit Kappadione (U.S.A.)
Acetomenaphthone (B.P.)	Acetomenadione	Adaprin Amisyn Pernione Pernivit Prokayvit Oral Vitavel K (Oral)

Therapeutic Uses

Liver Disease.—Vitamin K is far more effective in correcting the hypoprothrombinaemia associated with biliary obstruction than with that associated with hepatocellular disease. However, even in the latter condition some improvement may result, particularly if there is an element of intrahepatic obstruction to the outflow of bile.

Phytomenadione (vitamin K_1) or menaphthone (vitamin K_3) may be given orally in a dose of 10 mg. daily, with bile salts to promote absorption, or the vitamin may be given parenterally in the same dosage.

Intestinal Disorders.—Hypoprothrombinaemia may arise in a variety of malabsorption syndromes, including adult coeliac disease, regional enteritis, ulcerative colitis, dysentery, and after extensive bowel resection. Oral sulphonamides and broad-spectrum antibiotics may alter the bacterial flora and so reduce the availability of vitamin K. Parenteral therapy with phytomenadione (vitamin K_1) or menaphthone (vitamin K_3) is indicated; the dose is 10 mg. daily.

Hypoprothombinaemia of the Newborn.—The levels of prothrombin and factors VII, IX, and X may be quite low even in the *normal* full-term infant, and they do not rise until the normal intestinal flora becomes established. In premature infants these factors may be further depressed, and this may lead to haemorrhagic disease of the newborn.

Routine prophylactic administration of vitamin K_1 or K_3 0·5–1·0 mg. parenterally to the newborn infant is to be recommended. The benefit to the offspring of prophylactic administration of vitamin K to the mother is less sure. In the treatment of established haemorrhagic disease of the newborn 0·5–1·0 mg. of vitamin K_1 or K_3 or one of the water-soluble analogues should be given, intravenously if possible to avoid haematoma formation. Large doses of the synthetic and water-soluble analogues may produce a Heinz-body anaemia with hyperbilirubinaemia and kernicterus, but small doses such as 1 mg. are quite safe. This problem does not arise with the naturally occurring vitamin K_1.

Drug-induced Hypoprothrombinaemia.—A mild overdose of an oral anticoagulant leading to bruising or transient haematuria should be treated simply by withdrawing the drug. When worrying haemorrhage occurs vitamin K_1 should be administered immediately. The oral route (10 to 20 mg.) is effective and not much slower than parenteral therapy, which is needed only in a severe emergency, when 20 to 50 mg. may be given by *slow* intravenous injection at a rate not exceeding 5 mg. per minute. Too rapid administration may lead to flushing of the face, sweating, constriction of the chest, cyanosis, and even peripheral vascular collapse. Menaphthone (vitamin K_3) is far less effective than phytomenadione (vitamin K_1). When anticoagulant therapy is to be resumed after the haemorrhage has been controlled the use of vitamin K_1 should be restricted to cases where some anxiety exists. This is because a prolonged refractory state, lasting from days to weeks, may result, and it may prove difficult to reintroduce a satisfactory level of anticoagulation after vitamin K_1 has been given. In any case the dosage of vitamin K_1 should be kept as low as possible compatible with a good therapeutic response.