

There is still no agreement on the most effective oral dose and frequency, and study of this has been complicated by the lack of a suitable oral preparation of phytonadione.^{12,13} Options currently available for oral use include the polyoxyl castor oil and polysorbate-80 containing preparations (unlicensed for oral use) and the colloidal, micelle formulation (licensed for oral use in some countries). These preparations are packaged in glass ampoules, therefore are unsuitable for parents to give at home.

The 1992 recommendations of the British Paediatric Society⁸ for oral use of the polyoxyl castor oil formulation suggested a single dose of 500 micrograms on the day of birth. For breast-fed babies, additional doses of 500 micrograms at 7 to 10 days and at 4 to 6 weeks, or 200 micrograms at weekly intervals for 26 weeks, or 50 micrograms daily for 26 weeks, were recommended. Current UK doses¹⁴ for the colloidal preparation in healthy term neonates are 2 mg soon after birth, then 2 mg at 4 to 7 days. Exclusively breast-fed infants should be given a third oral dose of 2 mg one month after birth. Further monthly doses of 2 mg have been recommended while the infant remains exclusively breast-fed. A report¹⁵ of the failure of prophylaxis in 3 breast-fed babies (2 of whom had unidentified cholestatic liver disease) who received 2 doses of this formulation, as recommended in Switzerland, emphasises the importance of the third, and possibly, other, follow-up doses. Plasma vitamin K concentrations in breast-fed infants receiving 3 oral doses of this formulation were at least equal to concentrations in those receiving a single intramuscular dose.¹⁶ A study in Germany, however, found the mixed micellar oral formulation to be no more efficacious than older vitamin K preparations,¹⁷ and a pharmacokinetic study found its absorption to be unreliable with conjugated hyperbilirubinaemia;¹⁸ the authors suggest that even 3 oral doses may not provide sufficient protection against VKDB in infants with latent cholestasis. The most recent advice from the UK Department of Health¹⁴ advocates that all newborn infants should receive vitamin K prophylaxis, both oral and intramuscular routes should be available, and that parents should be involved in the decision on which route is used.

Other oral regimens have been investigated or are in use. In the Netherlands a regimen of 1 mg orally or intramuscularly at birth, followed by 25 micrograms daily or 1 mg weekly by mouth from 1 week to 3 months of age has been found satisfactory.^{19,20} In Germany,^{9,20} and Australia²⁰ the suggested oral regimen for the polyoxyl castor oil formulation was 1 mg at birth, at 3 to 10 days and at weeks 3 to 6, although some failures have been reported in babies receiving this regimen,⁹ and the Australian data confirm it is less effective than a single intramuscular dose.²⁰ One hospital in the USA has satisfactorily used, for many years, a single 2-mg dose given via nasogastric tube to neonates after birth,²¹ although the American Academy of Pediatrics still advocates use of the intramuscular route.¹¹ In Denmark, a 2-mg dose at birth followed by a weekly dose of 1 mg during the first 3 months of life has effectively prevented any late VKDB in healthy breast-fed babies.²² In France, for formula-fed neonates at no risk of haemorrhage, 2 mg is given orally at birth, followed by a second dose between day 2 and 7; infants who are breast-fed are given weekly oral doses of 2 mg until cessation of exclusive breast feeding. For neonates at high risk of haemorrhage, however, the first dose is given intramuscularly, or even by slow intravenous injection, according to the clinical state of the infant.²

Although phytonadione crosses the placenta slowly and to a limited extent, it is nevertheless recommended that pregnant women receiving drugs that are vitamin K antagonists (particularly antiepileptics) should receive phytonadione 10 to 20 mg daily from 36 weeks gestation.^{2,23} This is in addition to the requirement that their neonates, who are at high risk of VKDB, receive intramuscular phytonadione soon after birth. Maternal phytonadione has been investigated as a means of improving vitamin K status in breast-fed neonates. In 1 study,²⁴ 5 mg daily for 12 weeks was effective for this purpose.

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Preparations

BP 2008: Menadiol Phosphate Injection; Menadiol Phosphate Tablets; Phytonadione Injection; Phytonadione Tablets;

USP 31: Menadiol Sodium Diphosphate Injection; Menadiol Sodium Diphosphate Tablets; Menadiol Injection; Phytonadione Emulsion; Phytonadione Tablets.

Proprietary Preparations (details are given in Part 3)

Arg: K1; Konakion; Mestil-Ka; Rupek; **Austral:** K Thrombin; Konakion; **Austria:** Kavitol; Konakion; **Belg:** Konakion; Vitamon K; **Braz:** Konakion; Kanavit; Vikator; Vita K; **Chile:** Auriderm K2; Fitouquinona; Konakion; **Cz:** Kanavit; **Denm:** Konakion; Menadion; **Fin:** Konakion; **Ger:** Kanavit; Konakion; **Gr:** Konakion; **Hong Kong:** Auriderm K2; Konakion; **Hung:** Konakion; **Ind:** Kenadion; **Indon:** Neo-K; **Ir:** Konakion; **Israel:** Konakion; **Ital:** Konakion; Vitak; **Jpn:** Glakay; Kaytvo; **Malaysia:** Konakion; **Mex:** K-50; Konakion; Røyken; **Neth:** Konakion; **Norw:** Konakion; **NZ:** K-Thrombin; Konakion; **Philipp:** Clotigen; Cymonin; Hema-K; Hemadone; Hemo-K; Konakion; **Pol:** Vitacon; **Port:** Konakion; **S.Afr:** Konakion; **Spain:** Kaergona Hidrosoluble; Konakion; **Swed:** Konakion; **Switz:** Konakion; **Thai:** Glakay; Konakion; KP; **Turk:** Konakion MM; Libavit K; **UK:** Konakion; **USA:** Aquamephyton; Mephyton.

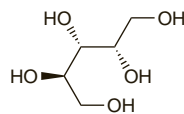
Multi-ingredient: **Arg:** Antidiar; Estreptocarbocafiazol; Kacerutin; **Austral:** Chilibain Formula; **Chile:** Hepabil; Katin; Microret K; **India:** Cadisper; CCKP; Gynae-CVP; K5 Hair Tincture; Kalpastic; Siochrome; Stypocid; Stypocid; **Indon:** Hi-Bone; **Ir:** Bio-Calcium + D + K; **Mex:** Hemo-sin-K; Mikroka; Microret K; **Rus:** Vectrum Calcium (Вектрум Кальций); **Spain:** Caprofiles Hemostatico; Cromoxin K; **Thai:** Bio-Calcium + D3 + K; Sidul; **Venez:** Dremo-Kf.

Xylitol (BAN)

E967; Ksilitolis; Ksylitol; Ksylitoli; Xilit; Xilitol; Xylit; meso-Xylitol; Xylitolum.

$C_5H_{12}O_5 = 152.1$.

CAS — 87-99-0 (xylitol); 16277-71-7 (D-xylitol).



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.* Also in *USNF*.

Ph. Eur. 6.2 (Xylitol). A white or almost white crystalline powder or crystals. M.p. 92° to 96°. Very soluble in water; sparingly soluble in alcohol.

USNF 26 (Xylitol). White crystals or crystalline powder. Crystalline xylitol has a melting range between 92° and 96°. It has a sweet taste and produces a cooling sensation in the mouth. Soluble 1 in about 0.65 of water; sparingly soluble in alcohol.

Adverse Effects

Large amounts of xylitol taken orally may cause diarrhoea and flatulence. Hyperoxaluria, which can occur with intravenous infusion, is unlikely after oral use. Hyperuricaemia, changes in liver-function tests, and acidosis (including lactic acidosis) have occurred after intravenous infusion.

Hypersensitivity. A report of oral erosions caused by contact hypersensitivity to xylitol-containing chewing gum.¹

- Hanakawa Y, et al. Xylitol as a causative agent of oral erosive eczema. *Br J Dermatol* 2005; **152**: 821-2.

Uses and Administration

Xylitol is a polyhydric alcohol (polyol) related to the pentose sugar, xylose (p.2416). It is used as a bulk sweetener in foods and as a sweetener or excipient in pharmaceuticals. Xylitol is also

used as a sweetening agent in sugar-free preparations as it is non-cariogenic and is less likely to cause dental caries than sucrose. It is under investigation for the prevention of dental caries and acute otitis media. It was formerly considered as a substitute for glucose in intravenous nutrition but such use has generally been abandoned due to adverse effects.

Dental caries. Chewing-gum containing xylitol appears to have a useful role in the prevention of dental caries (p.180).^{1,5}

- Edgar WM. Sugar substitutes, chewing gum and dental caries—a review. *Br Dent J* 1998; **184**: 29-32.
- Gales MA, Nguyen T-M. Sorbitol compared with xylitol in prevention of dental caries. *Ann Pharmacother* 2000; **34**: 98-100.
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- Burt BA. The use of sorbitol- and xylitol-sweetened chewing gum in caries control. *J Am Dent Assoc* 2006; **137**: 190-6. Correction. *ibid.*; 447.

Otitis media. It has been suggested that xylitol chewing gum^{1,2} and xylitol syrup^{2,3} may have a preventative effect against acute otitis media (p.182). However, a randomised study⁴ found xylitol to be ineffective when given only during an acute respiratory tract infection.

- Uhari M, et al. Xylitol chewing gum in prevention of acute otitis media: double blind randomised trial. *BMJ* 1996; **313**: 1180-4.
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Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Trident; **Arg:** Xylit; **Philipp:** Xylogel.

Multi-ingredient: **Arg:** Emoform Total; Fluorogel 2001 Chiquitos; Fluorogel 2001 para Dientes Sensibles; Hyper Sensitive; Penobacter; Penident; Solucion Oral; **Chile:** Oralgene; **Fr:** Exova; **Ger:** Cardioplegin N; Kalium-Magnesium-Asparaginat; Saseem; **Mex:** Dentsible; Fluoxylit; Periodontyl; Perioxidin; **Philipp:** Xylomise; **UK:** Biotene Oralbalance; BioX-tra; Salva Natura; Salva Orhana; **USA:** Optimoist.

Dried Yeast

Brewers' Yeast; Cerevisiae Fermentum Siccatum; Faex Siccata; Fermento de Cerveja; Levadura desecada; Levadura Sêca; Levure de Bière; Saccharomyces Siccum; Trockenhefe.

Сушёные Дрожжи

Pharmacopoeias. In *Jpn.*

Profile

Dried yeast consists of unicellular fungi belonging to the family Saccharomycetaceae, dried by a process that avoids decomposition of the vitamins present. The chief species are *Saccharomyces cerevisiae*, *S. carlsbergensis*, and *S. monacensis*. Dried yeast contains thiamine, nicotinic acid, riboflavin, pyridoxine, pantothenic acid, biotin, folic acid, cyanocobalamin, aminobenzoic acid, inositol, and chromium.

Dried yeast is a rich source of vitamins of the B group. It has been used for the prevention and treatment of vitamin B deficiency in doses of 1 to 8 g daily by mouth. Yeast is an ingredient of some preparations for treating haemorrhoids, and some preparations intended to restore normal gastrointestinal flora. Yeast is widely used in brewing.

Antibiotic-associated colitis. Although other organisms, including *Candida* spp., have been implicated in antibiotic-associated diarrhoea, colonisation of the colon with *Clostridium difficile*, a toxin-producing Gram-positive anaerobe, is the most common identifiable cause of antibiotic-associated colitis (p.171) and pseudomembranous colitis. There are reports of benefit with dried yeast in patients with *C. difficile*-associated diarrhoea;^{1,2} commercially available brewers' yeast tablets were used, at a dose of 3 tablets three times daily (strength unspecified), in 3 patients refractory to standard treatment,¹ or as adjunctive therapy in 11 patients, using the same dose.²

- Schellenberg D, et al. Treatment of *Clostridium difficile* diarrhoea with brewer's yeast. *Lancet* 1994; **343**: 171-2.
- Barthram J, et al. Further research warranted. *Pharm J* 1997; **259**: 371.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz: Bioflorin; Florax; Ginoflorax; Levedo; Lomvit; **Fr:** Microlev; **Ger:** AgioStop; Furunkulosin; Hamadin N; Imoflora; Levurinetten N; Omniflora Akut; Perocur; Santax; S; Yomogi; **India:** Lavist; **Ital:** Nutrivit; Zimocel; **Mex:** Levulisa; **Port:** Lio-Levedura; **Thai:** Brewers Yeast; **UK:** Bio-Strath.

Multi-ingredient: **Arg:** Bifena; Karbonetas; **Austral:** ML 20; Plantiodine Plus; Preparation H; **Austria:** Levurinetten; Sperti Preparation H; **Braz:** Composto Emagrecedor; Emagrevit; Manoli; **Canad.:** Preparation H; **Chile:** Sperti Preparation H; **Cz:** Preparation H; **Fr:** Actisoufre; Calciforte; Calciforte Vitamin D; Carbolévure; D'Contract; Levure Or; Phytophanere; Preparation H; Solacy; Spasmag; **Ger:** Pantovigar N; Sperti Preparation H; **Gr:** Preparation H; **India:** Efermij; Livogen; Medithane; Plastules; Softeron-Z; **Ir:** Preparation H; **Israel:** Preparation H; **Ital:** Bio-filact; Eurogel; Florelax; Lactisporin; Lactivis; Lactofite; Levudin; Lievitosol;