longed in patients with renal impairment and in neonates.

Cefuroxime is widely distributed in the body including pleural fluid, sputum, bone, synovial fluid, and aqueous humour, but only achieves therapeutic concentrations in the CSF when the meninges are inflamed. It crosses the placenta and has been detected in breast milk.

Cefuroxime is excreted unchanged, by glomerular filtration and renal tubular secretion, and high concentrations are achieved in the urine. On injection, most of a dose of cefuroxime is excreted within 24 hours, the majority within 6 hours. Probenecid competes for renal tubular secretion with cefuroxime resulting in higher and more prolonged plasma concentrations of cefuroxime. Small amounts of cefuroxime are excreted in bile.

Plasma concentrations are reduced by dialysis.

Uses and Administration

Cefuroxime is a second-generation cephalosporin antibacterial used in the treatment of susceptible infections. These have included bone and joint infections, bronchitis (and other lower respiratory-tract infections), gonorrhoea, meningitis (although treatment failures have been reported in *H. influenzae* meningitis), otitis media, peritonitis, pharyngitis, sinusitis, skin infections (including soft-tissue infections), and urinary-tract infections. It is also used for surgical infection prophylaxis. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Administration and dosage. Cefuroxime is given orally as the acetoxyethyl ester, cefuroxime axetil, in the form of tablets or suspension with or after food, or by injection as the sodium salt. Cefuroxime sodium may be given by deep intramuscular injection, by slow intravenous injection over 3 to 5 minutes, or by intravenous infusion. Doses of cefuroxime axetil and cefuroxime sodium are expressed in terms of the equivalent amount of cefuroxime; 1.20 g of cefuroxime axetil and 1.05 g of cefuroxime sodium are each equivalent to about 1 g of cefuroxime.

Usual oral doses for adults are 125 mg twice daily for uncomplicated urinary-tract infections and 250 to 500 mg twice daily for respiratory-tract infections. A dose for children more than 3 months of age is 125 mg twice daily or 10 mg/kg twice daily to a maximum of 250 mg daily. Children over 2 years of age with otitis media may be given 250 mg twice daily or 15 mg/kg twice daily to a maximum of 500 mg daily.

By injection the usual adult dose is 750 mg of cefuroxime every 8 hours but in more severe infections 1.5 g may be given intravenously every 8, or in some cases every 6, hours. Infants and children can be given 30 to 60 mg/kg daily, increased to 100 mg/kg daily if necessary, given in 3 or 4 divided doses. Neonates may be given similar total daily doses but in 2 or 3 divided doses.

Adults with pneumonia or with acute exacerbations of chronic bronchitis may respond to sequential therapy with parenteral cefuroxime 1.5 g twice daily or 750 mg twice daily respectively, followed by oral cefuroxime 500 mg twice daily in each case.

For Lyme disease in adults, an oral dose of 500 mg is given twice daily for 20 days.

For details of reduced dosage of cefuroxime in patients with renal impairment, see below.

For the treatment of meningitis due to sensitive strains of bacteria, cefuroxime is given intravenously in adult doses of 3 g every 8 hours. Infants and children are given 200 to 240 mg/kg daily intravenously in 3 or 4 divided doses, which may be decreased to 100 mg/kg daily after 3 days or when there is clinical improvement. For neonates, a dose of 100 mg/kg daily, decreased to 50 mg/kg daily when indicated, may be used.

In the treatment of gonorrhoea, a single dose of 1.5 g by intramuscular injection, divided between 2 injection sites, has been used. A single 1-g oral dose of cefuroxime has been given for uncomplicated gonorrhoea. In each case an oral dose of probenecid 1 g may be given with cefuroxime.

For surgical infection prophylaxis, the usual dose is 1.5 g of cefuroxime intravenously before the procedure; this may be supplemented by 750 mg intramuscularly every 8 hours for up to 24 to 48 hours depending upon the procedure. For total joint replacement, 1.5 g of cefuroxime powder may be mixed with the methylmethacrylate cement.

◊ Reviews.
1. Perry CM, Brogden RN. Cefuroxime axetil: a review of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy. *Drugs* 1996; **52:** 125–58.
2. Scott LJ, *et al.* Cefuroxime axetil: an updated review of its use in the management of bacterial infections. *Drugs* 2001; **61:** 1455–1500.

Administration in renal impairment. Parenteral doses of cefuroxime may need to be reduced in renal impairment. Licensed product information suggests the following doses based on creatinine clearance (CC):

- CC 10 to 20 mL/minute: 750 mg twice daily
- CC less than 10 mL/minute: 750 mg once daily

Patients undergoing haemodialysis should receive an additional 750-mg dose following each dialysis; those undergoing continuous peritoneal dialysis may be given 750 mg twice daily.

Preparations

BP 2008: Cefuroxime Axetil Tablets; Cefuroxime Injection;
USP 31: Cefuroxime Axetil for Oral Suspension; Cefuroxime Axetil Tablets; Cefuroxime for Injection; Cefuroxime Injection.

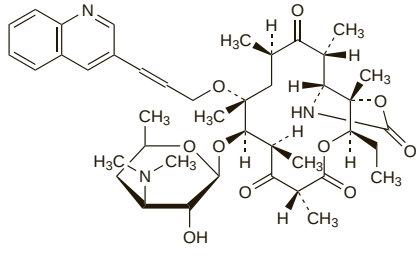
Proprietary Preparations (details are given in Part 3)
Arg.: Ceflux†; Cefogram†; Cefurox; Deltrox†; Ligramex†; ***Austral.:*** Zinnat; ***Austria:*** Curocef; Furoxim; Zinnat; ***Belg.:*** Axetine; Cefurim; Doccefuro; Kefurox†; Zinacef; Zinnat; ***Braz.:*** Cefunorth†; Cefuran†; Medcef; Zinacef; Zinnat; ***Canad.:*** Ceftin; Kefurox†; Zinacef; ***Chile:*** Curocef; Zinnat; ***Cz.:*** Axetine; Lifurox†; Xorimax; Zinacef; Zinnat; Zinoxime; ***Denm.:*** Zinacef; Zinnat; ***Fin.:*** Zinacef; Zinnat; ***Fr.:*** Cepazine; Zinnat; ***Ger.:*** Cefu; Cefudura; Cefuhexal; Cefurax; Cefuro-Puren; Cefurox-Wolff; Elobact; Zinacef†; Zinnat; ***Gr.:*** Anaptivan; Cefoprim†; Cefur; Cefuroprol; Cerofene; Ceruxim; Cupax; Ecoline†; Feacef; Foucacillin; Fredyr; Furaxil; Galemin; Genephoxal; Gonif; Interbion; Lyoprovir; Medoxem; Mevecan†; Mosalan; Nelabocin; Nipogalin; Normafenac; Receant; Saxetil; Sedopan; Vekfazolin; Yokel; Zagorine; Zetagal; Zilisten; Zinacef; Zinadol; ***Hong Kong:*** Anikef; Axetine†; Zinacef; Zinnat; ***Hung.:*** Cefurin; Ceroxim; Cexim†; Xorim; Xorimax; Zinacef; Zinnat; ***India:*** Altacef; Cefasyn; Cefogen; Cefoxim; Forcef; Supacef; ***Indon.:*** Anbacim; Cefurox; Celocid; Cethixim; Kalcef; Kenacef; Oxtercid; Roxbi; Sharox; Zinacef; Zinnat; ***Irl.:*** Ceftal; Zinacef; Zinnat; ***Israel:*** Cefurax; Kefurim; Zinacef; Zinnat; ***Ital.:*** Biociclin; Biofurex†; Cefoprim; Cefumax†; Cefur†; Cefurex†; Cefurin; Colifossim†; Curoxim; Deltacef†; Duxima; Ipacef†; Itorex; Kefox†; Kesint; Lafurex; Oraxim; Supero; Tilexim; Zinnat; Zinocep; Zoref; ***Malaysia:*** Ceflour; Efurox; Furoxime; Zinacef; Zinnat; Zocef; ***Mex.:*** Cefagen; Cefuracet; Cetoxil; Froxal; Fucerox; Lemoxin†; Magnaspor; Novador; Ximaken; Xorufec; Zinnat; ***Neth.:*** Cefofix; Zinacef; Zinnat; ***Norw.:*** Zinacef; ***NZ:*** Zinacef; Zinnat; ***Philipp.:*** Aeruginox; Cervin; Clovixime; Fubaxyn; Furocef; Furocem; Furoxy; Infekor; Kefox; Keunzef; Laxinat; Loxatrel; Panaxim; Profurex; Romicef; Ruxim; Sharox; Shincef; Unoximed; Xorimax; Zegen; Zinacef; Zinnat; ***Pol.:*** Biofuroksym; Bioracef; Ceroxim; Novocef; Oframax; Plixym; Tarsime; Xorim; Xorimax; Zamur; Zinacef; Zinnat; ***Port.:*** Antibioxime; Cefaricida†; Cefofix; Cefrix†; Curoxime; Furaxetil†; Lusocef; Pluscef; Zipos; Zoref; ***Rus.:*** Axetine (Аксетин); Kefstar (Кефстар); Ketocef (Кетоцеф); Zinacef (Зинацеф); Zinnat (Зиннат); ***S.Afr.:*** Cefasyn; Cefu-Hexal; Ceroxim; Cipofix†; Intracef; Lifurom†; Medaxime; Zefroxe; Zinacef; Zinnat; ***Singapore:*** Bearcef; Ceftil; Shincef; Zinacef; Zinnat; ***Spain:*** Curoxima; Lifurox†; Nivador; Selan; Zinnat; ***Swed.:*** Zinacef; Zinnat; ***Switz.:*** Cefurim; Zinacef; Zinat; ***Thai.:*** Axetine†; Axurocef; Cefamar; Cefogen†; Cefurim; Farmacef; Furoxime; Magnaspor; Zinacef; Zinnat; Zonef; ***Turk.:*** Aksef; Cefatin; Enfexia; Multisef; Oraceftin; Sefaktil; Sefuroks; Zinnat; ***UAE:*** Cefuzime; ***UK:*** Zinacef; Zinnat; ***USA:*** Ceftin; Zinacef; ***Venez.:*** Xorim; Zencef; Zinacef; Zinnat.

Cethromycin *(USAN, rINN)*

A-195773; Abbott-195773; ABT-773; Céthromycine; Cethromycinum; Cetromicina. (3a*S*,4*R*,7*R*,9*R*,10*R*,11*R*,13*R*,15*R*,15a*R*)-4-Ethyl-3a,7,9,11,13,15-hexamethyl-11-{[3-(quinolin-3-yl)prop-2-enyl]oxy}-10-{[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy}octahydro-2*H*-oxacyclotetradecino[4,3-*d*]oxazole-2,6,8,14(1*H*,7*H*,9*H*)-tetrone.

Цетромицин

$C_{42}H_{59}N_3O_{10}$ = 765.9.
CAS — 205110-48-1.



Profile

Cethromycin is a ketolide antibacterial under investigation for the treatment of susceptible respiratory-tract infections.

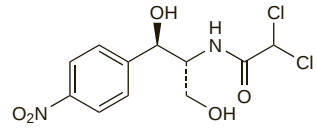
◊ References.
1. Dougherty TJ, Barrett JF. ABT-773: a new ketolide antibiotic. *Expert Opin Invest Drugs* 2001; **10:** 343–51.
2. Zhanel GG, *et al.* The ketolides: a critical review. *Drugs* 2002; **62:** 1771–1804.
3. Zhanel GG, *et al.* Ketolides: an emerging treatment for macrolide-resistant respiratory infections, focusing on S. pneumoniae. *Expert Opin Emerg Drugs* 2003; **8:** 297–321.
4. Reinert RR. Clinical efficacy of ketolides in the treatment of respiratory tract infections. *J Antimicrob Chemother* 2004; **53:** 918–27.
5. Anonymous. Cethromycin: A-195773, A-195773-0, A-1957730, Abbott-195773, ABT 773. *Drugs R D* 2007; **8:** 95–102.
6. Hammerschlag MR, Sharma R. Use of cethromycin, a new ketolide, for treatment of community-acquired respiratory infections. *Expert Opin Invest Drugs* 2008; **17:** 387–400.

Chloramphenicol *(BAN, rINN)*

Chloramfenikol; Chloramfenikolis; Chloramphénicol; Chloramphenicolum; Chloranfenicol; Cloranfenicol; Klóramfenikol; Kloramfenikol; Kloramfenikoli; Laevomycetinum. 2,2-Dichloro-*N*-[(α*R*,β*R*)-β-hydroxy-α-hydroxymethyl-4-nitrophenethyl]acetamide.

Хлорамфеникол

$C_{11}H_{12}Cl_2N_2O_5$ = 323.1.
CAS — 56-75-7.
ATC — D06AX02; D10AF03; G01AA05; J01BA01; S01AA01; S02AA01; S03AA08.
ATC Vet — QD06AX02; QD10AF03; QG01AA05; QJ01BA01; QJ51BA01; QS01AA01; QS02AA01; QS03AA08.



NOTE. CPL is a code approved by the BP 2008 for use on single unit doses of eye drops containing chloramphenicol where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Chloramphenicol). A substance produced by the growth of certain strains of *Streptomyces venezuelae*, but now mainly prepared synthetically. A white, greyish-white or yellowish-white, fine crystalline powder or fine crystals, needles, or elongated plates. Slightly soluble in water; freely soluble in alcohol and in propylene glycol. Protect from light.

USP 31 (Chloramphenicol). Fine, white to greyish-white or yellowish-white, needle-like crystals or elongated plates. Soluble 1 in 400 of water; freely soluble in alcohol, in acetone, in ethyl acetate, and in propylene glycol. pH of a 2.5% suspension in water is between 4.5 and 7.5. Its solutions are practically neutral to litmus. It is reasonably stable in neutral or moderately acid solutions. Store in airtight containers.

Chloramphenicol Palmitate *(BANM, rINNM)*

Chloramfenikolio palmitatas; Chloramfenikol-palmitát; Chloramfenikolu palmitynian; Chloramphenicol α-Palmitate; Chloramphénicol, palmitate de; Chloramphenicoli palmitas; Kloramfenikolipalmitaatti; Kloramfenikolpalmitat; Klóramfenikol-palmitát; Palmitato de cloranfenicol; Palmitylchloramphenicol.

Хлорамфеникола Пальмитат

$C_{27}H_{42}Cl_2N_2O_6$ = 561.5.
CAS — 530-43-8.
ATC — D06AX02; D10AF03; G01AA05; J01BA01; S01AA01; S02AA01; S03AA08.
ATC Vet — QD06AX02; QD10AF03; QG01AA05; QJ01BA01; QS01AA01; QS02AA01; QS03AA08.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Chloramphenicol Palmitate). A fine, white or almost white, unctuous, powder. M.p. 87° to 95°. Chloramphenicol palmitate shows polymorphism and the thermodynamically stable form has low bioavailability following oral administration. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in acetone; very slightly soluble in hexane. Protect from light.

USP 31 (Chloramphenicol Palmitate). A fine, white, unctuous, crystalline powder, having a faint odour. M.p. 87° to 95°. Insoluble in water; sparingly soluble in alcohol; freely soluble in acetone and in chloroform; soluble in ether; very slightly soluble in hexane. Store in airtight containers.

Chloramphenicol Sodium Succinate

(BANM, rINNM)

Chloramfenikolio natrio sukcinatas; Chloramfenikol-sukcinát sodná sůl; Chloramphenicol α-Sodium Succinate; Chloramphénicol, succinate sodique de; Chloramphenicoli natrii succinas; Kloramfenikol Süksinat Sodyum; Klóramfenikol-hidrogénszukcinátnátrium; Kloramfenikolinatriumsuksinaatti; Kloramfenikolnatriumsuccinat; Succinato sódico de cloranfenicol.

Хлорамфеникола Натрия Сукцинат

$C_{15}H_{15}Cl_2N_2NaO_8$ = 445.2.

CAS — 982-57-0.

ATC — D06AX02; D10AF03; G01AA05; J01BA01; S01AA01; S02AA01; S03AA08.

ATC Vet — QD06AX02; QD10AF03; QG01AA05; QJ01BA01; QS01AA01; QS02AA01; QS03AA08.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet. Chin*. includes Chloramphenicol Hydrogen Succinate.

Ph. Eur. 6.2 (Chloramphenicol Sodium Succinate). A white or yellowish-white hygroscopic powder. Very soluble in water; freely soluble in alcohol. A 25% solution in water has a pH of 6.4 to 7.0. Store in airtight containers. Protect from light.

USP 31 (Chloramphenicol Sodium Succinate). A light yellow powder. Freely soluble in water and in alcohol. pH of a solution in water containing the equivalent of chloramphenicol 25% is between 6.4 and 7.0. Store in airtight containers.

Incompatibility. Incompatibility or loss of activity has been reported between chloramphenicol and a wide variety of other substances. Other factors, especially drug concentration, may play a part and many incompatibilities are chiefly seen with concentrated solutions.

Adverse Effects and Treatment

Chloramphenicol may cause serious and sometimes fatal adverse effects. Some of its toxicity is thought to be due to effects on mitochondrial protein synthesis. The most serious adverse effect of chloramphenicol is bone-marrow depression, which can take two different forms. The first is a fairly common dose-related reversible depression occurring usually when plasma-chloramphenicol concentrations exceed 25 micrograms/mL and is characterised by morphological changes in the bone marrow, decreased iron utilisation, reticulocytopenia, anaemia, leucopenia, and thrombocytopenia. This effect may be due to inhibition of protein synthesis in the mitochondria of bone marrow cells.

The second and apparently unrelated form of bone-marrow toxicity is severe irreversible aplastic anaemia. This is fairly rare, with a suggested incidence of about 1:20 000 to 1:50 000, although the incidence varies throughout the world, and is not considered to be dose-related. The aplasia usually develops after a latent period of weeks or even months and has been suggested to be the result of a nitrated benzene radical produced *in vivo*. It is considered that there may be some genetic or biochemical predisposition, but there is no way of identifying susceptible patients. Although the majority of cases were after oral use, aplasia has also occurred after intravenous and topical (eye drops) use of chloramphenicol. Survival is most likely in those with early onset aplasia, but they may subsequently develop acute myeloid leukaemia.

A toxic manifestation—the 'grey syndrome'—characterised by abdominal distension, vomiting, ashen colour, hypothermia, progressive pallid cyanosis, irregular respiration, and circulatory collapse followed by death in a few hours or days, has occurred in premature and other newborn infants given large doses of chloramphenicol. The syndrome is associated with high plasma concentrations of chloramphenicol, due to reduced capacity for glucuronidation and decreased glomerular filtration in children of this age, leading to drug accumulation. Recovery is usually complete if the drug is withdrawn early enough after onset, but up to 40% of infants with the full-blown syndrome may die. The syndrome has also been reported in infants born to mothers given chloramphenicol in late pregnancy. A similar syndrome has been reported in adults and older children given very high doses.

Prolonged oral use of chloramphenicol may induce bleeding, either by bone-marrow depression or by reducing the intestinal flora with consequent inhibition of vitamin K synthesis. Haemolytic anaemia has occurred in some patients with the Mediterranean form of glucose 6-phosphate dehydrogenase deficiency, but is rare in patients with milder forms of the deficiency.

Peripheral as well as optic neuritis has been reported, usually in patients treated over prolonged periods. Although ocular symptoms are often reversible if treatment is withdrawn early, permanent visual impairment or blindness has occurred.

Other neurological symptoms have included encephalopathy with confusion and delirium, mental depression, and headache. Ototoxicity has also occurred, especially after the use of ear drops.

Hypersensitivity reactions including rashes, fever, and angioedema may occur especially after topical use; anaphylaxis has occurred but is rare. Jarisch-Herxheimer reactions may also occur. Gastrointestinal symptoms including nausea, vomiting, and diarrhoea can follow oral use. Disturbances of the oral and intestinal flora may cause stomatitis, glossitis, and rectal irritation. Patients may experience an intensely bitter taste after rapid intravenous use of chloramphenicol sodium succinate.

Aplastic anaemia. A review[1] of the toxicity of chloramphenicol and related drugs, including the potential role of the *p*-nitro group in producing aplastic anaemia, indicated that derivatives such as thiamphenicol, which lack this grouping, are not associated with increased incidence of aplastic anaemia.

1. Yunis AA. Chloramphenicol: relation of structure to activity and toxicity. *Ann Rev Pharmacol Toxicol* 1988; **28:** 83–100.

Overdosage. Charcoal haemoperfusion was found to be far superior to exchange transfusion in the removal of chloramphenicol from blood, although it did not prevent death in a 7-week-old infant with the 'grey syndrome' after a dosage error.[1]

1. Freundlich M, *et al*. Management of chloramphenicol intoxication in infancy by charcoal hemoperfusion. *J Pediatr* 1983; **103:** 485–7.

Precautions

Chloramphenicol is contra-indicated in patients with a history of hypersensitivity or toxic reaction to the drug. It should never be given systemically for minor infections or for prophylaxis. Repeated courses and prolonged treatment should be avoided and it should not be used in patients with pre-existing bone-marrow depression or blood dyscrasias. Routine periodic blood examinations are advisable in all patients, but will not warn of aplastic anaemia.

Use of chloramphenicol with other drugs liable to depress bone-marrow function should be avoided.

Reduced doses should be given to patients with hepatic impairment. Excessive blood concentrations may also occur after usual doses in patients with severe renal impairment and in premature and full-term neonates who have immature metabolic processes. Monitoring of plasma-chloramphenicol concentrations may be desirable in patients with risk factors. A suggested range for peak plasma concentrations is 10 to 25 micrograms/mL and for trough concentrations 5 to 15 micrograms/mL.

Neonates should never be given chloramphenicol systemically, unless it may be life-saving and there is no alternative treatment, because of the risk of the 'grey syndrome'. The use of chloramphenicol is probably best avoided during pregnancy.

Chloramphenicol may interfere with the development of immunity and it should not be given during active immunisation.

Breast feeding. Chloramphenicol is distributed into breast milk[1] and the American Academy of Pediatrics[2] considers that its use by mothers during breast feeding may be of concern, since there have been reports of possible idiosyncratic bone-marrow suppression in the infant.

1. Havelka J, *et al.* Excretion of chloramphenicol in human milk. *Chemotherapy* 1968; **13:** 204–11.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid*.; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Ocular use. Ocular chloramphenicol is widely used in the UK for the treatment of superficial eye infections. In view of the potential for serious toxicity, such as aplastic anaemia, after systemic absorption some, particularly in the USA, have advised that its ocular use should be restricted to situations where there is no alternative treatment.[1] However, apart from patients with a personal or family history of blood dyscrasias, the use, particularly of short courses, was defended by several specialists in the UK,[2-4] and the arguments have been the subject of several reviews.[5-7] Prospective case-control studies were considered necessary to clarify the risk.[8] One such study,[9] involving 145 patients with aplastic anaemia and 1226 controls, found that only 3 of the patients had been exposed to ocular chloramphenicol, and calculated that the absolute risk was no more than 0.5 cases per million treatment courses. Similarly, data[10] from 2 other studies revealed that none of 426 patients with aplastic anaemia and 7 of 3118 controls had used chloramphenicol eye drops. In a survey[11] of patients who received prescriptions for chloramphenicol eye drops the risk of serious haematological toxicity was 3 per 442 543 patients or 3 per 674 148 prescriptions.

1. Doona M, Walsh JB. Use of chloramphenicol as topical eye medication: time to cry halt? *BMJ* 1995; **310:** 1217–18.
2. Mulla RJ, *et al.* Is it time to stop using chloramphenicol on the eye: fears are based on only six cases. *BMJ* 1995; **311:** 450.
3. Buckley RJK, *et al.* Is it time to stop using chloramphenicol on the eye: safe in patients with no history of blood dyscrasia. *BMJ* 1995; **311:** 450.
4. Hall AV, *et al.* Is it time to stop using chloramphenicol on the eye: risk is low in short courses. *BMJ* 1995; **311:** 450–1.
5. McGhee CNJ, Anastas CN. Widespread ocular use of topical chloramphenicol: is there justifiable concern regarding idiosyncratic aplastic anaemia? *Br J Ophthalmol* 1996; **80:** 182–4.
6. Rayner SA, Buckley RJ. Ocular chloramphenicol and aplastic anaemia: is there a link? *Drug Safety* 1996; **14:** 273–6.
7. Titcomb L. Ophthalmic chloramphenicol and blood dyscrasias: a review. *Pharm J* 1997; **258:** 28–35.
8. Gordon-Smith EC, *et al.* Is it time to stop using chloramphenicol on the eye: prospective study of aplastic anaemia should give definitive answer. *BMJ* 1995; **311:** 451.
9. Laporte J-R, *et al.* Possible association between ocular chloramphenicol and aplastic anaemia—the absolute risk is very low. *Br J Clin Pharmacol* 1998; **46:** 181–4.
10. Wiholm B-E, *et al.* Relation of aplastic anaemia to use of chloramphenicol eye drops in two international case-control studies. *BMJ* 1998; **316:** 666.
11. Lancaster T, *et al.* Risk of serious haematological toxicity with use of chloramphenicol eye drops in a British general practice database. *BMJ* 1998; **316:** 667.

Porphyria. Chloramphenicol has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Sodium content. Each g of chloramphenicol sodium succinate represents about 2.2 mmol of sodium.

Interactions

Chloramphenicol is inactivated in the liver and may, therefore, interact with drugs that are metabolised by hepatic microsomal enzymes. For example, chloramphenicol enhances the effects of coumarin anticoagulants, such as dicoumarol and warfarin, some hypoglycaemics such as chlorpropamide and tolbutamide, and antiepileptics such as phenytoin. Conversely, the metabolism of chloramphenicol may be increased by inducers of hepatic enzymes such as phenobarbital or rifampicin. Some other interactions affecting the activity of chloramphenicol are discussed below.

Chloramphenicol may decrease the effects of iron and vitamin B_{12} in anaemic patients and has occasionally impaired the action of oral contraceptives.

For the effects of chloramphenicol on the activity of other antibacterials, see Antimicrobial Action, below.

Antiepileptics. Serum concentrations of chloramphenicol are usually reduced by the hepatic enzyme induction that occurs with *phenobarbital*,[1,2] and similar reductions have been reported in a case study during *phenytoin* use.[3] Conversely, elevated and potentially toxic serum-chloramphenicol concentrations have resulted during phenytoin use,[2] apparently due to competition for binding sites, although increased metabolism may alternatively lead to decreased serum-chloramphenicol concentrations.

For reference to the effects of chloramphenicol on phenobarbital and phenytoin, see p.493 and p.498, respectively.

1. Bloxham RA, *et al.* Chloramphenicol and phenobarbitone—a drug interaction. *Arch Dis Child* 1979: **54:** 76–7.
2. Krasinski K, *et al.* Pharmacologic interactions among chloramphenicol, phenytoin and phenobarbital. *Pediatr Infect Dis* 1982; **1:** 232–5.
3. Powell DA, *et al.* Interactions among chloramphenicol, phenytoin, and phenobarbital in a pediatric patient. *J Pediatr* 1981; **98:** 1001–3.

Ciclosporin. For the effect of chloramphenicol on ciclosporin, see p.1825.

Cimetidine. Fatal aplastic anaemia of rapid onset has occurred in 2 patients who received intravenous chloramphenicol and cimetidine.[1,2] As there is usually a latent period of 2 weeks to 12 months before aplastic anaemia develops after chloramphenicol therapy it is plausible that an additive or synergistic effect may