Cetrimonium Bromide *(BAN, rINN)*

Bromuro de cetrimonio; Cetrimonii Bromidum; Cétrimonium, Bromure de; Cetylotrimetyloamoniowy bromek; Cetyltrimethylammonium Bromide; CTAB. Hexadecyltrimethylammonium bromide.

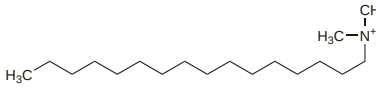
Цетримония Бромид

$C_{19}H_{42}BrN$ = 364.4.

CAS — 6899-10-1 (cetrimonium); 57-09-0 (cetrimonium bromide).

ATC — D08AJ02; R02AA17.

ATC Vet — QD08AJ02; QR02AA17.



(cetrimonium)

NOTE. The name cetrimonium bromide was formerly applied to cetrimide (see above).

Pharmacopoeias. In *USNF.*

USNF 26 (Cetrimonium Bromide). A white to creamy white, voluminous, free-flowing powder, with a characteristic faint odour. Freely soluble in water and in alcohol; practically insoluble in ether.

Cetrimonium Chloride *(BAN)*

Cetrimonio, cloruro de. Hexadecyltrimethylammonium chloride.

$C_{19}H_{42}ClN$ = 320.0.

CAS — 112-02-7.

Profile

Cetrimonium bromide is a quaternary ammonium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). Cetrimonium chloride and cetrimonium tosilate are also used.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz.: Tiracaspa†; ***Ital.:*** Golaval†; Senol; Sterilene; ***Switz.:*** Aknex Cleaning; Turisan.

Multi-ingredient: ***Arg.:*** Bagociletas sin Anestesia†; Bagoderm; Eryteal; Klorane Bebe Eryteal; Salvicutan†; ***Austria:*** Xylestesin; ***Belg.:*** Cetavlex; HAC; Hacdil-S; ***Braz.:*** Amigdalol; Drapolene; Leucocida†; ***Fr.:*** Eryteal†; Nostril; ***Ger.:*** Lemocin; Xylestesin Pumpspray†; ***Indon.:*** Lemocin; ***Israel:*** Lemocin; ***Ital.:*** Golamixin; Xylonor; ***Mex.:*** Dermatolona; ***Pol.:*** Cetriscabin; ***Spain:*** Diformiltricina; Hongosan; Xylonor; ***Switz.:*** Desitur†; Lemocin; Septivon N; Turexan Capilla; Xylestesin†; Xylonor; ***Venez.:*** Kertyol.

Cetylpyridinium Chloride *(BAN, rINN)*

Cetilpiridinio chloridas; Cetilpiridinium-klorid; Cetylpyridinii chloridum; Cetylpyridinii Chloridum Monohydricum; Cétylpyridinium, chlorure de; Cetylpyridinium-chlorid monohydrát; Cetylpyridiniumklorid; Cloruro de cetilpiridinio; Setilpiridinyum Klorür; Setyylipyridiniumkloridi. 1-Hexadecylpyridinium chloride monohydrate.

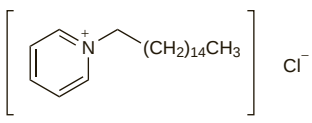
Цетилпиридиния Хлорид

$C_{21}H_{38}ClN,H_2O$ = 358.0.

CAS — 7773-52-6 (cetylpyridinium); 123-03-5 (anhydrous cetylpyridinium chloride); 6004-24-6 (cetylpyridinium chloride, monohydrate).

ATC — B05CA01; D08AJ03; D09AA07; R02AA06.

ATC Vet — QB05CA01; QD08AJ03; QD09AA07; QR02AA06.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Cetylpyridinium Chloride). A white or almost white powder, slightly soapy to the touch. Soluble in water, frothing copiously when shaken; soluble in alcohol.

USP 31 (Cetylpyridinium Chloride). A white powder with a slight characteristic odour. Soluble 1 in 4.5 of water and of chloroform, and 1 in 2.5 of alcohol; slightly soluble in ether and in benzene.

Incompatibility. Cetylpyridinium chloride is incompatible with soaps and other anionic surfactants.

Profile

Cetylpyridinium chloride is a quaternary pyridinium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used chiefly as lozenges or solutions for the treatment of minor infections of the mouth and throat. It is also used topically for the treatment of skin and eye infections.

Cetylpyridinium bromide is used similarly for minor mouth and throat disorders.

Preparations

USP 31: Cetylpyridinium Chloride Lozenges; Cetylpyridinium Chloride Topical Solution.

Proprietary Preparations (details are given in Part 3)

Austral.: Cepacol Antibacterial; Cepacol Antiseptic Throat Lozenges; Cepacol Mint; Cepacol Regular; Lemsip Lozenges; ***Austria:*** Dobendan; Halset; ***Braz.:*** Gargocetil; Laringex; ***Canad.:*** Cepacol; Mouthwash†; Rince Bouche Antiseptique; Throat Lozenges; ***Chile:*** Freesept; ***Cz.:*** Halset; ***Fr.:*** Cetylyre†; Novoptine†; ***Ger.:*** Dobendan; Halstabletten akute; ***Hong Kong:*** Cepacol; Cetocomp; ***Hung.:*** Halset; ***Irl.:*** Merocets; ***Ital.:*** Bat; Borocaina Gola; Bronchenolo†; Cetilsan; Citromed Soap; Exil; Farin Gola; Golacetin; Golafair; Honeygola; Neo Cepacol Pastiglie; Neo Coricidin Gola†; Neo Formitrol; Periogard Plus; Ragaden; Stomygen; ***Mex.:*** Trociletas; ***Norw.:*** Pyrisept; ***NZ:*** Cepacol; Lemsip Throat Lozenges; ***Pol.:*** Halset; Menthosept; ***Port.:*** Septus; ***S.Afr.:*** Cepacol; Universal Throat Lollies; ***Singapore:*** Cepacol; ***Spain:*** Angifonil†; ***Thai.:*** Cepacol; Orasept; ***Turk.:*** Aseptol; Penipastil; ***UK:*** Listermint; Merocets; ***USA:*** Cepacol Mouthwash; Cepacol Throat; Choice DM Gentle Care; Scope; ***Venez.:*** Cepacol; Tablibut†.

Multi-ingredient: ***Arg.:*** Desenfriol Caramelos†; Ernex Duo; Oral-B Enjuague Bucal†; Periodil; Solumenin; ***Austral.:*** Cepacaine; Cepacol Anaesthetic; Cepacol Antibacterial; Cepacol Cough & Sore Throat; Difflam Anti-inflammatory Lozenges with Cough Suppressant; Difflam Lozenges; Difflam Mouth Gel; Duro-Tuss Cough Lozenges; Gentlees; Seda-Gel†; ***Austria:*** Coldistan; Dentinox; Gurfix; Paididont; Tetesept; ***Braz.:*** Cepacaina; Cepacol Menta; Cetildrops†; Dentalivio†; Fenotricin†; Lima C; Limao Bravo com Vitamina C†; Limao Bravo†; Malvona†; Neopiridin; Pondicilina; Proplax†; Psiu; Sanilin; ***Canad.:*** Cepacol Extra Strength; Cepacol with Fluoride; Green Antiseptic Mouthwash & Gargle; Kank-A; Oral Plan†; Oral-B Anti-Bacterial with Fluoride; Throat Lozenges; ***Chile:*** Halita; Kank-Eze; Oralfresh Menta; Pancrit; Perio-Aid c Cloruro de Cetilpiridinio; Vitis Encias Colutorio; Vitis Encias Pasta; ***Cz.:*** Brand- und Wundgel†; Calgel; Neoseptolete; Panlid; Stas†; Tetesept Angidin†; ***Fin.:*** Bafucin; ***Fr.:*** Alodont; Broncorinol maux de gorge†; Lysopaine; Parogencyl prevention gencives; ***Ger.:*** Biogel†; Brand- und Wund-Gel Eu Rho†; Broncho-Tyrosolvetten†; Dolo-Dobendan; Emmedical†; Frubienzym; Frubizin Forte†; Nordathricin N†; Trachiform†; Tyrosolvetten-C†; Tyrosolvetten†; Tyrosur; Wick Sulagil; ***Hong Kong:*** Dentinox Teething Gel; Difflam Anti-inflammatory Lozenges; Difflam Mouth Gel; Pharynx; Setronges†; ***Hung.:*** Mebucain; Tyrosur; ***Indon.:*** Sentril; ***Irl.:*** Anbesol; Merocaine; ***Israel:*** Cepadont; Kank-A; ***Ital.:*** Delta 80; Delta 80 Plus; Farmagola†; Ginvapast; Gola Action; Neo-Stomygen; Oral-B Collutorio per la Protezione di Denti e Gengive; Orosanyl†; Ridiodent; Rikospray; Stomygen; ***Malaysia:*** Cetylpyridinium B; Dentinox Teething Gel; Difflam Anti-inflammatory Lozenges (with Antibacterial); Difflam Anti-Inflammatory Lozenges (with cough suppressant); Difflam Mouth Gel; Orregel; Pharynx; Setronges†; ***Mex.:*** Cepacaina; Mentalgina; Trociletas B; ***Neth.:*** Agre-Gola; ***Norw.:*** Aselli; ***NZ:*** Cepacaine; Cepacol Anaesthetic; Cepacol Cough Discs; Difflam Cough; Difflam Mouth Gel; Duro-Tuss Lozenges; ***Philipp.:*** Xylorinse; ***Pol.:*** Calgel; Lidodent; Septolete Plus; Tetesept; Undofen; ***Port.:*** Anbegele†; Biofluor Ortodoncia†; Biofluor Sensitive†; Dropcina; Mebocaina; ***Rus.:*** Calgel (Калгель); Septolete Plus (Септолете Плюс); ***S.Afr.:*** Anbesol; Andolex-C; Cepacaine; Cepacol; Cepacol Cough Discs; Cetoxol; Colphen; Endcol Lozenges; Medi-Kain†; Medi-Keel A; Prodol; Vagarsol; Vicks Acta Plus; Vicks Cough Syrup; ***Singapore:*** Dentinox Teething Gel; Difflam Anti-inflammatory Anti-Bacterial Lozenges; Difflam Mouth Gel; Duro-Tuss Cough Lozenges; Pharynx; Soragel; ***Spain:*** Alcohocel; Alcohol Cetil†; Alcohol Cetilpi Cuve†; Babysiton; Farmalcohol; Pastillas Antisep Garg L; Pastillas Antisep Garg M; Silidermil†; Vicks Formula 44†; ***Swed.:*** Bafucin; ***Switz.:*** Alodont†; Angina MCC; Anginazol; Desaquick forte†; Flavangin†; Hextrileten; Hextrimint; Lidazon; Mebucaine; Nasex†; Neo-Angin Lido; Otothricinol; Pharmacard Family Maux de gorge†; Wulnasin; ***Thai.:*** Sentril; Sore Mouth Gel; ***Turk.:*** Calgel; Nesgarin; ***UAE:*** B-Cool; New B-Cool; ***UK:*** Adult Meltus for Chesty Coughs & Catarrh; Allens Dry Tickly Cough; Anbesol; Calgel; Dentinox Teething Gel; Kilkof; Listermint with Fluoride; Macleans Mouthguard; Meltus Expectorant; Meltus Junior Expectorant; Merocaine; Merocets Plus; Rinstead; Rinstead Teething Gel†; Woodwards Teething Gel; ***USA:*** Cepacol Anesthetic; Cepacol Maximum Strength Sore Throat; Cepacol Regular Strength; Cylex; MouthKote O/R; MouthKote P/R†; Orajel Mouth Aid; ***Venez.:*** Borogin; Calgel†; Cepacol-BE; Isospray; Lafarcaina; Solunovar Compuesto.

Chlorhexidine *(BAN, rINN)*

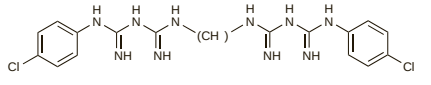
Chlorhexidinum; Clorhexidina; Klooriheksidiini; Klorheksidin; Klorhexidin.

Хлоргексидин

CAS — 55-56-1.

ATC — A01AB03; B05CA02; D08AC02; D09AA12; R02AA05; S01AX09; S02AA09; S03AA04.

ATC Vet — QA01AB03; QB05CA02; QD08AC02; QD09AA12; QR02AA05; QS01AX09; QS02AA09; QS03AA04.



Chlorhexidine Acetate *(BANM, rINNM)*

Acetato de clorhexidina; Chlorheksidino diacetatas; Chlorhexidin-diacetát; Chlorhexidine, Acétate de; Chlorhexidine Diacetate; Chlorhexidine, diacétate de; Chlorhexidini Acetas; Chlorhexidini diacetas; Chloroheksydyny octan; Klooriheksidiinidiasetaatti; Klorhexidindiacetat; Klórhexidin-diacetát. 1,1′-Hexamethylenebis[5-(4-chlorophenyl)biguanide] diacetate.

Хлоргексидина Ацетат

$C_{22}H_{30}Cl_2N_{10},2C_2H_4O_2$ = 625.6.

CAS — 56-95-1.

ATC — A01AB03; B05CA02; D08AC02; D09AA12; R02AA05; S01AX09; S02AA09; S03AA04.

ATC Vet — QA01AB03; QB05CA02; QD08AC02; QD09AA12; QR02AA05; QS01AX09; QS02AA09; QS03AA04.

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

Ph. Eur. 6.2 (Chlorhexidine Diacetate). A white or almost white, microcrystalline powder. Sparingly soluble in water; soluble in alcohol; slightly soluble in glycerol and in propylene glycol.

Incompatibility. The incompatibilities of chlorhexidine salts are discussed under Chlorhexidine Hydrochloride, below.

Stability. The stability of chlorhexidine salts is discussed under Chlorhexidine Hydrochloride, below.

Chlorhexidine Gluconate *(BANM, USAN, rINNM)*

Chlorheksidino digliukonato tirpalas; Chlorhexidin-diglukonát; Chlorhexidine Digluconate; Chlorhexidine, digluconate de; Chlorhexidine, Gluconate de; Chlorhexidini digluconas; Chlorhexidini Digluconatis Solutio; Chlorhexidini Gluconas; Chloroheksydyny diglukonianu roztwór; Gluconato de clorhexidina; Klooriheksidiinidiglukonaattiliuos; Klorheksidin Glukonat; Klorhexidindiglukonatlösning; Klórhexidin-diglükonát-oldat. 1,1′-Hexamethylenebis[5-(4-chlorophenyl)biguanide] digluconate.

Хлоргексидина Глюконат

$C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$ = 897.8.

CAS — 18472-51-0.

ATC — A01AB03; B05CA02; D08AC02; D09AA12; R02AA05; S01AX09; S02AA09; S03AA04.

ATC Vet — QA01AB03; QB05CA02; QD08AC02; QD09AA12; QR02AA05; QS01AX09; QS02AA09; QS03AA04.

Pharmacopoeias. *Chin., Eur.* (see p.vii), and *US* include a solution which contains 19 to 21% of chlorhexidine gluconate.

Ph. Eur. 6.2 (Chlorhexidine Digluconate Solution; Chlorhexidini Digluconatis Solutio; Chlorhexidine Gluconate Solution BP 2008). An aqueous solution which contains not less than 190 g/litre and not more than 210 g/litre of chlorhexidine gluconate. An almost colourless or pale-yellowish liquid. Miscible with water, with not more than 5 parts of alcohol, and with not more than 3 parts of acetone. A 5% v/v dilution in water has a pH of 5.5 to 7.0. Protect from light.

USP 31 (Chlorhexidine Gluconate Solution). An aqueous solution which contains not less than 19% and not more than 21% of chlorhexidine gluconate. An almost colourless or pale yellow, clear liquid. Miscible with water and with glacial acetic acid; miscible with five times its volume of dehydrated alcohol and with three times its volume of acetone; further addition of dehydrated alcohol or of acetone yields a white turbidity. A 5% v/v dilution in water has a pH of 5.5 to 7.0. Store in airtight containers. Protect from light.

Incompatibility. The incompatibilities of chlorhexidine salts are discussed under Chlorhexidine Hydrochloride, below.

Stability. The stability of chlorhexidine salts is discussed under Chlorhexidine Hydrochloride, below.

Sterilisation. Dilutions of commercial concentrated solutions may be sterilised by autoclaving.

Chlorhexidine Hydrochloride *(BANM, USAN, rINNM)*

AY-5312; Chlorheksidino dihidrochloridas; Chlorhexidin-dihydrochlorid; Chlorhexidine, Chlorhydrate de; Chlorhexidine, dichlorhydrate de; Chlorhexidine Dihydrochloride; Chlorhexidini dihydrochloridum; Chlorhexidini Hydrochloridum; Hidrocloruro de clorhexidina; Klooriheksidiinidihydrokloridi; Klorheksidin Hidroklorür; Klórhexidin-dihidroklorid; Klorhexidindihydroklorid. 1,1′-Hexamethylenebis[5-(4-chlorophenyl)biguanide] dihydrochloride.

Хлоргексидина Гидрохлорид

$C_{22}H_{30}Cl_2N_{10},2HCl$ = 578.4.

CAS — 3697-42-5.

ATC — A01AB03; B05CA02; D08AC02; D09AA12; R02AA05; S01AX09; S02AA09; S03AA04.

ATC Vet — QA01AB03; QB05CA02; QD08AC02; QD09AA12; QR02AA05; QS01AX09; QS02AA09; QS03AA04.

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

Ph. Eur. 6.2 (Chlorhexidine Dihydrochloride; Chlorhexidine Hydrochloride BP 2008). A white or almost white, crystalline powder. Sparingly soluble in water and in propylene glycol; very slightly soluble in alcohol.

Incompatibility. Chlorhexidine salts are incompatible with soaps and other anionic materials. Activity may be reduced in the presence of suspending agents such as alginates and tragacanth, insoluble powders such as kaolin, and insoluble compounds of calcium, magnesium, and zinc. Chlorhexidine acetate is incompatible with potassium iodide. At a concentration of 0.05%, chlorhexidine salts are incompatible with borates, bicarbonates, carbonates, chlorides, citrates, nitrates, phosphates, and sulfates, forming salts of low solubility which may precipitate out of solution. At dilutions of 0.01% or more, these salts are generally soluble. Insoluble salts may form in hard water. Chlorhexidine salts are inactivated by cork.

References to incompatibilities of chlorhexidine with suspending agents and insoluble solids.[1-3]

1. McCarthy TJ. The influence of insoluble powders on preservatives in solution. *J Mond Pharm* 1969; **12:** 321–8.
2. Yousef RT, *et al.* Effect of some pharmaceutical materials on the bactericidal activities of preservatives. *Can J Pharm Sci* 1973; **8:** 54–6.
3. McCarthy TJ, Myburgh JA. The effect of tragacanth gel on preservative activity. *Pharm Weekbl* 1974; **109:** 265–8.

Stability. Chlorhexidine and its salts are stable at normal storage temperatures but when heated may decompose with the production of trace amounts of 4-chloroaniline. Chlorhexidine hydrochloride is less readily decomposed than chlorhexidine acetate and may be heated at 150° for 1 hour without appreciable production of 4-chloroaniline. Aqueous solutions of chlorhexidine salts decompose with the formation of trace amounts of 4-chloroaniline. This decomposition is increased by heating and alkaline pH.

Adverse Effects and Treatment

Skin sensitivity to chlorhexidine has occasionally been reported. Severe hypersensitivity reactions, including anaphylactic shock, have been reported rarely after topical use of chlorhexidine. Strong solutions may cause irritation of the conjunctiva and mucous membranes. The use of chlorhexidine dental gel and mouthwash has been associated with reversible discoloration of the tongue, teeth, and silicate or composite dental restorations. Transient taste disturbances and a burning sensation of the tongue may occur on initial use. Oral desquamation and occasional parotid gland swelling have been reported with the mouthwash. If desquamation occurs, 50% dilution of the mouthwash with water and less vigorous rinsing may allow continued use.

The main consequence of ingestion is mucosal irritation and systemic toxicity is rare due to minimal absorption from the gastrointestinal tract (see Poisoning, below). Haemolysis has been reported after accidental intravenous administration. Gastric lavage with demulcents has been suggested for acute ingestion.

Effects on the eyes. Corneal damage was reported in 4 patients after use of chlorhexidine gluconate for pre-operative preparation of facial skin.[1] Severe corneal endothelium damage occurred in a further 3 patients[2] when chlorhexidine was inadvertently used as an intra-ocular irrigating solution and 2 of the patients subsequently required penetrating keratoplasty. Other adverse effects included pronounced iris atrophy, anterior chamber flattening, and a retrocorneal membrane; one patient developed raised intra-ocular pressure. In another case progressive ulcerative keratitis and almost total loss of the corneal epithelium was reported[3] after use of chlorhexidine gluconate 0.02% and propamidine 0.1% eye drops for 8 weeks for *Acanthamoeba* keratitis. In 2 patients[4] treated similarly for 4 to 6 months, deep marginal ulceration of the cornea developed, in each case requiring a penetrating graft; a mature cataract and an atrophic iris were seen in each patient after removal of the cornea. Due to the similarity of both cases, it was suggested that these complications were caused by the drugs rather than by amoeba-induced inflammation.

1. Tabor E, *et al.* Corneal damage due to eye contact with chlorhexidine gluconate. *JAMA* 1989; **261:** 557–8.
2. Anders N, Wollensak J. Inadvertent use of chlorhexidine instead of balanced salt solution for intraocular irrigation. *J Cataract Refract Surg* 1997; **23:** 959–62.
3. Murthy S, *et al.* Progressive ulcerative keratitis related to the use of topical chlorhexidine gluconate (0.02%). *Cornea* 2002; **21:** 237–9.
4. Ehlers N, Hjortdal J. Are cataract and iris atrophy toxic complications of medical treatment of acanthamoeba keratitis? *Acta Ophthalmol Scand* 2004; **82:** 228–31.

Effects on the nose. Temporary hyposmia (reduced sense of smell) in some patients after transsphenoidal pituitary adenoma operation was assumed to be caused by pre-operative disinfection of the nasal cavity with chlorhexidine gluconate solution.[1]

1. Yamagishi M, *et al.* Impairment of olfactory epithelium treated with chlorhexidine digluconate (Hibitane). *Pract Otol* 1985; **78:** 399–409.

Hypersensitivity. Both immediate and delayed hypersensitivity reactions have been reported after topical use of chlorhexidine[1] and from the use of chlorhexidine-containing urethral lubricants.[2] However, the incidence is low given the frequent use of chlorhexidine. Delayed hypersensitivity reactions such as contact dermatitis, fixed drug eruptions, and photosensitivity reactions are more common than immediate hypersensitivity reactions (acute urticaria, angioedema, and bronchospasm which may progress to anaphylactic shock).[1,3]

Immediate hypersensitivity reactions have also occurred with surgical disinfection. Signs appear 15 to 45 minutes after the start of surgery and include hypotension, urticaria, tachycardia, bronchospasm, and sometimes anaphylactic shock, cardiovascular collapse, or cardiac arrest.[3,4] In 1998 the FDA issued a public notice[5] warning of potential hypersensitivity reactions to chlorhexidine-impregnated intravenous catheters, topical antimicrobial skin dressings, and implanted antimicrobial surgical mesh, based on reports of adverse events that had occurred in the USA and other countries.

Occupational asthma has been attributed to an alcoholic chlorhexidine spray.[6]

1. Krautheim AB, *et al.* Chlorhexidine anaphylaxis: case report and review of the literature. *Contact Dermatitis* 2004; **50:** 113–16.
2. Jayathillake A, *et al.* Allergy to chlorhexidine gluconate in urethral gel: report of four cases and review of the literature. *Urology* 2003; **61:** 837iv–837vi.
3. Beaudouin E, *et al.* Immediate hypersensitivity to chlorhexidine: literature review. *Allerg Immunol (Paris)* 2004; **36:** 123–6.
4. Chisholm DG, *et al.* Intranasal chlorhexidine resulting in an anaphylactic circulatory arrest. *BMJ* 1997; **315:** 785.
5. FDA. FDA Public Health notice potential hypersensitivity reactions to chlorhexidine-impregnated medical devices (issued 11/03/98). Available at: http://www.fda.gov/cdrh/chlorhex.html (accessed 15/03/06)
6. Waclawski ER, *et al.* Occupational asthma in nurses caused by chlorhexidine and alcohol aerosols. *BMJ* 1989; **298:** 929–30.

Poisoning. Reports of adverse effects after ***ingestion*** of chlorhexidine salts include a neonate who developed multiple episodes of cyanosis and bradycardia;[1] the infant's mother had sprayed chlorhexidine onto her breasts to prevent mastitis. In contrast an 89-year-old woman only experienced mild giddiness, unusual laughter, and an increased appetite after mistakenly drinking 30 mL of a solution containing chlorhexidine gluconate 4% and isopropyl alcohol 4%.[2] A review[3] of 7 adult cases of deliberate ingestion of a commercially available mixture of cetrimide 3% and chlorhexidine gluconate 0.3%, concluded that symptoms were generally mild and included nausea, vomiting, sore throat, and abdominal pain. There has also been a report of a patient who developed gastritis after ingesting a pre-operative skin preparation containing chlorhexidine gluconate 4% when using it as a mouthwash.[4]

Another person had much more serious effects after drinking about 150 mL of chlorhexidine gluconate solution, corresponding to about 30 g of the pure substance.[5] Besides pharyngeal oedema and necrotic oesophageal lesions, the patient had aminotransferase concentrations that rose to 30 times normal 5 days after ingestion and were still 8 times normal one week later. After one month the serum aspartate aminotransferase was returning to normal while the serum alanine aminotransferase was still 3 times normal. Six months after ingestion the aminotransferase levels were normal. A liver biopsy performed soon after the peak in aminotransferase levels showed diffuse fatty degeneration and lobular hepatitis suggesting that chlorhexidine was absorbed from the gastrointestinal tract in a concentration high enough to produce liver necrosis. An 80-year-old woman had spontaneous vomiting and aspiration followed by acute respiratory distress syndrome within 5 hours of accidental ingestion of 200 mL of a chlorhexidine gluconate 5% solution .[6] Despite supportive treatment, the patient's condition continued to deteriorate and she developed shock and metabolic acidosis and died from cardiac arrest 12 hours after ingestion.

Accidental ***intravenous*** administration of 4 mL of a 20% chlorhexidine gluconate solution in a 67-year-old man undergoing a colectomy resulted in the sudden development of acute respiratory distress syndrome.[7] Respiratory failure progressed despite plasma exchange therapy over 3 consecutive days. Veno-arterial extracorporeal membrane oxygenation was started on the third day and after 72 hours improvement was noted and the patient subsequently recovered completely.

1. Quinn MW, Bini RM. Bradycardia associated with chlorhexidine spray. *Arch Dis Child* 1989; **64:** 892–3.
2. Emerson D, Pierce C. A case of a single ingestion of 4% Hibiclens. *Vet Hum Toxicol* 1988; **30:** 583.
3. Chan TYK. Poisoning due to Savlon (cetrimide) liquid. *Hum Exp Toxicol* 1994; **13:** 681–2.
4. Roche S, *et al.* Chlorhexidine-induced gastritis. *Postgrad Med J* 1991; **67:** 210–11.
5. Massano G, *et al.* Striking aminotransferase rise after chlorhexidine self-poisoning. *Lancet* 1982; **i:** 289.
6. Hirata K, Kurokawa A. Chlorhexidine gluconate ingestion resulting in fatal respiratory distress syndrome. *Vet Hum Toxicol* 2002; **44:** 89–91.
7. Ishigami S, *et al.* Intravenous chlorhexidine gluconate causing acute respiratory distress syndrome. *J Toxicol Clin Toxicol* 2001; **39:** 77–80.

Precautions

Since chlorhexidine is irritant it is recommended that it should not be used on the brain, meninges, middle ear, or other sensitive tissues. Contact with the eye should be avoided except for dilute solutions expressly for use in the eyes. Chlorhexidine may be adsorbed by some soft contact lenses and cause eye irritation, although it may be suitable for use with others (see Contact Lens Care, p.1622). Syringes and needles that have been immersed in chlorhexidine solutions should be thoroughly rinsed with sterile water or saline before use.

Aqueous solutions of chlorhexidine salts may be susceptible to contamination with micro-organisms. To reduce this risk, a sterilised preparation should be used or, where necessary, solutions must be freshly prepared at the recommended concentration and appropriate measures should be taken to prevent contamination during storage or dilution.

Aqueous solutions of chlorhexidine used for instrument storage should contain sodium nitrite 0.1% to inhibit metal corrosion, and should be changed every 7 days. Commercial 5% concentrate contains a nonionic surfactant to prevent precipitation on dilution with hard water and is not suitable for use in body cavities or for disinfection of instruments containing cemented glass components; dilutions of the 20% concentrate should be used for this purpose.

Contamination. *Ralstonia pickettii* (*Burkholderia pickettii*; *Pseudomonas pickettii*) septicaemia developed in 6 patients after the use of aqueous chlorhexidine 0.05%, prepared with contaminated twice-distilled water, for skin disinfection before venepuncture and it was considered that unsterilised 0.05% solutions should not be used for such skin preparation.[1] Positive blood cultures of *Burkholderia cepacia* (*Pseudomonas cepacia*) were found in 2 patients after inappropriate use of a chlorhexidine handwash for the same purpose.[2] Further studies showed that the handwash supported pseudomonal growth only when diluted.[3]

1. Kahan A, *et al.* Is chlorhexidine an essential drug? *Lancet* 1984; **ii:** 759–60.
2. Gosden PE, Norman P. Pseudobacteraemia associated with contaminated skin cleansing agent. *Lancet* 1985; **ii** 671–2.
3. Norman P, *et al.* Pseudobacteraemia associated with contaminated skin cleansing agent. *Lancet* 1986; **i:** 209.

Neonates. Haemorrhagic skin necrosis associated with umbilical artery catheterisation in a premature infant was attributed to damage by the alcohol from the use of chlorhexidine 0.5% in spirit 70% as a disinfectant.[1]

For reference to the percutaneous absorption of chlorhexidine following topical use in neonates and infants, see Pharmacokinetics, below.

1. Harpin V, Rutter N. Percutaneous alcohol absorption and skin necrosis in a preterm infant. *Arch Dis Child* 1982; **57:** 477–9.

Oral hygiene. As toothpastes may contain anionic surfactants such as sodium laurilsulfate, which are incompatible with chlorhexidine, it has been recommended that at least 30 minutes should be allowed to elapse between the use of toothpaste and oral chlorhexidine preparations.[1]

1. Barkvoll P, *et al.* Interaction between chlorhexidine digluconate and sodium lauryl sulfate in vivo. *J Clin Periodontol* 1989; **16:** 593–5.

Washing precautions. Fabrics that have been in contact with chlorhexidine solution may develop a brown stain if bleached with a hypochlorite. A peroxide bleach may be used instead.

Pharmacokinetics

Chlorhexidine is poorly absorbed from the gastrointestinal tract and skin.

Neonates. Occasional reports of the percutaneous absorption of chlorhexidine in neonates and infants include a study in which chlorhexidine was detected in low concentrations in the venous blood of 5 of 24 infants after washing them with a preparation containing chlorhexidine gluconate 4% (*Hibiscrub*); no adverse effects were observed.[1] Low concentrations have been found[2] in the venous blood of neonates following the topical use of a powder containing chlorhexidine 1%. Percutaneous absorption of chlorhexidine was reported in preterm neonates (but not full-term infants) treated with chlorhexidine 1% in alcohol for neonatal cord care; no such absorption occurred when a dusting powder containing chlorhexidine 1% and zinc oxide 3% was used.[3]

1. Cowen J, *et al.* Absorption of chlorhexidine from the intact skin of newborn infants. *Arch Dis Child* 1979; **54:** 379–83.
2. Alder VG, *et al.* Comparison of hexachlorophane and chlorhexidine powders in prevention of neonatal infection. *Arch Dis Child* 1980; **55:** 277–80.
3. Aggett PJ, *et al.* Percutaneous absorption of chlorhexidine in neonatal cord care. *Arch Dis Child* 1981; **56:** 878–91.

Uses and Administration

Chlorhexidine is a bisbiguanide antiseptic and disinfectant that is bactericidal or bacteriostatic against a wide range of Gram-positive and Gram-negative bacteria. It is more effective against Gram-positive than Gram-negative bacteria, and some species of *Pseudomonas* and *Proteus* have low susceptibility. It is relatively ineffective against mycobacteria. Chlorhexidine inhibits some viruses and is active against some fungi. It is inactive against bacterial spores at room temperature. Chlorhexidine is most active at a neutral or slightly acid pH. Combinations of chlorhexidine with cetrimide (p.1634) or in alcoholic solution are used to enhance efficacy.

Chlorhexidine is formulated as lotions, washes, and creams for disinfection and cleansing of skin and wounds (p.1585), and as oral gels, sprays, and mouthwashes for mouth infections including candidiasis and to reduce dental plaque accumulation. It has also been used with neomycin to eliminate nasal carriage of staphylococci (p.195) and for disinfection of some contact lenses (but see Precautions, above). It has been suggested for use with propamidine isetionate for the treatment of Acanthamoeba keratitis and in spermicides to prevent transmission of HIV infection (p.858).

For pre-operative skin disinfection and hand-washing, chlorhexidine is used as a 0.5% solution of the acetate or gluconate in alcohol (70%) or as a 2 or 4% detergent solution of the gluconate. For disinfection of wounds, burns, or other skin damage or disorders chlorhexidine is used as a 0.05% aqueous solution of the acetate or gluconate, as a tulle dressing impregnated with chlorhexidine acetate 0.5%, or as a cream or powder containing chlorhexidine acetate or gluconate 1%. Preparations containing chlorhexidine acetate or gluconate 0.015% and cetrimide 0.15% are also used for cleansing and disinfection of skin and wounds. In obstetrics, chlorhexidine gluconate is used as a 0.05% aqueous solution or a 1% cream. The cream is also used as a barrier against bacterial hand infection.

Chlorhexidine gluconate is used in a 1% dental gel, 0.2% oral spray, and 0.1 to 0.2% mouthwash for the prevention of plaque and the prevention and treatment of gingivitis and in the treatment of oral candidiasis. A slow-release formulation containing 2.5 mg of chlorhexidine gluconate for insertion into periodontal pockets is also available.

A 0.02% solution may be used as a bladder irrigation in some urinary-tract infections. A gel containing 0.25% chlorhexidine gluconate solution and lidocaine hydrochloride has been used in catheterisation and cystoscopy.

For the emergency disinfection of clean instruments, a 2-minute immersion in chlorhexidine acetate or gluconate 0.5% in alcohol (70%) is used; for the storage and disinfection of clean instruments a 30-minute immersion in a 0.05% aqueous solution containing 0.1% sodium nitrite to inhibit metal corrosion is used.

As an antimicrobial preservative, chlorhexidine is used at a concentration of 0.01% of the acetate or gluconate in eye drops. Solutions containing 0.002 to 0.006% of chlorhexidine gluconate have also been used for disinfection of hydrophilic contact lenses.

Acanthamoeba infections. As discussed on p.822, the optimal antiamoebic therapy for *Acanthamoeba* keratitis has yet to be determined. Propamidine isetionate is commonly used, usually in combinations including a biguanide. A multicentre study[1] evaluated the efficacy of a combination of topical chlorhexidine 0.02% and propamidine 0.1% in 12 contact lens-wearing patients with confirmed *Acanthamoeba* keratitis. Patients were treated for between 2 to 6 months and resolution of signs occurred gradually over 5 to 28 weeks (mean 11 weeks). Resolution of symptoms occurred within 1 to 7 weeks (mean 3 weeks); patients noted a reduction of pain, photophobia and lid oedema after 3 weeks of treatment. No drug toxicity was noted in any of the patients. However, concern has been expressed over the possible toxicity of chlorhexidine at this concentration on the cornea (see Adverse Effects and Treatment, above).

Chlorhexidine is also an effective disinfectant against *Acanthamoeba* cysts and most bacteria found in contact lens storage cases.[2]

Chlorhexidine has also been used to treat skin lesions associated with disseminated *Acanthamoeba* infection[3] as an adjunct to systemic therapy (see p.822).

1. Seal D, *et al.* Successful medical therapy of Acanthamoeba keratitis with topical chlorhexidine and propamidine. *Eye* 1996; **10:** 413–21.
2. Seal DV. Acanthamoeba keratitis. *BMJ* 1994; **308:** 1116–17.
3. Slater CA, *et al.* Brief report: successful treatment of disseminated Acanthamoeba infection in an immunocompromised patient. *N Engl J Med* 1994; **331:** 85–7.

Contraception. Bisbiguanides of the chlorhexidine type are reported to have the ability to diffuse into cervical mucus and render it impenetrable to sperm at concentrations as low as 1 mg/mL.[1] Higher concentrations of chlorhexidine structurally modify the mucus, producing a barrier to both the entry of sperm and chlorhexidine. The potency[1] of chlorhexidine in inhibiting sperm motility *in vitro* is identical to that of nonoxinol 9, but unlike spermicides containing nonoxinol 9, which tend to trickle out, the clearance of chlorhexidine from the vagina is delayed.[2] Chlorhexidine also has potential for reducing transmission of HIV infection as it does not disrupt the vaginal epithelium and has activity *in vitro* against the HIV virus in low concentrations.[2]

For a review of contraception, including the view that spermicides are not a particularly effective method unless used with other means of contraception, see p.2070.

1. Pearson RM. Update on vaginal spermicides. *Pharm J* 1985; **234:** 686–7.
2. Anonymous. Multipurpose spermicides. *Lancet* 1992; **340:** 211–13.

Disinfection. Viable bacterial counts on the hands were reduced by a mean of 97.9% by the application of chlorhexidine gluconate 0.5% in alcohol 95%.[1] The reduction was not so substantial with a 0.5% chlorhexidine aqueous solution (65.1% reduction in bacterial count) or a 4% detergent solution (86.7%). Hand disinfection with chlorhexidine gluconate 4% appeared to be more effective than the use of isopropyl alcohol 60% and soap in preventing nosocomial infections in a study conducted in intensive care units but this may have been partly due to better compliance with hand-washing instructions when using chlorhexidine.[2] In another study,[3] pre-operative total body bathing with a 4% detergent did not decrease the risk of wound infection in patients compared with bathing in detergent alone.

Chlorhexidine 1% nasal cream failed to control an epidemic of meticillin-resistant *Staphylococcus aureus* in a neurosurgical ward[4] and handwashing with chlorhexidine soap failed to control an outbreak of infection with *Staph. aureus* resistant to meticillin and gentamicin in a neonatal intensive care unit.[5] The organisms were subsequently eradicated by the use of nasal mupirocin and hexachlorophene handwashing, respectively.

1. Lowbury EJL, *et al.* Preoperative disinfection of surgeons' hands: use of alcoholic solutions and effects of gloves on skin flora. *BMJ* 1974; **4:** 369–72.
2. Doebbeling BN, *et al.* Comparative efficacy of alternative handwashing agents in reducing nosocomial infections in intensive care units. *N Engl J Med* 1992; **327:** 88–93.
3. The European Working Party on Control of Hospital Infections. A comparison of the effects of preoperative whole-body bathing with detergent alone and with detergent containing chlorhexidine gluconate on the frequency of wound infections after clean surgery. *J Hosp Infect* 1988; **11:** 310–20.
4. Duckworth G. New method for typing Staphylococcus aureus resistant to methicillin. *BMJ* 1986; **293:** 885.
5. Reboli AC, *et al.* Epidemic methicillin-gentamicin-resistant Staphylococcus aureus in a neonatal intensive care unit. *Am J Dis Child* 1989; **143:** 34–9.

INJECTION SITE AND CATHETER CARE. See p.1624.

Endocarditis. Antiseptics applied immediately before dental procedures may reduce postextraction bacteraemia. Chlorhexidine mouthwash or gel may be used as an adjunct to antibacterial prophylaxis in dental patients at risk of bacterial endocarditis.[1,2] The protective cover required for such patients is discussed on p.168.

1. Dajani AS, *et al.* Prevention of bacterial endocarditis: recommendations by the American Heart Association. *JAMA* 1997; **277:** 1794–1801. Also available at: http://circ.ahajournals.org/cgi/content/full/96/1/358 (accessed 07/03/06)
2. Simmons NA, *et al.* Antibiotic prophylaxis and infective endocarditis. *Lancet* 1992; **339:** 1292–3.

Mouth disorders. Chlorhexidine mouthwashes, sprays, and gels are used to prevent accumulation of dental plaque (see Mouth Infections, p.180). Early studies[1-4] generally showed chlorhexidine mouthwash 0.1 to 0.2% used 2 or 3 times daily to be effective in reducing plaque accumulation and gingivitis and provided limited evidence of effectiveness in preventing caries in permanent teeth of children and adolescents. A retrospective review[5] of 22 controlled studies of chlorhexidine for caries prevention, found the evidence inconclusive in schoolchildren and adolescents with active caries and regular fluoride exposure; there was also no good evidence that it arrested root caries in patients with dry mouth and in frail elderly subjects. However, chlorhexidine varnishes showed a preventative effect for fissure caries compared with no treatment in children with low fluoride exposure. Other studies have shown that chlorhexidine reduces gingivitis by 60 to 90% but its use is limited by its unpleasant taste and staining properties; special circumstances in which chlorhexidine is helpful include management of acute gingivitis, control of periodontal involvement in immunocompromised patients, and promotion of healing after periodontal treatment.[6]

Chlorhexidine gluconate may be useful in controlling secondary bacterial infections of aphthous ulcers (see Mouth Ulceration, p.1700). Local application of chlorhexidine has been reported to reduce the incidence[7] and duration and severity[8] of recurrent ulcers, although one study showed no benefit compared with placebo.[9] However, a retrospective review[10] of 7 studies comparing chlorhexidine with placebo or no treatment found no evidence that chlorhexidine prevents oral mucositis in patients receiving cancer treatment.

Chlorhexidine may be a useful adjunct to antifungal treatment of oral candidiasis[11] (p.518).

For the need for a delay when using chlorhexidine with other oral hygiene preparations, see under Precautions, above.

1. Flötra L, *et al.* A 4-month study on the effect of chlorhexidine mouth washes on 50 soldiers. *Scand J Dent Res* 1972; **80:** 10–17.
2. O'Neil TCA, Figures KH. The effects of chlorhexidine and mechanical methods of plaque control on the recurrence of gingival hyperplasia in young patients taking phenytoin. *Br Dent J* 1982; **152:** 130–3.
3. de la Rosa M, *et al.* The use of chlorhexidine in the management of gingivitis in children. *J Periodontol* 1988; **59:** 387–9.
4. O'Neil TCA. The use of chlorhexidine mouthwash in the control of gingival inflammation. *Br Dent J* 1976; **141:** 276–80.
5. Twetman S. Antimicrobials in future caries control: a review with special reference to chlorhexidine treatment. *Caries Res* 2004; **38:** 223–9.
6. Greene JC, *et al.* Preventive dentistry II: periodontal diseases, malocclusion, trauma, and oral cancer. *JAMA* 1990; **263:** 421–5.
7. Hunter L, Addy M. Chlorhexidine gluconate mouthwash in the management of minor aphthous ulceration. *Br Dent J* 1987; **162:** 106–10.
8. Addy M, *et al.* Management of recurrent aphthous ulceration: a trial of chlorhexidine gluconate gel. *Br Dent J* 1976; **141:** 118–20.
9. Matthews RW, *et al.* Clinical evaluation of benzydamine, chlorhexidine, and placebo mouthwashes in the management of recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol* 1987; **63:** 189–91.
10. Worthington HV, *et al.* Interventions for preventing oral mucositis for patients with cancer receiving treatment. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 27/08/08).
11. WHO. *WHO model prescribing information: drugs used in skin diseases*. Geneva: WHO, 1997.

Obstetric use. Disinfection of the birth canal with chlorhexidine gluconate 0.05 to 0.4% during labour has been investigated as a method for reducing mother-to-child transmission of infections, including early-onset group B streptococcal infection and HIV.[1-6] Studies have shown that it has not reduced perinatal transmission of HIV except when membranes were ruptured for more than 4 hours before delivery[1] or if used before the membranes rupture and at higher concentrations.[4] A systematic review of 5 studies[5] to determine the efficacy of chlorhexidine vaginal disinfection for preventing early-onset group B streptococcal infection concluded that, although there was a statistically significant reduction in colonisation there was no significant reduction in early-onset infection, morbidity or mortality. Comparable results have been reported with the use of chlorhexidine gluconate 1% obstetric cream at each examination during labour.[3] A systematic review of 3 studies[6] to determine the efficacy of chlorhexidine vaginal disinfection for preventing perinatal transmission of infections other than group B streptococcal infection and HIV found no evidence to support its use. However, a study[2] conducted in Malawi reported a reduction in neonatal morbidity and mortality from other neonatal infections.

1. Biggar RJ, *et al.* Perinatal intervention trial in Africa: effect of a birth canal cleansing intervention to prevent HIV transmission. *Lancet* 1996; **347:** 1647–50.
2. Taha TE, *et al.* Effect of cleansing the birth canal with antiseptic solution on maternal and newborn morbidity and mortality in Malawi: clinical trial. *BMJ* 1997; **315:** 216–20.
3. Lindemann R, *et al.* Vaginal chlorhexidine disinfection during labour. *Lancet* 1992; **340:** 792.
4. Gaillard P, *et al.* Vaginal lavage with chlorhexidine during labour to reduce mother-to-child HIV transmission: clinical trial in Mombasa, Kenya. *AIDS* 2001; **15:** 389–96.
5. Stade B, *et al.* Vaginal chlorhexidine during labour to prevent early-onset neonatal group B streptococcal infection. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2004 (accessed 15/03/06).
6. Lumbiganon P, *et al.* Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding group B streptococcal and HIV). Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 15/03/06).

Urinary catheter-related infection. Chlorhexidine solutions have been used in the management of catheter-related bladder infections and for urinary catheter maintenance. Twice-daily bladder irrigation with chlorhexidine acetate 0.02% did not produce a reduction in urinary bacterial counts in geriatric patients with indwelling catheters, and there was a tendency for overgrowth of *Proteus* spp. in patients given chlorhexidine.[1] In patients undergoing prostatectomy, intermittent pre-operative bladder irrigation with chlorhexidine gluconate 0.05% reduced the incidence of bacteraemia and severe wound infection, although urinary infections were eradicated in only 3 of the 13 patients treated.[2]

Addition of chlorhexidine to catheter drainage bags was not shown to reduce the frequency of urinary infections,[3] but infection rates were reduced by combining this technique with the use of a catheter lubricant containing chlorhexidine, disinfection of the urethral meatus, and aseptic nursing procedures.[4] The use of lubricating gel containing chlorhexidine did not reduce the risk of urinary-tract infections associated with short-term catheterisation,[5] and in general external disinfection of the periurethral area alone does not seem to be of benefit in reducing the rate of catheter-related bacteriuria.[6,7]

The treatment of urinary-tract infections is discussed on p.199.

1. Davies AJ, *et al.* Does instillation of chlorhexidine into the bladder of catheterized geriatric patients help reduce bacteriuria? *J Hosp Infect* 1987; **9:** 72–5.
2. Adesanya AA, *et al.* The use of intermittent chlorhexidine bladder irrigation in the prevention of post-prostatectomy infective complications. *Int Urol Nephrol* 1993; **25:** 359–67.
3. Gillespie WA, *et al.* Does the addition of disinfectant to urine drainage bags prevent infection in catheterised patients? *Lancet* 1983; **i:** 1037–9.
4. Southampton Infection Control Team. Evaluation of aseptic techniques and chlorhexidine on the rate of catheter-associated urinary-tract infection. *Lancet* 1982; **i:** 89–91.

5. Schiøtz HA. Antiseptic catheter gel and urinary tract infection after short-term postoperative catheterization in women. *Arch Gynecol Obstet* 1996; **258:** 97–100.
6. Webster J, *et al*. Water or antiseptic for periurethral cleaning before urinary catheterization: a randomized controlled trial. *Am J Infect Control* 2001; **29:** 389–94.
7. Koskeroglu N, *et al*. The role of meatal disinfection in preventing catheter-related bacteriuria in an intensive care unit: a pilot study in Turkey. *J Hosp Infect* 2004; **56:** 236–8.

Preparations

BP 2008: Chlorhexidine Irrigation Solution; Chlorhexidine Mouthwash; Lidocaine and Chlorhexidine Gel;
USP 31: Chlorhexidine Gluconate Oral Rinse.

Proprietary Preparations (details are given in Part 3)
Arg.: Antiminth; Biguanex; Bucogel; Elugel; Finaplac; Hexidin; Hexil; Hexil-P; Hibiscrub; Hiboquad†; Laclorhex; Periodil; Pervinox Clorhexidina; Pervinox Incoloro; Plac Out; Strictus†; ***Austral.:*** Anti-Plaque Chewing Gum†; Bactigras; Bush Formula†; Catheter Preparation; Clorhexitulle†; Hexol†; Microshield 2, 4, and 5; Periogard Clorohex†; Plaqacide†; Savacol Mouth and Throat Rinse; ***Austria:*** Chlorhexamed; Plak Out; ***Belg.:*** Astrexine; Baxil; Cedium Chlorhexidine; Corsodyl; Golaseptine; Hansamedic; Hibidil; Hibiguard; Hibiscrub; Hibitane; Medisepta; Mefren; Nolargin; Pixidin; Sterilon; Uro-Tainer†; ***Braz.:*** Asseptic; Glucohex†; Hibitane; Marclorhex; Merthiolate†; Noplak; ***Canad.:*** Bactigras; Baxedin; Hibidil; Hibitane; Peridex†; Spectro Gram; Stanhexidine; ***Chile:*** AB; Agermin†; Bucoseptil; Freshmel; Garonsept; Graneodin; Hibicrick†; Hibiscrub†; Oralgene; Ortoxine; Peridentt†; Perio-Aid; Periokin; Perioxidin†; ***Cz.:*** Corsodyl; Hibiscrub†; Septofort; ***Denm.:*** Hibitane; Periochip; ***Fin.:*** Corsodyl; Klorhexol; Travahex; ***Fr.:*** Biorgasept; Collunovar; Corsodyl; Dermachrome; Diaseptyl; Dosiseptine; Elgydium; Eluge; Euraxsepti; Exoseptoplix†; Hibidil; Hibiscrub; Hibisprint; Hibitane; Paroex; Plurexid; Prexidine; Septeal; Septiapaisyl; Septivon; ***Ger.:*** Bactigras†; Cathejell S; Chlorhexamed; CHX Dental Gel; Cidegol C; Dentosmin P; Frubilurgyl†; Gurgellosung Chauvin†; Hansamed Spray†; Lemocin CX; Nur 1 Tropfen Chlorhexidin; Periogard Chlorohex†; Trachisan N†; ***Gr.:*** Hibitane; Periochip; ***Hong Kong:*** Bactigras†; Corsodyl; Hexol†; Hibiscrub†; Hibitane†; Hydrex; Qualikin; Scanlin; ***Hung.:*** Septofort; ***India:*** Orinse; ***Indon.:*** Mediscrub; ***Irl.:*** Corsodyl; Hibiscrub; Hibitane; ***Israel:*** Alcoxidine; Bactoscrub; Bactosept; Cleardent; Corsodyl; Medident; Periochip; Pharma-Dentix; Septadine Scrub; Septal; Septalone; Septol; Tarodent; Uniscrub†; Unisept†; ***Ital.:*** Benodent; Benodent CLX; Broxodin; Clarifex; Clomirex; Clorosan; Corsodyl; Dempol; Dentosan Clorexidina; Dentosan Parodontale; Eburos; Ekuba; Esoform Mani; Golasan; Iodosan Clorexidina; Lenil; Master-Aid; Neo Perginol†; Neo-Destomygen; Neomercurocromo; Neoxene; Neoxinal; Parodontax; Periogard Chlorohex; Plak Out; Sicura 3; Triseptil; ***Malaysia:*** Antibex†; Antisol†; Baby Shield Plus; Bactigras; Hibiscrub†; Hibisol†; Hibitane†; Oradex†; Sepsol†; ***Mex.:*** Hibiscrub†; Perioxidin; ***Neth.:*** Chlorhexamed; Corsodyl; Hibiscrub; Hibitane; Hydrex; Irrisol; Lifo-Scrub; Periochip; Sterilon; Urogliss-S; ***Norw.:*** Corsodyl; Hibiscrub; Hibitane; Periochip; ***NZ:*** DP Hand Rub; Hibitane; Riotane; ***Philipp.:*** Bactigras; Orahex; ***Pol.:*** Septofervex; ***Port.:*** Bexident; Cloraldin; Corsodyl; Dialens; Handscrub; Hibitane; Lifo-Scrub; Periochip; Plak Out†; ***Rus.:*** Elgydium (Эльгидиум); Elugel (Элюгель); Hexicon (Гексикон); Intim (Интим)†; ***S.Afr.:*** Bactigras; Corsodyl; D-Germ; Hexidin; Hibidil†; Hibiscrub; Hibitane; Orosept; ***Singapore:*** Acnederm Wash; Baby Shield Plus; Chlorohex; Elgydium; Elugel; Hexodane Mouthwash; Hexoscrub; Pfizer Obstetric Lotion†; ***Spain:*** Clorxil†; Cristalcrom; Cristalmina; Curafil; Cuvefilm; Deratin; Hibimax; Hibiscrub; Menalmina; Septisan; ***Swed.:*** Cervitec†; Corsodyl; Descutan; Hexident; Hibiscrub; Hibitane; Periochip; ***Switz.:*** Chlorhexamed; Chlorohex†; Corsodyl; Dentohexine; Hibidil; Hibiscrub; Hibitane; Lifo-Scrub; Periochip; Plak Out; ***Thai.:*** Bacard Antiseptic; Bactigras; C-20; Chlorhex; Desmanol G†; Hexene; Hexide; Hexol†; Hibiscrub†; Hibitane†; Hidine†; Hydrex; Q-Bac; ***Turk.:*** Cloder; Disinfecting; Klorheksol; Klorhex; Mediscrub; Oroheks; ***UAE:*** Zordyl; ***UK:*** Acriflex; Bactigras; Cepton; Chlorohex; Corsodyl; Curasept; CX Powder; Elgydium; Hibiscrub; Hibitane; Hydrex; Savlon Antiseptic Wound Wash; Serotulle; Spotoway; Steripod Chlorhexidine Gluconate; Unisept; Uriflex C; ***USA:*** Betasept; Dyna-Hex; Exidine; Hibiclens; Hibistat; Peridex; Periochip; Periogard; ***Venez.:*** Peridont.

Multi-ingredient: ***Arg.:*** Antiseptic Plus; Buclorhex; Consil; Dexatopic†; Drill; Elgydium; Elgydium Dientes Sensibles; Elgyfluor†; Eludril; Fluorexidina†; Hexil Antiseptico; Instillagel; Merthiolate NF; Odontobiotic†; Parodium; Periobacter; Periobacter Prof Avio; Periodent; Periodil; ***Austral.:*** Acnederm Foaming Wash; Curacleanse†; Difflam-C; Hamilton Body Lotion†; Hamilton Cleansing Lotion†; Hemocane; Medi Creme; Medi Pulv; Microshield Antiseptic; Microshield Handrub; Microshield Tincture; Mycil Healthy Feet; Nasalate; Oralife Peppermint; Paraderm Plus; Pro-PS†; Savlon Antiseptic; Seda-Gel†; Silvazine; Soov Cream; Xylocaine Jelly with Chlorhexidine; ***Austria:*** Bepanthen Plus; Cathejell; Cathejell mit Lidocain; Dermaspray; Endosgel; Instillagel; Skinsept mucosa; Uromont; Vitawund; ***Belg.:*** Angiocine; Cathejell; Cetavlex; Dermaspray†; Eludril; HAC; Hacdil-S; Hibitane; Instillagel; Medica; Neo-Cutigenol; Neo-Golaseptine; Nestosyl; Sabenyl; Vita-Mefren†; ***Braz.:*** Effaclar; ***Canad.:*** Avagard CHG; Baxedin 2% - 70%; Flamazine C†; Savlodil; Spectro Tar†; ***Chile:*** AB Antitusivo; Cariax; Endogel Esteril; Freshmel Tos; Graneodin N†; Graneodin-Tos; Halita; Medisept†; Oralgene; Orthokin; Perio-Aid c Cloruro de Cetilpiridinio; ***Cz.:*** Bepanthen Plus; Cyteal; Drill; Hexoral; Hexoraletten N; Hibicet Hospital Concentrate†; Instillagel; N-Septonex†; Skinsept mucosa†; ***Denm.:*** Hexokain; Instillagel; ***Fin.:*** Duocort; Sibicort; Toncils; ***Fr.:*** Alco-Aloe; Aphtoral; Biseptine; Cantalene; Chlorisprayt; Collu-Blache†; Collustan†; Cyteal; Dacryne; Dermaspraid Antiseptique; Dermobacter; Drill; Elgydium Dents Sensibiles; Elgyfluor†; Eludril; Instillagel; Mercryl; Mercrylsoins; Nostril; Parodium; Parogencyl sensibilite gencives; Paroplak; Posine†; Spitaderm†; Thiovalone; ***Ger.:*** Bepanthen Antiseptische; Cathejell mit Lidocain; Desmanol†; Endosgel; Hermalind†; Hexoraletten N; Instillagel; Nystalocal; Skinsept F; Skinsept mucosa; Trachisan†; Uro-Stilloson†; ***Gr.:*** Hibicet; Instillagel; Octrene; Trachisan; ***Hong Kong:*** Acnederm Wash; Dermobacter; Difflam-C; Hibicet Hospital Concentrate†; Hibisol†; Instillagel; Medicreme; Medipulv†; Mycil; Oragesic; Pilelife; Soov Cream; Trachisan†; ***Hung.:*** Alkcema; Alksebor; Bepanthen Plus; Drill; Instillagel; Vita-Merfen†; ***India:*** Argisept†; Burnheal†; Iteol-3; Silverex; ***Indon.:*** Dexatopic; Neo Resiguard; Pravlon; Spitaderm; ***Irl.:*** Alltracel S†; Hibicet; Hibisol; Instillagel; Mycil; Naseptin; Nystaform-HC†; Nystaform†; Savlon; ***Israel:*** Alcosept; Bepanthen Plus; Cathejell; Cetrin; Instillagel†; Merfen; Neocutan Silver; Savior; Septacare†; Septadine; Sterets H; Tisept; Travasept; V-Tabur; Vita-Merfen NF; ***Ital.:*** Bactigras; Baxidin; Benodent; Benodent Gel Gengivale†; Biopatch; Cetrexidin; Cetrisan; Citroclorex; Citromed; Citromed 80 and 85; Citromed Chirurgico; Citromedics Pronto; Citrosteril Pronto; Clorexan; Clorexan Ferri; Clotramid†; Cuprosodio Plus; Decon Lavanda; Dentaton; Dentosan Azione Intensiva; Dentosan Mese; Dentosan Placca & Carie; Disinfene; Eso Ferri Plus; Eso S 80; Esosan Pronto; Farvicett; Handexin; Hibizene; Neo-Stomygen; Neogyn; Ninfagin; Panseptil; Parogencyl Gengive Delicate; Rexichlor; Sicura3 Medical; Simp; Simpottantacinque; Spitaderm; Steridol†; Videorelax†; ***Malaysia:*** Acnederm Foaming Wash; Cathejell with Lidocaine; Difflam-C; Elan-Forte; Hibicet†; Horf; Oral-Aid; Trachisan†; ***Mex.:*** Instillagel†; Perioxidin; ***Neth.:*** Dexatopic†; Endosgel; Hibicet concentraat; Hibicet verdunning; Hibisol; Instillagel; Spitaderm; Urogliss; ***Norw.:*** Bacimycin; ***NZ:*** Acnederm Foaming Wash; Acnederm Wash†; Conditioning Solution†; Difflam-C; Egomycol†; Medicreme; Medipulv; Oralife Peppermint; Paraderm Plus; Savlon; Silvazine; Soov Cream; Xylocaine with Chlorhexidine†; ***Philipp.:*** Cathejell; ***Pol.:*** Bepanthen Plus; Sebidin; ***Port.:*** Alkagin; Alphacedre; Bepanthene; Bepanthene Plus; Biofluor Plus†; Biofluor Prevencao†; Cathejell; Cyteal; Drill; Eludril; Hibitane Menta†; Hibitane†; Instillagel; Lactigriet; Lubrificante Anestesico; ***Rus.:*** Bepanthen Plus (Бепантен Плюс); Cathejell with Lidocaine (Катеджель С Лидокаином)†; Cyteal (Цитеал); Drill (Дрилл); Elgyfluor (Эльгифлуор); Eludril (Элюдрил); Lysoplac (Лизоплак); Metrogyl Denta (Метрогил Дента); Parodium (Пародиум); Sebidin (Себидин); ***S.Afr.:*** Andolex-C; Cathejell with Lidocaine; Germolene; Hibicet†; Naseptin; Orochlor; ***Singapore:*** Cyteal; Difflam-C; Elgyfluor; Eludril; Hexodane Handrub; Oral-Aid; Savlon†; Silvazine; Silvin; Soov Cream; Trachisan; ***Spain:*** Angileptol; Bucodrin; Bucometasana; Bucospray; Drill; Eludril; Faringesic; Gargaril; Garydol; Hibitane; Mastiol; Menalcol; Mercryl Plus; ***Swed.:*** Instillagel; ***Switz.:*** Antebor N; Bepanthene Plus; Collu-Blache; Collunosol-N; Eludril; Eubucal†; Galamila; Gleitmittel†; Hibital; Hibitane Teinture; Lidohex†; Merfen; Nystacortone†; Nystalocal; Trachisan†; Vita-Hexin; Vita-Merfen; ***Thai.:*** Bacard; Cathejell with Lidocaine; Chlorhex-C; Dekka; Frebac; Hibicet†; Inhibac; Sepdine†; Septone†; ***Turk.:*** Bepanthene Plus; Dervanol; Gleitgelen; Hemoralgine; Kloroben; Pantenol Plus; Savlex; Savonol; Savrolin; Setilin; ***UK:*** Cathejell with Lidocaine; ChloraPrep; Clearasil Pore Cleansing Lotion; Covonia Throat Spray; Cyteal; Dermol; Eludril; Germolene; Germoloids†; Hibicet†; Hibisol; Instillagel; Medi-Swab H; Medi-Wipe; Mycil; Naseptin; Nystaform; Nystaform-HC; Quinoderm Antibacterial Face Wash; Savlon Antiseptic Cream; Savlon Antiseptic Liquid; Sterets H; Steripod Chlorhexidine Gluconate with Cetrimide†; Tisept; Torbetol; Travasept; ***USA:*** BactoShield; Fresh-N-Free.

Chlorinated Lime

Bleaching Powder; Cal clorada; Calcaria Chlorata; Calcii Hypochloris; Calcium Hypochlorite; Calcium Hypochlorosum; Calx Chlorata; Calx Chlorinata; Chloride of Lime; Chlorkalk; Chlorure de Chaux; Cloruro de Cal; Desmanche.
CAS — 7778-54-3.

Pharmacopoeias. In *Br.* and *Jpn*.
BP 2008 (Chlorinated Lime). A dull white powder with a characteristic odour, containing not less than 30.0% w/w of 'available chlorine'. It becomes moist and gradually decomposes on exposure to air, carbon dioxide being absorbed and chlorine evolved. Partly soluble in water and in alcohol.

Adverse Effects, Treatment, and Precautions
As for Sodium Hypochlorite, p.1661.

Uses and Administration
Chlorinated lime is a disinfectant and antiseptic with the general properties of chlorine (p.1638).

Its action is rapid but brief, the 'available chlorine' soon being exhausted by combination with organic material. It is used to disinfect faeces, urine, and other organic material, and as a cleansing agent for lavatories, drains, and effluents.

Chlorinated lime is used in the preparation of Surgical Chlorinated Soda Solution (BPC 1973) (Dakin's Solution) which has been employed as a wound disinfectant, and Chlorinated Lime and Boric Acid Solution (BP 1993), (Eusol), which has been used as a disinfectant lotion and wet dressing, sometimes with equal parts of liquid paraffin. However, such solutions are irritant when applied undiluted, and are no longer recommended for use in this way. In addition, there is some evidence that such chlorine-releasing solutions may delay wound healing (see Disinfection, Wounds under Uses and Administration of Sodium Hypochlorite, p.1662).

Preparations
BPC 1973: Surgical Chlorinated Soda Solution.

Chlorine

925; Chlor; Chlore; Chlorium; Cloro; Klor.
Хлор
Cl_2 = 70.906.
CAS — 7782-50-5.

Description. Chlorine is a greenish-yellow gas with a suffocating odour; commonly available as a pressurised liquid.

Adverse Effects and Treatment
Chlorine gas is irritant and corrosive producing inflammation, burns, and necrosis. Inhalation may result in coughing, choking, headache, dyspnoea, dizziness, expectoration of frothy white sputum (which may be blood stained), a burning chest pain, and nausea. Bronchospasm, laryngeal oedema, acute pulmonary oedema with cyanosis, and hypoxia may occur. There may be vomiting and development of acidosis. Death may result from hypoxia.

Some of the toxicity of chlorine may be due to its dissolution in tissue water to produce hydrochloric acid and hypochlorite. After exposure to chlorine, conjunctivitis may require a topical anaesthetic and frequent irrigations of water or saline. Respiratory distress should be treated with inhalations of humidified oxygen and bronchodilators; mechanical ventilation may be required. Corticosteroids have been given in an attempt to minimise pulmonary damage but their benefit is unproven. Acidosis may require the intravenous use of sodium bicarbonate or other suitable alkalising agent.

◊ Experience gained from 186 cases of acute chlorine exposure indicated that medical support was required for only a short time even when exposure was repeated;[1] late sequelae were not seen, even in patients with abnormal respiratory function tests or blood gases on admission. Thirteen children who were accidentally exposed to chlorine products and gas at a community swimming pool complained of eye and throat irritation, chest pain and tightness, shortness of breath, wheezing, and anxiety and 5 children with hypoxia required hospital admission. These children received humidified oxygen, salbutamol, and, in 4 patients, methylprednisolone, and all were discharged 1 to 2 days later.[2] Another report on 76 children with chlorine poisoning revealed that the longest period of hospitalisation was 12 hours after treatment with oxygen and corticosteroids.[3] A 14-year-old boy with a history of asthma exposed to chlorine gas developed acute respiratory distress syndrome and required intubation, ventilatory support, salbutamol, and corticosteroids. He was extubated after 19 days and recovered well.[4] There have been reports of deliberate inhalation of chlorine,[5,6] in one instance for pleasure,[5] leading to severe adverse effects. Some individuals may be unduly insensitive to chlorine-induced irritation and workers should be warned that concentrations of chlorine which can be tolerated for short periods without undue discomfort can still cause serious injury which may not be immediately apparent.[6]

Guidelines[7,8] have been issued for the management of chlorine exposure.

1. Barret L, Faure J. Chlorine poisoning. *Lancet* 1984; **i:** 561–2.
2. Sexton JD, Pronchik DJ. Chlorine inhalation: the big picture. *Clin Toxicol* 1998; **36:** 87–93.
3. Fleta J, *et al*. Intoxication of 76 children by chlorine gas. *Hum Toxicol* 1986; **5:** 99–100.
4. Traub SJ, *et al*. Case report and literature review of chlorine gas toxicity. *Vet Hum Toxicol* 2002; **44:** 235–9.
5. Rafferty P. Voluntary chlorine inhalation: a new form of self-abuse? *BMJ* 1980; **281:** 1178–9.
6. Dewhurst F. Voluntary chlorine inhalation. *BMJ* 1981; **282:** 565–6.
7. Department of Health. Chlorine: guidelines for action in the event of a deliberate release (issued February 2004). Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947362398 (accessed 27/08/08)
8. Agency for Toxic Substances and Disease Registry. Medical management guidelines (MMGs) for chlorine (Cl). Available at: http://www.atsdr.cdc.gov/MHMI/mmg172.html (accessed 15/03/06)

Effects on the eyes. Eye examinations of 50 subjects immediately before and after swimming in a chlorinated pool (chlorine range 1.0 to 1.5 ppm) showed that 68% had symptoms of corneal oedema and 94% had corneal epithelial erosions. No subject had a measurable decrease in visual acuity.[1]

1. Haag JR, Gieser RG. Effects of swimming pool water on the cornea. *JAMA* 1983; **249:** 2507–8.

Precautions
The antimicrobial activity of chlorine disinfectants is reduced by the presence of organic material and by increasing pH. Hypochlorite solutions may delay wound healing (see Disinfection: Wounds under Uses and Administration of Sodium Hypochlorite, p.1662).

Uses and Administration
Chlorine is a disinfectant with a rapid potent brief bactericidal action. It is capable of killing most bacteria, and some fungi, yeasts, algae, viruses, and protozoa. It is slowly active against spores.

It is used for the treatment of water (p.1623), but for most other purposes it is used in the form of hypochlorites, organic and inorganic chloramines, chlorinated hydantoins, chlorinated isocyanurates, and similar oxidising compounds capable of releasing chlorine. In the presence of water these compounds produce hypochlorous acid (HOCl) and hypochlorite ion (OCl^-) and it is generally considered that the lethal action on micro-organisms is due to chlorination of cell protein or enzyme systems by nonionised hypochlorous acid, although the hypochlorite ion may also contribute.

The activity of most of the compounds decreases with increase of pH, the activity of solutions of pH 4 to 7 being greater than those of higher pH values. However, stability is usually greater at an alkaline pH.

The potency of chlorine disinfectants is expressed in terms of **available chlorine**. This is based on the concept of chlorine gas (Cl_2) as the reference substance. Two atoms of chlorine (2 × Cl) yield in water only one