rence in industrial wastes as well as its use as a fungicide; its use is banned in some countries.

Hexachlorobenzene is reported to be distributed into breast milk. ♦ References.

- 1. WHO. Hexachlorobenzene. Environmental Health Criteria 195. Geneva: WHO, 1997. Available at: http://www.inchem.org/documents/ehc/ehc/ehc195.htm (accessed 26/04/04)
- 2. WHO. Hexachlorobenzene health and safety guide. *IPCS Health and Safety Guide 107*. Geneva: WHO, 1998. Available at: http://www.inchem.org/documents/hsg/hsg/hsg107.htm (accessed

Toxicity. Porphyria cutanea tarda1 and parkinsonism2 have both been reported in subjects who had ingested seed crops treated with hexachlorobenzene. In a further report the symptoms of porphyria in some patients have been said to persist for many years.

- Cam C, Nigogosyan G. Acquired toxic porphyria cutanea tarda due to hexachlorobenzene. JAMA 1963; 183: 88–91.
- Chapman LJ, et al. Parkinsonism and industrial chemicals. Lancet 1987; i: 332–3.
- 3. Cripps DJ, et al. Porphyria turcica due to hexachlorobenzene: a 20 to 30 year follow-up study on 204 patients. *Br J Dermatol* 1984; **111:** 413–22.

Hydrocyanic Acid

Cianhídrico, ácido; Prussic Acid. CAS - 74-90-8.

HC≡N

Description. Hydrocyanic acid is an aqueous solution containing hydrogen cyanide, HCN = 27.03. A colourless liquid with a characteristic almond odour.

Adverse Effects and Precautions

Hydrocyanic acid and its vapour are intensely poisonous. Cyanides interfere with the oxygen uptake of cells by inhibition of cytochrome oxidase, an enzyme necessary for cellular oxygen transport.

Poisoning by cyanides may occur from inhalation of the vapour, ingestion, or absorption through the skin. Poisoning may arise from cyanide pesticides, industrial accidental exposure, or the inhalation of fumes from some burning plastics. Poisoning may also occur from cyanide-containing plants or fruits.

When large doses of hydrocyanic acid are taken, unconsciousness occurs within a few seconds and death within a few minutes. With smaller toxic doses the symptoms, which occur within a few minutes, may include constriction of the throat, nausea, vomiting, giddiness, headache, palpitation, hyperpnoea then dyspnoea, bradycardia (although initially there may be tachycardia), unconsciousness, and violent convulsions, followed by death. The characteristic smell of bitter almonds may not be obvious and not all individuals can detect it. Cyanosis is not prominent. Similar but usually slower effects occur with cyanide salts.

The fatal dose of hydrocyanic acid for man is considered to be about 50 mg and of the cyanides about 250 mg.

Treatment of Adverse Effects

Treatment must be given rapidly but should not involve the use of antidotes unless it is certain that cyanide has been absorbed and poisoning is severe.

Cyanide is absorbed very rapidly on inhalation and the poisoned patient should be removed from the area and given oxygen. Steps should be taken to ensure that the airway is adequate. Contaminated clothing should be removed and skin washed. If the patient is conscious, amyl nitrite may be inhaled for up to 30 seconds in every minute but the value of this practice is questionable. Should the patient be unconscious or nearly so, then in the UK and some other countries it is the practice to give dicobalt edetate (p.1443) by injection since it forms a stable complex with the cyanide ion. However, cyanide poisoning should be confirmed, as absence of cyanide puts the patient at risk from the adverse effects of dicobalt edetate. The recommended dose of dicobalt edetate is 300 mg given intravenously over about 1 to 5 minutes, depending on the severity of the poisoning, and repeated once or twice depending on the response. It is customary to give 50 mL of glucose 50% intravenously after each injection. In the USA cyanide antidote kits containing amyl nitrite, sodium nitrite, and sodium thiosulfate are available. After the use of inhaled amyl nitrite, 10 mL of sodium nitrite injection (3%) is given intravenously over 5 to 20 minutes, then, using the same needle and vein, an injection of 12.5 g of sodium thiosulfate (50 mL of a 25% solution or 25 mL of a 50% solution) is given over a period of about 10 minutes. The nitrite components from amyl nitrite and sodium nitrite convert haemoglobin to methaemoglobin which competes with cytochrome oxidase for cyanide, with the formation of cyanmethaemoglobin; sodium thiosulfate acts as a sulfur donor and aids the conversion or inactivation of cyanide from cyanmethaemoglobin to thiocyanate. If toxic symptoms recur, the injections of nitrite and thiosulfate may be repeated at half the initial doses. Appropriate measures should be instituted to correct hypotension and acidosis. The methaemoglobinaemia

induced by the nitrites in the antidote kits can be dangerous and fatalities have been reported.

Hydroxocobalamin may be used for the management of cyanide toxicity. The usual dose is 70 mg/kg by intravenous infusion, repeated once or twice according to severity. Alternatively, hydroxocobalamin 5 g may be given by intravenous infusion over 15 minutes, followed if necessary by a second dose of 5 g intravenously, infused over 15 minutes to 2 hours.

If cyanide has been ingested, one of the above procedures should be used. Activated charcoal or gastric lavage may be considered if the patient presents within 1 hour.

◊ Some references concerning the management of cyanide poisoning. 1-4 The use of solutions A and B (15.8% ferrous sulfate in 0.3% citric acid, and 6% sodium carbonate respectively) as so called oral antidotes in persons exposed to cyanide has been condemned as ineffective and lacking scientific evidence.

- Langford RM, Armstrong RF. Algorithm for managing injury from smoke inhalation. BMJ 1989; 299: 902-5.
- 2. Koizumi A. Fighting myths. Lancet 1994; 344: 559-60.
- 3. Proudfoot A, ed. Pesticide poisoning: notes for the guidance of medical practitioners. 2nd ed. London: DoH, The Stationery Office, 1996.
- 4. Geller RJ, et al. Pediatric cyanide poisoning: causes, manifestations, management, and unmet needs. Pediatrics 2006; 118: 2146-58

Uses

Cyanides have various industrial applications. Hydrocyanic acid and cyanide salts produce hydrogen cyanide, which has been used as a gas for the eradication of rabbits, rodents, and some other pests. Cyanide salts that might be encountered include calcium cyanide, mercuric cyanide, potassium cyanide, potassium ferricyanide, potassium sodium cyanide, and sodium cyanide.

Preparations

Proprietary Preparations (details are given in Part 3) Multi-ingredient: Spain: Oftalmol Ocular.

Imidacloprid

Bay-NTN-33893. I-[(6-Chloro-3-pyridinyl)methyl]-4,5-dihydro-N-nitro-1H-imidazol-2-amine. $C_9H_{10}CIN_5O_2 = 255.7.$

CAS — 105827-78-9; 138261-41-3. ATC Vet — QP53AX17.

Imidacloprid is used as a topical ectoparasiticide in veterinary practice, and as an insecticide in agriculture. It has also been investigated for use in the treatment of head lice.

lodofenphos (BAN)

lodofenfós; Jodfenphos. O-2,5-Dichloro-4-iodophenyl O,O-dimethyl phosphorothioate.

 $C_8H_8Cl_2IO_3PS = 413.0.$ CAS - 18181-70-9.

Iodofenphos is an organophosphorus insecticide (p.2047) used in veterinary practice for the control of ectoparasites in the environment. It has also been used as an agricultural insecticide. It is an effective mosquito larvicide.

Iodopropynyl Butyl Carbamate

3-lodo-2-propynyl-N-butyl carbamate. $C_8H_{12}INO_2 = 281.1.$ CAS — 55406-53-6.

Iodopropynyl butyl carbamate is a carbamate pesticide (p.2037). It is used as a preservative in cosmetic preparations; contact sensitisation has been reported. It is also used as a wood preserva♦ References.

- 1. Bryld LE, et al. Iodopropynyl butylcarbamate: a new contact al-
- lergen. Contact Dermatitis 1997; **36:** 156–8.

 2. Badreshia S, Marks JG. Iodopropynyl butylcarbamate. Am J Contact Dermat 2002; 13: 77-9.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Arg.: Pityval†; Saliker†; Braz.: Effaclar; Pityval; Saliker; Fr.: Effaclar; Pityval; Saliker†; Irl.: Effaclar; Effaclar Al; Effaclar K.

Lindane (BAN, USAN, rINN)

666; Benhexachlor; Gamma Benzene Hexachloride; Gamma-BHC: Gamma-HCH: HCH: Hexicide: Lindaani: Lindan: Lindan: Lindanas; Lindano; Lindanum. Ια, 2α, 3β, 4α, 5α, 6β-Hexachlorocyclohexane

Линдан

 $C_6H_6CI_6 = 290.8.$ CAS - 58-89-9. ATC - P03AB02.ATC Vet — QP53AB02; QS02QA01.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Int.*, and *US.* **Ph. Eur. 6.2** (Lindane). A white or almost white crystalline powder. Practically insoluble in water; soluble in dehydrated alcohol; freely soluble in acetone. Protect from light.

USP 31 (Lindane). A white, crystalline powder with a slight musty odour. Practically insoluble in water; soluble in dehydrated alcohol; freely soluble in chloroform; sparingly soluble in ether; slightly soluble in ethylene glycol.

Adverse Effects, Treatment, and Precautions

As for Chlorinated Insecticides, p.2037.

Serious adverse effects, including seizures and deaths, have been reported in patients who have used higher than recommended concentrations of lindane, or after a second application of lindane to the skin in the treatment of scabies and pediculosis: lindane should not be used as a first-line treatment in the management of the latter conditions. Babies, children, the elderly and people weighing less than 50 kg are considered to be particularly at risk. Lindane should not be used in patients who have a body-weight less than 50 kg, a history of epilepsy, have open or crusted sores on the skin around the head and neck or broken skin around the treatment areas, or skin conditions such as psoriasis or atopic dermatitis. Lindane is excreted into the breast milk but the amount excreted is not considered to be clinically significant; breastfeeding should, however, be avoided for at least 4 days after stopping treatment. There is limited human data on the use of lindane in pregnancy and animal data indicate a low risk for congenital defects, but because of its serious toxic potential safer alternative products are recommended.

♦ Seizures have been reported after the topical use of lindane. In reply, one of the manufacturers stated that up to the end of 1983 they were aware of 21 cases of convulsive disorders apparently associated with the use of their product; it had been used by over 40 million people. Of the 21 cases, the seizures were definitely or probably caused by the product in 11, but in 9 the seizures were associated with ingestion or excessive use.² From 1998 to 2003, 870 cases of unintentional lindane ingestion were reported in the USA.3 Signs and symptoms of illness after ingestion included abdominal cramps, confusion, cough, headache, nausea, oral irritation, seizures, and vomiting.

Isolated reports of adverse effects associated with lindane include disseminated intravascular coagulation and subsequent death after oral ingestion4 and aplastic anaemia after prolonged topical exposure (twice daily application for 3 weeks).

- Etherington JD. Major epileptic seizures and topical gammaben-zene hexachloride. BMJ 1984; 289: 228.
- Kelly VT. Major epileptic seizures and topical gammabenzene hexachloride. BMJ 1984; 289: 837.
- CDC. Unintentional topical lindane ingestions—United States, 1998–2003. MMWR 2005; 54: 533–5. Also available at: http:// www.cdc.gov/mmwr/preview/mmwrhtml/mm5421a2.htm (accessed 22/04/08)
- 4. Rao CVSR, et al. Disseminated intravascular coagulation in case of fatal lindane poisoning. Vet Hum Toxicol 1988; 30: 132-4.
- Rauch AE, et al. Lindane (Kwell)-induced aplastic anemia. Arch Intern Med 1990; 150: 2393–5.

Uses and Administration

Lindane is a chlorinated insecticide (p.2037). It has been used topically in a concentration of 1% for scabies (p.2035) in selected patients and has also been used in pediculosis (p.2034), but use for head lice is restricted by resistance.

The symbol † denotes a preparation no longer actively marketed

Lindane has been used for the control of disease vectors including mosquitoes, lice, and fleas, but resistance has developed. It has also been used as an agricultural and a horticultural insecticide, but its use is prohibited or restricted in many countries.

♦ References.

- WHO, Lindane. Environmental Health Criteria 124. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/ehc/ehc/ehc/l24.htm (accessed 26/04/04)
 WHO, Lindane health and safety guide. IPCS Health and Safety Guide 54. Geneva: WHO, 1991. Available at: http://
- www.inchem.org/documents/hsg/hsg/hsg054.htm (accessed

Preparations

USP 31: Lindane Cream; Lindane Lotion; Lindane Shampoo.

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Arg.: Gamma-Scab; Heaz-Defital; Austria: Jacutin; Braz.: Escabron†; Pediletan; Pilensar; Canad.: Hexit; Chile: Plomurol; Scabexyl†; Cz.: Jacutin†; Skabicid†; Fr.: Scabecid†; Ger.: Delitex N; InfectoPedicul; Jacutin; Hung.: Jacutin; India: Ascabio!; Gab; Nit-N-Mrite; Scaboma; Indon.: Obat Kutu Rambut Cap Dua Jempol; Irl.: Quellada†; Israel: Bicide; Malaysia: Jacutin; Mex.: Herklin; NZ: Benhex; Pol.: Jacutin; Port.: Musside†; Sarcoderma†; S.Afr.: Gambex; Quellada†; Singopore: Jacutin; Switz.: Jacutin; Thol.: Jacutin; Venez.: Demar†; Somergan.

Multi-ingredient: Arg.: Gamma-Scab; Hexa-Defital; Lyndan; Fr.: Elenol; India: Emscab; Nit-N-Mite†; Scabine; Scaboma; Scarab; Indon.: Scabicid; Topicide; Mex.: Herklin; Spain: Yacutin.

Lufenuron (BAN rINN)

CGA-184699; Lufenurón; Lufénurone; Lufenuronum. 1-[2,5-Dichloro-4-(1,1,2,3,3,3-hexafluoropropoxy)phenyl]-3-(2,6-dif-(RS)-N-[2,5-Dichloro-4-(1,1,2,3,3,3-hexluorobenzovl)urea: afluoropropoxy)phenylcarbamoyl]-2,6-difluorobenzamide.

Луфенурон

 $C_{17}H_8Cl_2F_8N_2O_3 = 511.2.$ CAS — 103055-07-8. ATC Vet - QP53BC01

Profile

Lufenuron is used as a systemic ectoparasiticide in veterinary practice; it is given by mouth or injection to the host animal

Malathion (BAN)

Carbofos; Compound 4047; Malathionum; Malatión; Malation; Malationas; Malationi; OMS-1. Diethyl 2-(dimethoxyphosphinothioylthio)succinate.

 $C_{10}H_{19}O_6PS_2 = 330.4.$ CAS - 121-75-5. ATC - PO3AXO3.ATC Vet - QP53AF12.

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

Ph. Eur. 6.2 (Malathion). A clear, colourless or slightly yellowish liquid. It freezes at about 3°. Slightly soluble in water; miscible with alcohol, with acetone, with cyclohexane, and with vegetable oils. Store in airtight containers. Protect from light.

USP 31 (Malathion). A clear, colourless, or slightly yellowish liquid with a characteristic odour. Congeals at about 2.9°. Slightly soluble in water; miscible with alcohols, with ethers, with esters, with ketones, with aromatic and alkylated aromatic hydrocarbons, and with vegetable oils. Store in airtight containers. Protect from light.

Stability. The manufacturers have reported that malathion is sensitive to heat and is degraded at temperatures above 30°.

Adverse Effects and Treatment

As for Organophosphorus Insecticides, p.2047.

Malathion is one of the safer organophosphorus insecticides but its toxicity may be increased by the presence of impurities

Acute renal insufficiency has been described in a patient associated with excessive exposure to a malathion spray. The condition resolved without specific treatment. Renal toxicity had not previously been associated with organophosphorus pesticides. In a second case of acute poisoning,2 due to ingestion of malathion, mild transient renal insufficiency and proteinuria with several other late complications including cardiac arrhythmias, pulmonary oedema, diffuse interstitial fibrosis, and muscle weakness due to peripheral neuropathy, were seen subsequent to recovery from the initial cholinergic toxicity.

- Albright RK, et al. Malathion exposure associated with acute re-nal failure. JAMA 1983; 250: 2469.
- 2. Dive A, et al. Unusual manifestations after malathion poisoning. Hum Exp Toxicol 1994; 13: 271-4.

Uses and Administration

Malathion is an organophosphorus insecticide (p.2047). It is used in the treatment of head and pubic pediculosis (p.2034) and in scabies (p.2035); lotions of 0.5% and shampoos of 1% are commonly available. Lotions are generally preferred to shampoos as the contact time is longer. Aqueous lotions are preferred to treat pubic lice and scabies because alcoholic lotions are irritant to excoriated skin and the genitalia; aqueous lotions may also be preferable in asthmatic subjects or children to avoid alcoholic fumes. Skin or hair treated with an alcohol-based preparation should be allowed to dry naturally.

Malathion is also used in veterinary practice, agriculture, and horticulture. It is widely used for adult and larval mosquito control although resistance occurs.

Preparations

USP 31: Malathion Lotion

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Austral: Lice Rid†, Belg: Prioderm; Radika!, Denm:: Prioderm; Fin.: Prioderm; Fr.: Prioderm; Fr.: Prioderm; Fr.: Sicarils Specifibril; Irl.: Derbac-Nt; Prioderm; Quellada Mt; Israel: Prioderm; Ital.: Aftir Gel; Neth.: Noury Hoofdlotion; Prioderm; Norw.: Prioderm; Norw.: Prioderm; Norw.: Prioderm; Port.: Olide†; Rus.: Pædlin (Tle_Auwh); Singapore: A-Lices; Lice Care; Swed.: Prioderm; Switz.: Lusap†; Prioderm; UK: Derbac-Nt; Prioderm; Quellada Mt; Suleo-M†; USA: Ovide.

Multi-ingredient: Arg.: Aero Helpp Forte†; Para Plus; Belg.: Para Plus; Fr.: Para Plus; Gr.: Para-plus; Israel: Para Plus; NZ: Para Plus; Rus.: Para Plus (Παρα Πλιος).

Metaldehyde

Metaldehído.

 $(C_2H_4O)_x$ CAS - 9002-91-9.

Description. Metaldehyde is a cyclic polymer of acetaldehyde.

Adverse Effects and Treatment

Symptoms of poisoning by metaldehyde, which may be delayed, include vomiting and diarrhoea, fever, drowsiness, convulsions, and coma. Death from respiratory failure may occur within 48 hours. Kidney and liver damage may occur.

Treatment is symptomatic, although activated charcoal may be considered if more than 50 mg/kg has been ingested within the preceding hour.

♦ References

- Longstreth WT, Pierson DJ. Metaldehyde poisoning from slug bait ingestion. West J Med 1982; 137: 134–7.
- 2. Proudfoot A, ed. Pesticide poisoning: notes for the guidance of medical practitioners. 2nd ed. London: DoH, The Stationery Office, 1996.
- 3. Bleakley C, et al. Self-poisoning with metaldehyde. Emerg Med J 2008; 25: 381-2.

Uses

Metaldehyde is a molluscicide used in pellets against slugs and snails. It is an ingredient of some firelighters.

'Meta' is compressed metaldehyde which has been used as a solid fuel burning with a non-luminous carbon-free flame.

Methomyl

 $Metomilo. \ S-Methyl \ \textit{N-} (methylcarbamoyloxy) thio acetimidate.$ $C_5H_{10}N_2O_2S = 162.2$ CAS — 16752-77-5.

Methomyl is a carbamate insecticide (p.2037) that has been used in agriculture.

◊ References.

- 1. WHO. Methomyl health and safety guide. IPCS Health and Safety Guide 97. Geneva: WHO, 1995. Available at: http:// www.inchem.org/documents/hsg/hsg/hsg097.htm (accessed
- WHO. Methomyl. Environmental Health Criteria 178. Geneva: WHO, 1996. Available at: http://www.inchem.org/documents/ehc/ehc/ehc178.htm (accessed 26/04/04)

- ♦ Reports of poisoning with methomyl and its management.
- Martinez-Chuecos J, et al. Management of methomyl poisoning. Hum Exp Toxicol 1990; 9: 251–4.
- Buchholz U, et al. An outbreak of food-borne illness associated with methomyl-contaminated salt. JAMA 2002; 288: 604–10.

Methoprene (rINN)

Méthoprène; Methoprenum; Metopreno; ZR-515. Isopropyl 11methoxy-3,7,11-trimethyldodeca-2(E),4(E)-dienoate.

Метопрен $C_{19}H_{34}O_3 = 310.5.$ CAS — 40596-69-8.

ATC Vet — QP53BD01

Profile

Methoprene is an insect growth regulator which mimics the action of insect juvenile hormones and, if it is applied at the appropriate period of sensitivity, it causes death by preventing the transformation of larva to pupa. It is used against a variety of insects including fleas and mosquitoes. It is used in veterinary practice for the control of ectoparasites in the environment, rather than being applied to the animals themselves. It is also used in agriculture

Preparations

Proprietary Preparations (details are given in Part 3) Multi-ingredient: Fr.: Aspipur

Methoxychlor

Methoxy-DDT; Metoksychlor; Metoxicloro. I,I,I-Trichloro-2-2bis(p-methoxyphenyl)-ethane.

 $C_{16}H_{15}CI_3O_2 = 345.6.$ CAS - 72-43-5.

Methoxychlor is a chlorinated insecticide (p.2037) used in agriculture, horticulture, and veterinary practice.

Methyl Bromide

Metilo, bromuro de. Bromomethane; Monobromomethane $CH_3Br = 94.94.$ CAS — 74-83-9.

Adverse Effects, Treatment, and Precautions

Methyl bromide is a vesicant. Toxic effects after inhalation or percutaneous absorption are mainly due to neurotoxicity and include dizziness, headache, vomiting, blurred vision, weakness, ataxia, confusion, mania, hallucinations, mental depression, convulsions, pulmonary oedema, and coma. Renal and hepatic toxicity may also occur and death may be due to circulatory collapse or respiratory failure. Onset of symptoms may be preceded by a latent period. Concentrations of 1% or more are irritant to the eyes. Treatment is symptomatic although dimercaprol or acetylcysteine therapy has been tried.

Rubber absorbs and retains methyl bromide and should not therefore be used in protective clothing.

- ◊ References to toxicity of methyl bromide including reports of poisoning.
- 1. Chavez CT, et al. Methyl bromide optic atrophy. Am J Ophthalmol 1985; **99:** 715–19.

 2. Langard S, et al. Fatal accident resulting from methyl bromide
- poisoning after fumigation of a neighbouring house: leakage through sewage pipes. *J Appl Toxicol* 1996; **16:** 445–8.
- 3. De Haro L, et al. Central and peripheral neurotoxic effects of chronic methyl bromide intoxication. *J Toxicol Clin Toxicol* 1997; **35:** 29–34. 4. Michalodimitrakis MN, et al. Death following intentional me-
- thyl bromide poisoning: toxicological data and literature review. Vet Hum Toxicol 1997; **39:** 30–4.
- 5. Horowitz BZ, et al. An unusual exposure to methyl bromide leading to fatality. J Toxicol Clin Toxicol 1998; 36: 353-7.