zyme values, and there have been some reports of nephrotic syndrome. Nervousness and, sometimes, hallucinations, have also been reported.

Intolerance. Three patients with nephropathic cystinosis developed fever, maculopapular eruption, leucopenia, or headache within 2 weeks of starting mercaptamine at doses of 53, 67, and 75 mg/kg daily by mouth, respectively.[1] These adverse effects resolved within 48 hours of drug withdrawal and all 3 patients were able to tolerate mercaptamine when restarted at a dose of 10 mg/kg daily, slowly increased to therapeutic levels over 2 to 3 months. Higher doses of mercaptamine had been associated with lethargy and seizures.

1. Schneider JA, *et al.* Cysteamine therapy in nephropathic cystinosis. *N Engl J Med* 1981; **304:** 1172.

Pharmacokinetics

◊ Results of a pharmacokinetic-pharmacodynamic study[1] in paediatric patients with nephropathic cystinosis showed that although mercaptamine is rapidly cleared from plasma, dosing every 6 hours was sufficient to maintain the content of cystine in the white blood cells below the target value (see below).

1. Belldina EB, *et al.* Steady-state pharmacokinetics and pharmacodynamics of cysteamine bitartrate in paediatric nephropathic cystinosis patients. *Br J Clin Pharmacol* 2003; **56:** 520–5.

Uses and Administration

Mercaptamine reduces intracellular cystine levels and is given orally as the bitartrate in the treatment of cystinosis (see below); it has also been given as the hydrochloride. Doses are expressed in terms of the base; 2.94 g of the bitartrate or 1.47 g of the hydrochloride are each equivalent to 1 g of mercaptamine. Mercaptamine bitartrate is given in an initial dose that is one-sixth to one-quarter of the expected maintenance dose, and is then increased gradually over 4 to 6 weeks. The usual maintenance dose in adults weighing over 50 kg is 2 g daily in 4 divided doses with or after food. Children up to 12 years of age are given 1.3 g/m^2 (approximately 50 mg/kg) daily in 4 divided doses. Doses are given in conjunction with monitoring of leucocyte-cystine levels which should be kept below 1 nanomol of hemicystine per mg of protein.

Phosphocysteamine, a phosphorothioester of mercaptamine, has been said to be more palatable, and is used similarly.

Mercaptamine facilitates glutathione synthesis and was formerly used intravenously in the treatment of severe paracetamol poisoning to prevent hepatic damage, but other forms of treatment are now preferred (see p.108).

Cystinosis. Mercaptamine and phosphocysteamine (which appears to be rapidly hydrolysed to mercaptamine after ingestion) have been reported to be of benefit in children with cystinosis, a rare autosomal recessive metabolic disorder characterised by the intracellular accumulation of cystine. Cystinosis is marked by growth retardation, rickets, Fanconi syndrome, and renal failure; acute episodes of acidosis and dehydration may develop, and there may be photophobia associated with deposition of cystine in the eye.[1] Use of mercaptamine, which results in a reduction in the concentrations of cystine in leucocytes, has been shown to be effective in controlling many of the symptoms,[2-5] especially if begun early, although it has not been clear from contradictory results[4,6] how much benefit would be seen on renal function. Excellent clinical outcomes were reported[7] on long-term follow-up of 2 siblings with severe nephropathic cystinosis, reinforcing the need for early and diligent treatment in order to avoid progressive renal disease. Compliance may be a problem, because of the taste and odour of mercaptamine, and the more palatable prodrug phosphocysteamine has been developed as an alternative;[8,9] more palatable formulations of mercaptamine are also being investigated. Mercaptamine eye drops are reportedly of benefit in reversing or preventing deposition of corneal cystine crystals.[10] A strength of 0.11% has been used. Renal transplantation may be necessary if renal failure develops.

1. Gahl WA, *et al.* Cystinosis. *N Engl J Med* 2002; **347:** 111–21.
2. Yudkoff M, *et al.* Effects of cysteamine therapy in nephropathic cystinosis. *N Engl J Med* 1981; **304:** 141–5.
3. Gahl WA, *et al.* Cysteamine therapy for children with nephropathic cystinosis. *N Engl J Med* 1987; **316:** 971–7.
4. Reznik VM, *et al.* Treatment of cystinosis with cysteamine from early infancy. *J Pediatr* 1991; **119:** 491–3.
5. Gahl WA, *et al.* Nephropathic cystinosis in adults: natural history and effects of oral cysteamine therapy. *Ann Intern Med* 2007; **147:** 242–50.
6. Markello TC, *et al.* Improved renal function in children with cystinosis treated with cysteamine. *N Engl J Med* 1993; **328:** 1157–62.
7. Kleta R, *et al.* Long-term follow-up of well-treated nephropathic cystinosis patients. *J Pediatr* 2004; **145:** 555–60.
8. Gahl WA, *et al.* Cystinosis: progress in a prototypic disease. *Ann Intern Med* 1988; **109:** 557–69.
9. van't Hoff WG, *et al.* Effects of oral phosphocysteamine and rectal cysteamine in cystinosis. *Arch Dis Child* 1991; **66:** 1434–7.
10. Kaiser-Kupfer MI, *et al.* A randomized placebo-controlled trial of cysteamine eye drops in nephropathic cystinosis. *Arch Ophthalmol* 1990; **108;** 689–93.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Cystagon; ***Belg.:*** Cystagon; ***Cz.:*** Cystagon; ***Denm.:*** Cystagon; ***Fin.:*** Cystagon; ***Fr.:*** Cystagon; ***Ger.:*** Cystagon; ***Ital.:*** Cystagon; ***Neth.:*** Cystagon; ***Pol.:*** Cystagon; ***Port.:*** Cystagon; ***Spain:*** Cystagon; ***Swed.:*** Cystagon; ***UK:*** Cystagon.

Mercuric Chloride

Bicloruro de Mercurio; Chlorid rtut'natý; Cloreto Mercúrico; Corrosive Sublimate; Gyvsidabrio dichloridas; Higany(II)-klorid; Hydrarg. Perchlor.; Hydrargyri dichloridum; Hydrargyri Perchloridum; Hydrargyrum Bichloratum; Kvicksilverdiklorid; Mercuric Chlor.; Mercúrico, cloruro; Mercurique (Chlorure); Mercurique, chlorure; Mercury Bichloride; Mercury Perchloride; Merkuridikloridi; Quecksilberchlorid; Rtęci(II) chlorek.

$HgCl_2$ = 271.5.
CAS — 7487-94-7.
ATC — D08AK03.
ATC Vet — QD08AK03.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Mercuric Chloride). A white or almost white, crystalline powder, or colourless or white or almost white crystals or heavy crystalline masses. Soluble in water and in glycerol; freely soluble in alcohol. Protect from light.

Profile

The use of mercuric chloride as an antibacterial substance is limited by its toxicity, its precipitating action on proteins, its irritant action on raw surfaces, its corrosive action on metals, and by the fact that its activity is greatly reduced in the presence of excreta or body fluids.

Details of the adverse effects of inorganic mercury compounds are provided under Mercury, below.

Preparations

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

Yellow Mercuric Oxide

Gelbes Quecksilberoxyd; Hydrargyri Oxidum Flavum; Hydrargyri Oxydum Flavum; Mercúrico amarillo, óxido; Mercurique (Oxyde) Jaune; Oxido Amarillo de Mercurio; Yellow Precipitate.

HgO = 216.6.
CAS — 21908-53-2.

Pharmacopoeias. In *Fr.* and *It.*

Profile

Yellow mercuric oxide has been used in eye ointments for the local treatment of minor infections including the eradication of pubic lice from the eyelashes. Absorption can occur and produce the adverse effects of inorganic mercury (see Mercury, below).

Pediculosis. Yellow mercuric oxide 1% eye ointment was considered to be a safe and effective treatment in pediculosis (p.2034) of the eyelashes caused by pubic lice (pthiriasis palpebrarum).[1]

1. Ashkenazi I, *et al.* Yellow mercuric oxide: a treatment of choice for phthiriasis palpebrarum. *Br J Ophthalmol* 1991; **75:** 356–8.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Golden Eye Ointment†; ***Fr.:*** Pommade Maurice.
Multi-ingredient: ***Hung.:*** Dermaforine†; ***India:*** Bell Diono Resolvent; Bell Resolvent.

Mercurous Chloride

Calomel; Calomelanos; Cloreto Mercuroso; Hydrarg. Subchlor.; Hydrargyri Subchloridum; Hydrargyrosi Chloridum; Hydrargyrum Chloratum (Mite); Mercureux (Chlorure); Mercurioso, cloruro; Mercurius Dulcis; Mercury Monochloride; Mercury Subchloride; Mild Mercurous Chloride; Protocloruro de Mercurio; Quecksilberchlorür.

HgCl = 236.0; Hg_2Cl_2 = 472.1.
CAS — 7546-30-7 (HgCl); 10112-91-1 (Hg_2Cl_2).

NOTE. Precipitated Mercurous Chloride (Hydrargyri Subchloridum Praecipitatum), is a white amorphous powder, for which the synonym 'White Precipitate' (Praecipitatum Album) has been used. White Precipitate has also been used as a name for Ammoniated Mercury.

Pharmacopoeias. In *Chin.* as Hg_2Cl_2.

Profile

Mercurous chloride was formerly given as a laxative and was applied topically as an antibacterial. It was one of the mercury compounds employed in the management of syphilis in the pre-antibiotic era.

The mercurous form of mercury does not possess the corrosive properties of the mercuric form and is not absorbed to any great extent. However, the mercurous form can be converted to the mercuric, with consequent toxicity as described under Mercury (see below).

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Hung.:*** Dermaforine†.

Mercury

Hydrarg.; Hydrargyrum; Hydrargyrum Depuratum; Mercure; Mercurio; Quecksilber; Quicksilver; Rtęć.

Hg = 200.59.
CAS — 7439-97-6.
ATC — D08AK05.

Description. Mercury is a shining, silvery white, very mobile liquid, easily divisible into globules, which readily volatilises on heating.

Adverse Effects

Poisoning with liquid mercury or inorganic mercury salts has arisen from sources such as batteries, cosmetics, dental materials, medical equipment, and jewellery manufacture. Barometers, sphygmomanometers, and thermometers are still sources of liquid mercury. Trace amounts of organic and inorganic mercury may also be ingested in the diet.

The effects of **acute** exposure depend on the nature of the compound.

- *Elemental (liquid) mercury* if ingested is poorly absorbed and, unless there is aspiration or pre-existing gastrointestinal disorders, is not considered to be a severe toxicological hazard. The greatest dangers from elemental mercury arise from the inhalation of mercury vapour, which can cause gastrointestinal effects including nausea, vomiting, and diarrhoea; more importantly it is toxic to the respiratory system and this effect can be fatal. Some CNS involvement has also been reported. Adverse effects have also been reported after accidental or intentional parenteral dosage.
- *Inorganic salts* such as mercuric chloride are corrosive when ingested causing severe nausea, vomiting, pain, bloody diarrhoea, and necrosis. The kidney is also involved and tubular necrosis may develop. Mercurous salts are considered to be less hazardous, but the mercurous form can be converted to the mercuric.
- *Organic mercurial compounds* produce similar toxic effects to inorganic compounds, but they have a more selective action on the CNS that has proved difficult to treat. The degree of toxicity varies; those used as preservatives or disinfectants are less toxic than the ethyl or methyl compounds that are not used pharmaceutically or clinically. Methylmercury is notorious for its toxicity; there have been cases of fetal neurotoxicity during outbreaks of methylmercury poisoning.

Chronic mercury poisoning may result from inhalation of mercury vapour, skin contact with mercury or mercury compounds, or ingestion of mercury salts over prolonged periods. It is characterised by many symptoms including tremor, motor and sensory disturbances, mental deterioration, gastrointestinal symptoms, dermatitis, kidney damage, salivation, and gingivitis. A blue line may be present on the gums. There is little difference between acute and chronic poisoning with organic mercurials.

The syndrome of *acrodynia* (pink disease), with symptoms of sweat, rash, erythema of the extremities, photophobia, wasting, weakness, hypertension, tachycardia, and diminished reflexes, occurred in children given mercury in teething powders or in ointments or dusting powders. Such preparations have long since been withdrawn from use. However, the syndrome is still a feature of mercury poisoning from other sources.

Hypersensitivity to mercury and mercurial compounds has been reported.

Mercurialentis has been reported in patients treated with eye drops containing an organomercurial preservative.

Chronic exposure. Acute *occupational exposure* to mercury vapour in 53 men resulted in an initial phase described as metal fume fever, an intermediate phase of severe symptoms with CNS, gastrointestinal, respiratory, and urological involvement, and a late phase with persistent CNS symptoms, dysuria, and pain on ejaculation.[1,2] Although persistent hyperchloraemia was noted in the 11 patients with the highest mercury levels, renal impairment tended to be temporary.[2]

Long-term follow-up of a patient who had an intravenous *injection* of mercury 12 years previously also revealed no persistent renal impairment,[3] despite the presence of mercury microemboli in lungs, kidneys, liver, and subcutaneous tissues and high concentrations in the urine. At this time, the patient had residual reductions in respiratory function, polyneuropathy, and marked asthenozoospermia. Spermatozoal abnormalities may also have contributed to his wife's miscarriage. Mercury deposits mimicking gallbladder cancer were found in the gallbladder of a patient 35 years after he had injected himself with elemental mercury.[4]

Fetal neurotoxicity after *maternal exposure* to methylmercury is well recognised, and there has been widespread concern about the effect of maternal diets on the developing fetus because of mercury concentrations in freshwater and marine organisms. Results from a study in the Faroe Islands showed an association between delays in neurological development in children and maternal consumption of pilot whale meat.[5] Follow-up studies of this population when they reached 14 years of age suggest that the neurotoxic effects of methylmercury might compromise brain development into the teenage years,[6] as well as affecting autonomic regulation of heart function.[7] However, data from a study conducted in a fish-consuming population in the Seychelles failed to find a similar connection.[8]