Fuller's Earth

Terra Fullonica; Tierra de Fuller.

CAS — 8031-18-3.

Profile

Fuller's earth consists largely of montmorillonite, a native hydrated aluminium silicate, with which very finely divided calcite (calcium carbonate) may be associated. It is an adsorbent and has been used in dusting powders, toilet powders, and lotions. Fuller's earth of high adsorptive capacity has been used in industry as a clarifying and filtering medium.

It has been used in the treatment of paraquat poisoning (p.2047), usually as a 15% suspension given in an initial oral dose of about 100 g, followed by further doses of about 50 g every 2 hours for 3 doses. Purgatives such as magnesium sulfate or mannitol have been given at the same time to promote emptying of the gut, but some suggest they should only be given with the first dose.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Camomila.

Glucagon *(BAN, rINN)*

Gliukagonas; Glucagón; Glucagonum; Glukagon; Glukagoni; HGF. His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr.

Глюкагон

$C_{153}H_{225}N_{43}O_{49}S$ = 3482.7.

CAS — 16941-32-5.

ATC — H04AA01.

ATC Vet — QH04AA01.

Pharmacopoeias. In *US*.

USP 31 (Glucagon). A polypeptide hormone obtained from porcine and bovine pancreas glands. A fine, white or faintly coloured, practically odourless, crystalline powder. Soluble in dilute alkali and acid solutions; insoluble in most organic solvents. Store under nitrogen in airtight glass containers at a temperature of 2° to 8°.

Adverse Effects

Nausea and vomiting may occur after use of glucagon. Hypersensitivity reactions, abdominal pain, hypotension, tachycardia, and hypokalaemia have also been reported.

Precautions

Glucagon should generally not be given to patients with phaeochromocytoma since it can cause a release of catecholamines producing marked hypertension. Glucagon should be given with care to patients with insulinoma as it may induce hypoglycaemia due to its insulin-releasing effect. Glucagon was formerly used to diagnose phaeochromocytoma and insulinoma but this use has been largely abandoned. Caution is also required when it is being used as a diagnostic aid in diabetic patients or in elderly patients with heart disease.

Glucagon is not effective in patients with marked depletion of liver glycogen stores, as in starvation, adrenal insufficiency, alcohol-induced hypoglycaemia, or chronic hypoglycaemia. Oral carbohydrates should be given after glucagon to prevent the development of secondary hypoglycaemia.

Interactions

Warfarin. For a report of glucagon enhancing the anticoagulant effect of warfarin, see p.1431.

Pharmacokinetics

Glucagon has a plasma half-life of about 3 to 6 minutes but longer values have been reported in diabetics (see Bioavailability, below). It is inactivated in the liver, kidneys, and plasma.

Bioavailability. In a study[1] in healthy subjects and diabetic patients the bioavailability of glucagon given intranasally was about 30% of that after intramuscular injection. However, the mean value for the apparent half-life after intramuscular injection was 28.6 and 31.4 minutes respectively in the two groups, compared with 6.6 and 11.9 minutes for intravenous infusion, and 5.5 and 13.8 minutes when given intranasally, possibly due to slow release of glucagon from the injection site.

1. Pontiroli AE, *et al.* Pharmacokinetics of intranasal, intramuscular and intravenous glucagon in healthy subjects and diabetic patients. *Eur J Clin Pharmacol* 1993; **45:** 555–8.

Uses and Administration

Glucagon is an endogenous polypeptide hormone that is produced by the alpha cells of the pancreatic islets of Langerhans. It is a hyperglycaemic that mobilises glucose by activating hepatic glycogenolysis. It can to a lesser extent stimulate the secretion of pancreatic insulin. Glucagon for therapeutic use may be derived from animal sources but is now more commonly produced using recombinant DNA techniques. It is given as the hydrochloride, but doses are usually expressed as glucagon (note that 1 unit is equivalent to 1 mg of glucagon).

Glucagon is used in the treatment of severe hypoglycaemic reactions when the patient cannot take glucose by mouth and intravenous glucose is not feasible. It is given by subcutaneous, intramuscular, or intravenous injection in a dose of 1 mg (or 500 micrograms in patients under about 25 kg body-weight). If there is no response within 10 minutes, intravenous glucose should be given, although there is no contra-indication to repeating the dose of glucagon. Once the patient has responded sufficiently to take carbohydrate orally this should be given to restore liver glycogen stores and prevent secondary hypoglycaemia.

As glucagon reduces the motility of the gastrointestinal tract it is used as a diagnostic aid in gastrointestinal examinations. The route of administration and dose is dependent upon the diagnostic procedure. A dose of 1 to 2 mg intramuscularly has an onset of action of 4 to 15 minutes and a duration of effect of 10 to 40 minutes; 0.2 to 2 mg intravenously produces an effect within 1 minute that lasts for 5 to 25 minutes.

Glucagon possesses positive cardiac inotropic activity but is not generally considered suitable for heart failure. However, as it can bypass blocked beta receptors, it is used in the treatment of beta-blocker overdosage, see Cardiovascular Effects, below.

Intranasal preparations have been studied.

Cardiovascular effects. Glucagon has chronotropic and inotropic effects due to its ability to raise cyclic AMP concentrations independently of a response to catecholamines.[1] It is used in the management of beta-blocker overdosage (p.1227), although evidence of benefit is mainly anecdotal;[2] doses of 2 to 10 mg (or 50 to 150 micrograms/kg in children) by intravenous injection, followed by an infusion of 50 micrograms/kg per hour, have been suggested.

Glucagon may also have a role in anaphylactic shock (see under Adrenaline, p.1205), particularly in patients receiving beta blockers, in whom adrenaline may be less effective. A dramatic improvement in refractory hypotension during an anaphylactic reaction to contrast media was described in a 75-year-old man receiving beta blockers after intravenous glucagon.[3]

There has also been a report[4] of benefit with intravenous glucagon following calcium-channel blocker overdosage, but evidence from controlled studies is not available[2] and glucagon is not generally regarded as standard treatment for such patients.

1. White CM. A review of potential cardiovascular uses of intravenous glucagon administration. *J Clin Pharmacol* 1999; **39:** 442–7.
2. Bailey B. Glucagon in β-blocker and calcium channel blocker overdoses: a systematic review. *J Toxicol Clin Toxicol* 2003; **41:** 595–602.
3. Zaloga GP, *et al.* Glucagon reversal of hypotension in a case of anaphylactic shock. *Ann Intern Med* 1986; **105:** 65–6.
4. Walter FG, *et al.* Amelioration of nifedipine poisoning associated with glucagon therapy. *Ann Emerg Med* 1993; **22:** 1234–7.

Diagnosis and testing. Glucagon stimulates secretion of growth hormone and cortisol (hydrocortisone) and has been used as a test of pituitary function in adults,[1-3] and in children.[4,5] It may be particularly suitable when first-line tests such as the insulin-tolerance test are contra-indicated.[3] The glucagon stimulation test should be used with caution in young children;[5] severe secondary hypoglycaemia and death has been reported[6] in a 2-year-old child after a glucagon test for growth hormone secretion.

1. Gómez JM, *et al.* Growth hormone release after glucagon as a reliable test of growth hormone assessment in adults. *Clin Endocrinol (Oxf)* 2002; **56:** 329–34.
2. Abs R. Update on the diagnosis of GH deficiency in adults. *Eur J Endocrinol* 2003; **148:** S3–S8.
3. Ho KKY. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia. *Eur J Endocrinol* 2007; **157:** 695–700. Also available at: http://www.ghresearchsociety.org/files/2007_Consensus_AGHD.pdf (accessed 18/07/08)
4. Hindmarsh PC, Swift PGF. An assessment of growth hormone provocation tests. *Arch Dis Child* 1995; **72:** 362–8.
5. GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *J Clin Endocrinol Metab* 2000; **85:** 3990–3. Also available at: http://www.ghresearchsociety.org/files/Eilat.pdf (accessed 04/10/05)
6. Shah A, *et al.* Hazards of pharmacologic tests of growth hormone secretion in childhood. *BMJ* 1992; **304:** 173–4.

Gastrointestinal disorders. The relaxant effect of glucagon on smooth muscle has been used to facilitate passage of swallowed foreign bodies[1] and impacted food boluses[2] that have become lodged in the lower oesophagus. However, a controlled trial[3] in children with impacted oesophageal coins found that glucagon was not effective.

1. Cooke MW, Glucksman EE. Swallowed coins. *BMJ* 1991; **302:** 1607.
2. Farrugia M, *et al.* Radiological treatment of acute oesophageal food impaction. *Br J Hosp Med* 1995; **54:** 410–11.
3. Mehta D, *et al.* Glucagon use for esophageal coin dislodgment in children: a prospective, double-blind, placebo-controlled trial. *Acad Emerg Med* 2001; **8:** 200–3.

Hypoglycaemia. Hypoglycaemia most commonly occurs in diabetic patients, particularly those receiving insulin therapy. Other rare causes include alcohol ingestion and tumours such as insulinomas. Neonatal hypoglycaemia occurs in small-for-gestational-age infants or infants of diabetic mothers. Persistent or recurrent hypoglycaemia in neonates is usually due to an endocrine or metabolic disorder, such as nesidioblastosis.

Glucose is the treatment of choice for **acute** hypoglycaemia since it corrects the problem at source. In patients who are unconscious or unable to take glucose orally, it may need to be given intravenously. Glucagon is an alternative in such situations, and first-line use has been suggested[1] since it is more convenient and easier to give than parenteral glucose, particularly in emergency situations. However, glucagon has a slower onset and may not always be effective, particularly where hepatic glycogen stores are depleted, such as in patients with alcohol-induced hypoglycaemia or with insulinoma. Low doses of glucagon have also been given prophylactically[2] in diabetic children at risk of developing hypoglycaemia due to gastrointestinal disorders or reduced oral intake.

Hypoglycaemia in neonates is usually managed by adjusting the enteral feeds or by giving parenteral glucose in symptomatic infants. Glucagon may be used if parenteral glucose is not effective or cannot be given.[3,4] In infants with persistent hyperinsulinaemic hypoglycaemia,[5] continuous infusion of glucagon has been used, although oral treatments such as diazoxide or chlorothiazide are usually preferred.

Intractable hypoglycaemia (such as that resulting from excessive endogenous insulin production from islet cell tumours or hyperplasia) is usually treated with diazoxide, but continuous infusion of glucagon has been used in patients with tumour-associated hypoglycaemia.[6,7]

1. Gibbins RL. Treating hypoglycaemia in general practice. *BMJ* 1993; **306:** 600–1.
2. Haymond MW, Schreiner B. Mini-dose glucagon rescue for hypoglycemia in children with type 1 diabetes. *Diabetes Care* 2001; **24:** 643–5.
3. Carter PE, *et al.* Glucagon for hypoglycaemia in infants small for gestational age. *Arch Dis Child* 1988; **63:** 1264.
4. Williams AF. Hypoglycaemia of the newborn: a review. *Bull WHO* 1997; **75:** 261–90.
5. Aynsley-Green A, *et al.* Practical management of hyperinsulinism in infancy. *Arch Dis Child Fetal Neonatal Ed* 2000; **82:** F98–F107.
6. Samaan NA, *et al.* Successful treatment of hypoglycemia using glucagon in a patient with an extrapancreatic tumor. *Ann Intern Med* 1990; **113:** 404–6.
7. Hoff AO, Vassilopoulou-Sellin R. The role of glucagon administration in the diagnosis and treatment of patients with tumor hypoglycemia. *Cancer* 1998; **82:** 1585–92.

Liver disorders. For references to the use of glucagon with insulin in the treatment of liver disorders, see under Insulin, p.452.

Preparations

USP 31: Glucagon for Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: GlucaGen; ***Austral.:*** GlucaGen; ***Austria:*** GlucaGen; ***Belg.:*** GlucaGen; ***Braz.:*** GlucaGen; ***Cz.:*** GlucaGen; ***Denm.:*** GlucaGen; ***Fin.:*** GlucaGen; ***Fr.:*** GlucaGen; ***Ger.:*** GlucaGen; ***Gr.:*** GlucaGen; ***Hong Kong:*** GlucaGen; ***Hung.:*** GlucaGen; ***India:*** GlucaGen; ***Irl.:*** GlucaGen; ***Israel:*** GlucaGen; ***Ital.:*** GlucaGen; ***Malaysia:*** GlucaGen; ***Neth.:*** GlucaGen; ***NZ:*** GlucaGen; ***Pol.:*** GlucaGen; ***Port.:*** GlucaGen; ***Rus.:*** GlucaGen (Глюкаген); ***S.Afr.:*** GlucaGen; ***Singapore:*** GlucaGen; ***Spain:*** GlucaGen; ***Switz.:*** GlucaGen; ***Turk.:*** GlucaGen; ***UK:*** GlucaGen; ***USA:*** GlucaGen.

Glucarpidase *(rINN)*

Carboxypeptidase G_2; Glucarpidasa; Glucarpidasum.

Глюкарпидаз

CAS — 9074-87-7.

ATC — V03AF09.

ATC Vet — QV03AF09.

Profile

Glucarpidase is a recombinant glutamate carboxypeptidase that hydrolyses methotrexate to inactive metabolites; it is under investigation for the management of methotrexate toxicity.

◊ References.

1. Widemann BC, *et al.* Carboxypeptidase-G2, thymidine, and leucovorin rescue in cancer patients with methotrexate-induced renal dysfunction. *J Clin Oncol* 1997; **15:** 2125–34.
2. Widemann BC, *et al.* Treatment of accidental intrathecal methotrexate overdose with intrathecal carboxypeptidase G2. *J Natl Cancer Inst* 2004; **96:** 1557–9.
3. Buchen S, *et al.* Carboxypeptidase G2 rescue in patients with methotrexate intoxication and renal failure. *Br J Cancer* 2005; **92:** 480–7.

Glutathione *(BAN)*

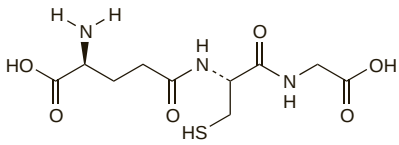
Glutathion; Glutathionum; Glutatión; Glutation; Glutationas; Glutationi; GSH. *N*-(*N*-L-γ-Glutamyl-L-cysteinyl)glycine.

$C_{10}H_{17}N_3O_6S$ = 307.3.

CAS — 70-18-8.

ATC — V03AB32.

ATC Vet — QV03AB32.



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

Ph. Eur. 6.2 (Glutathione). Fermentation product. A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; very slightly soluble in alcohol and in dichloromethane. Protect from light.

Profile

Glutathione is an endogenous peptide with antoxidant and other metabolic functions. Glutathione and glutathione sodium are used to prevent neurotoxicity associated with cisplatin or oxaliplatin; they have also been used to prevent other adverse effects of antineoplastic and radiation therapy, as well as in a wide range of other disorders including poisoning with heavy metals and other compounds, liver disorders, corneal disorders, and eczema. Glutathione has also been tried in idiopathic pulmonary fibrosis and peripheral vascular disorders.

Antineoplastic toxicity. Glutathione has been reported to reduce the incidence of neurotoxicity induced by cisplatin therapy. In a double-blind, randomised trial[1] in 50 patients receiving cisplatin for advanced gastric cancer, glutathione significantly reduced the incidence of neuropathy assessed within one week of completing cisplatin therapy. There did not appear to be any reduction in cytotoxic activity. Similar benefit was observed in a randomised, double-blind, placebo-controlled trial involving 52 patients receiving oxaliplatin.[2]

1. Cascinu S, *et al.* Neuroprotective effect of reduced glutathione on cisplatin-based chemotherapy in advanced gastric cancer: a randomized double-blind placebo-controlled trial. *J Clin Oncol* 1995; **13:** 26–32.
2. Cascinu S, *et al.* Neuroprotective effect of reduced glutathione on oxaliplatin-based chemotherapy in advanced colorectal cancer: a randomized, double-blind, placebo-controlled trial. *J Clin Oncol* 2002; **20:** 3478–83.

Lung disorders. Glutathione is an important extracellular antoxidant in the lung and high concentrations are found in lung epithelial lining fluid. A deficiency of glutathione may contribute to the epithelial damage that occurs in various lung disorders, and treatment with nebulised glutathione has therefore been investigated. Small studies have found beneficial biochemical results in patients with cryptogenic fibrosing alveolitis (idiopathic pulmonary fibrosis)[1] and in cystic fibrosis,[2] but the clinical effects of these changes are not clear. Another study in cystic fibrosis[3] found no effect on oxidative markers after treatment for 2 weeks, but there was a small improvement in lung function. Benefit has also been reported[4] in a patient with emphysema. However, in a study[5] of patients with mild asthma, inhalation of glutathione solution was associated with bronchoconstriction, leading to cough or breathlessness in some patients, possibly due to sulfite formation.

1. Borok Z, *et al.* Effect of glutathione aerosol on oxidant-antioxidant imbalance in idiopathic pulmonary fibrosis. *Lancet* 1991; **338:** 215–16.
2. Roum JH, *et al.* Glutathione aerosol suppresses lung epithelial surface inflammatory cell-derived oxidants in cystic fibrosis. *J Appl Physiol* 1999; **87:** 438–43.
3. Griese M, *et al.* Improvement of alveolar glutathione and lung function but not oxidative state in cystic fibrosis. *Am J Respir Crit Care Med* 2004; **169:** 822–8.
4. Lamson DW, Brignall MS. The use of nebulized glutathione in the treatment of emphysema: a case report. *Altern Med Rev* 2000; **5:** 429–31.
5. Marrades RM, *et al.* Nebulized glutathione induces bronchoconstriction in patients with mild asthma. *Am J Respir Crit Care Med* 1997; **156:** 425–30.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Glu-tathion; TAD; ***Ital.:*** Eudon†; Glutanil†; Gluthion; Ipatox†; Maglut†; Reglumax†; Ridutox; Rition; Scavenger†; TAD; Tationil; Thioxene†; ***Jpn:*** Glutathin; ***Rus.:*** Glutoxim (Глутоксим); ***USA:*** Cachexon.

Multi-ingredient: ***Austral.:*** BSS Plus; ***Austria:*** BSS Plus; ***Canad.:*** BSS Plus; ***Fr.:*** BSS Plus; ***Ger.:*** BSS Plus; ***Hong Kong:*** BSS Plus†; ***Hung.:*** BSS Plus; ***Israel:*** BSS Plus; ***Malaysia:*** BSS Plus; ***Philipp.:*** Illumina; ***S.Afr.:*** BSS Plus; ***Singapore:*** BSS Plus; ***Switz.:*** BSS Plus†; ***Thai.:*** BSS Plus; ***USA:*** BSS Plus; Sucrets Defense Kids Formula; ***Venez.:*** BSS Plus†.

Haem Derivatives

Heme Derivatives; Hemo, derivados del grupo.

ATC — B06AB01 (Haematin).

ATC Vet — QB06AB01 (haematin).

Profile

Haem is the iron protoporphyrin constituent of haemoglobin and is responsible for its colour and oxygen-carrying capacity. It is used in the management of porphyrias (below). Haem is given intravenously as its derivatives, although there is some confusion over their terminology. The names haematin (hematin) and haemin (hemin) have been used interchangeably although chemically haematin is the hydroxy derivative, formed by the reaction of haemin and sodium carbonate in solution. The arginine salt (haem arginate; haemin arginate; heme arginate) is reported to be more stable.

Haem arginate is used in the treatment of acute hepatic porphyrias, including acute intermittent porphyria, variegate porphyria, and hereditary coproporphyria. It is given by slow intravenous infusion in a dose of 3 mg/kg daily for 4 days, infused over at least 30 minutes. The maximum recommended dose is 250 mg daily. The course may be repeated, with close monitoring, in patients with an inadequate response.

Haematin is used intravenously for the amelioration of acute intermittent porphyria associated with the menstrual cycle in patients unresponsive to other therapy. It is given in a usual dose of 1 to 4 mg/kg daily for 3 to 14 days as an intravenous infusion over 10 to 15 minutes. In severe cases the dose may be repeated after 12 hours, but no more than 6 mg/kg should be given in any 24 hour period.

Phlebitis may occur after infusion of haem derivatives and they should be given into a large arm vein or central vein. Use of a filter is recommended due to the colour of the infusion.

Porphyrias. The porphyrias are a group of inherited and acquired disorders of haem biosynthesis in which defects in specific enzymes lead to the accumulation of haem precursors, including aminolevulinic acid, porphobilinogen, and porphyrins.[1-11] They are generally classified as acute or non-acute, reflecting their clinical presentation, or as hepatic or erythropoietic, depending on the site of the enzyme defect. The three most common forms are acute intermittent porphyria, porphyria cutanea tarda, and erythropoietic protoporphyria.

ACUTE PORPHYRIAS. These are inherited disorders characterised by the accumulation of porphyrin precursors, leading to acute attacks of neurovisceral symptoms. The most common form is *acute intermittent porphyria* (acute hepatic porphyria); *variegate porphyria* and *hereditary coproporphyria* are generally less common forms in which there is accumulation of both porphyrin precursors and porphyrins, leading to acute attacks with cutaneous symptoms similar to those seen in non-acute porphyrias (see below).

In acute porphyrias, some enzyme activity is present and the defect only becomes apparent when demand for hepatic haem is increased. Attacks are rare before puberty and the disorder may remain latent in many patients. The presenting symptom is most commonly severe abdominal pain; other gastrointestinal symptoms such as nausea and vomiting also occur, along with autonomic effects including hypertension, tachycardia, sweating, pallor, and pyrexia. Convulsions may occur at the peak of an attack and may persist between attacks. Neuropathy leads to weakness and paralysis and may progress rapidly to respiratory distress. Psychiatric symptoms are also common, particularly agitation, anxiety, and behavioural disturbances. Various factors can increase the demand for haem and attacks are usually precipitated by drugs, alcohol, steroid hormones, reduced caloric intake, or infection. They typically last for several days and are followed by complete recovery, although in some patients chronic abdominal pain may persist without other symptoms.

The primary management of an attack is to remove precipitants and to provide intensive support. *Symptomatic treatment* is complicated by the wide range of drugs that may precipitate porphyria. High doses of parenteral opioids may be required for pain; there is a danger of addiction occurring, but this is rare unless attacks are frequent or pain persists between attacks. Phenothiazines such as chlorpromazine are useful to control nausea and agitation and their sedative effect may also be beneficial. High doses of propranolol may be required for cardiovascular symptoms. Assisted ventilation may be necessary. Convulsions usually disappear as the attack resolves; management of patients who experience convulsions between attacks is a therapeutic problem since many antiepileptics are porphyrinogenic (see Porphyria, p.471). *Specific therapy* is aimed at suppressing the haem biosynthetic pathway, to prevent further accumulation of precursors. Haem, given as either haematin or haem arginate, is the most effective treatment and should be given as soon as possible after onset of the attack; it produces feedback suppression of the biosynthetic pathway. Tin-protoporphyrin, a haem oxygenase inhibitor, has been given with haem to prolong its action but is not commercially available. A high carbohydrate intake may also suppress haem precursor production and should be ensured in all patients, especially if haem is not immediately available; it is usually given orally to prevent fluid overload and exacerbation of hyponatraemia, but intravenous glucose may be required in patients who are vomiting. *Prevention* of attacks involves avoiding drugs that precipitate porphyria and maintaining an adequate carbohydrate intake. Gonadorelin analogues, such as buserelin, may have a role in preventing attacks related to the menstrual cycle. Long-term treatment with haem has been tried in patients with frequent attacks, although such use is not established.

NON-ACUTE PORPHYRIAS. These are characterised by the accumulation of porphyrins and usually present with cutaneous symptoms, although porphyrins also accumulate in the liver and liver damage commonly occurs. *Porphyria cutanea tarda* (cutaneous hepatic porphyria) is the most common form of porphyria. It is usually an acquired disorder and in most cases there is a history of moderate or heavy alcohol intake. There is usually a raised serum-iron concentration and use of oestrogen has also been implicated. The main clinical symptom is cutaneous photosensitivity leading to bullous dermatosis, pruritus, and skin fragility, in areas exposed to sunlight. *Management* involves protecting the skin from sunlight and trauma and avoiding causative agents such as alcohol and iron. Sunscreen preparations must be based on zinc oxide or titanium dioxide to be effective. Reduction of serum-iron concentrations by phlebotomy restores enzyme function and is effective in most patients; it should be carried out every 1 to 2 weeks until remission occurs, and may be required periodically for maintenance. Chloroquine and hydroxychloroquine have also been used and may be effective where phlebotomy is contra-indicated; they appear to act by complexing with porphyrins and increasing their excretion, but low doses are necessary to avoid exacerbating the condition. An alternative method of reducing serum-iron is with the iron chelator desferrioxamine, although it may be less effective than phlebotomy; it is usually reserved for patients unable to tolerate phlebotomy. In patients with renal failure who are too anaemic for phlebotomy and who cannot excrete chloroquine, erythropoietin may be used, and may be combined with desferrioxamine or low-volume phlebotomy.

Erythropoietic protoporphyria is a less common non-acute porphyria and is an inherited disorder leading to accumulation of protoporphyrin. Symptoms are cutaneous and there is an acute reaction to sunlight leading to urticaria, pruritus, swelling, redness, and a severe burning sensation; liver damage may also occur. *Management* involves protection of the skin, as for porphyria cutanea tarda. Betacarotene is widely used to increase tolerance to sunlight, although its efficacy is not established; canthaxanthin, another carotenoid, has also been used. Haem administration, as haematin or haem arginate, may be beneficial in suppressing protoporphyrin production. Colestyramine and activated charcoal reduce protoporphyrin levels by interrupting enterohepatic recycling; they also bind other porphyrins and may have a role in rare forms of porphyria such as *congenital erythropoietic porphyria*.

1. Murphy GM. The cutaneous porphyrias: a review. *Br J Dermatol* 1999; **140:** 573–81.
2. Thadani H, *et al.* Diagnosis and management of porphyria. *BMJ* 2000; **320:** 1647–51.
3. Sarkany RPE. The management of porphyria cutanea tarda. *Clin Exp Dermatol* 2001; **26:** 225–32.
4. Badminton MN, Elder GH. Management of acute and cutaneous porphyrias. *Int J Clin Pract* 2002; **56:** 272–8.
5. Murphy GM. Diagnosis and management of the erythropoietic porphyrias. *Dermatol Ther* 2003; **16:** 57–64.
6. Lecha M, *et al.* Diagnosis and treatment of the hepatic porphyrias. *Dermatol Ther* 2003; **16:** 65–72.
7. Kauppinen R. Porphyrias. *Lancet* 2005; **365:** 241–52.
8. Anderson KE, *et al.* Recommendations for the diagnosis and treatment of the acute porphyrias. *Ann Intern Med* 2005; **142:** 439–50. Correction. *ibid.*; **143:** 316.
9. European Porphyria Initiative. Information available at: http://www.porphyria-europe.com (accessed 04/10/05)
10. University of Cape Town Porphyria Service. Information available at: http://www.porphyria.uct.ac.za (accessed 04/10/05)
11. University of Queensland Porphyria Research Unit. Information available at: http://www.uq.edu.au/porphyria (accessed 04/10/05)