Glycine irrigation should be used cautiously in patients with hepatic impairment since any absorption and consequent metabolism may cause hyperammonaemia. The possible effects on fluid and electrolyte balance warrant cautious use in patients with cardiopulmonary or renal dysfunction; glycine irrigation is contraindicated in anuric patients.

Systemic absorption. Absorption of glycine irrigation solution during surgical procedures can cause disturbances of the circulatory and nervous systems.[1-3] Often seen after transurethral resection of the prostate, these symptoms and signs have been referred to as the transurethral resection syndrome,[1] although they have also been described after other urological or gynaecological surgical procedures.[4,5] Hyponatraemia and glycine toxicity are thought to be responsible for the clinical manifestations.[1,2,5]

Symptoms and signs include chest pains, hypertension, hypotension, bradycardia, anuria, dyspnoea, nausea, vomiting, restlessness, confusion, apprehension, irritability, headache, and seizures.[1,3-5] Chills, diarrhoea, and abdominal pain have also been reported,[1] as have visual disturbances and blindness.[3,6] Myocardial infarction,[7,8] coma, and death may occur.[5,7]

Absorption may occur rapidly, through the intravascular route, or, more rarely, slowly via extravascular absorption.[1,2,4] Extravasation should be suspected when abdominal pain and swelling are apparent.[4,9] Ethanol has been added to the irrigation fluid, and ethanol breath tests performed regularly during procedures in order to detect and monitor absorption.[1,2,4,9] However, the syndrome has still occurred despite monitoring;[9] awareness of the pattern of ethanol changes and clinical symptoms associated with extravascular as well as intravascular absorption are considered essential.[4,9]

1. Olsson J, *et al.* Symptoms of the transurethral resection syndrome using glycine as the irrigant. *J Urol (Baltimore)* 1995; **154:** 123–8.
2. Tauzin-Fin P. Complication des liquides d'irrigation à base de glycocolle: le syndrome de résorption. *Therapie* 2002; **57:** 48–54.
3. Radziwill AJ, *et al.* Visual disturbances and transurethral resection of the prostate: the TURP syndrome. *Eur Neurol* 1997; **38:** 7–9.
4. Hahn RG. Transurethral resection syndrome after transurethral resection of bladder tumours. *Can J Anaesth* 1995; **42:** 69–72.
5. Siddiqui MA, *et al.* Glycine irrigant absorption syndrome following cystoscopy. *Clin Nephrol* 1996; **45:** 365–6.
6. Karci A, Erkin Y. Transient blindness following hysteroscopy. *J Int Med Res* 2003; **31:** 152–5.
7. Byard RW, *et al.* Glycine toxicity and unexpected intra-operative death. *J Forensic Sci* 2001; **46:** 1244–6.
8. Hahn RG, Persson P-G. Acute myocardial infarction after prostatectomy. *Lancet* 1996; **347:** 335.
9. Hahn RG. Life-threatening transurethral resection syndrome despite monitoring of fluid absorption with ethanol. *Eur J Anaesthesiol* 1995; **12:** 431–3.

Uses and Administration

Glycine is a non-essential aliphatic amino acid. It is used as a dietary supplement.

Glycine is sometimes used with antacids in the treatment of gastric hyperacidity. It is also used as an ingredient of some aspirin preparations with the object of reducing gastric irritation.

Sterile solutions of glycine 1.5% in water, which are hypotonic and non-conductive, are used as urogenital irrigation solutions during certain surgical procedures, particularly transurethral resection of the prostate.

Glycine hydrochloride has also been used.

Preparations

BP 2008: Glycine Irrigation Solution;
USP 31: Glycine Irrigation.

Proprietary Preparations (details are given in Part 3)
Fr.: Derm Hydralin; Gyn-Hydralin; ***Hong Kong:*** Gyn-Hydralin; ***Mex.:*** Glisuret†.

Multi-ingredient: ***Arg.:*** Normoprost Compuesto; ***Austral.:*** Cal Alkyline; ***Austria:*** Centramin; ***Braz.:*** B-Vesil; ***Chile:*** Dolotol 12; ***Fr.:*** Cristopal†; Derm'Intim; Item Alphazole; Phakan†; Pruriced; ***India:*** Cotaryl; ***Ital.:*** Detoxicon; Digestivo Antonetto; ***Mex.:*** Segel†; ***Port.:*** Phakan†; ***Rus.:*** Eltacin (Элтацин); ***Spain:*** Sanieb†; Tebetane Compuesto; ***Switz.:*** DAM Antacidum; Phakolen†.

Used as an adjunct in: ***Austral.:*** Cardiprin; Disprin Direct; ***Cz.:*** Godasal; ***Ger.:*** Godamed; Praecineural; ***Hong Kong:*** Cardiprin; Glyprin; ***Indon.:*** Contrexyn; Inzana; Minigrip; ***Israel:*** Lysoprin†; ***Ital.:*** Aspiglicina; Geyfritz†; ***Malaysia:*** Cardiprin; Glyprin; ***NZ:*** Cardiprin†; ***Pol.:*** Alka-Prim; Asprocol; ***Singapore:*** Cardiprin; Glyprin; ***Thai.:*** Caparin; Cardiprin.

Halibut-liver Oil

Aceite de hígado de fletán; Aceite de Higado de Hipogloso; Heilbuttleberöl; Ol. Hippogloss.; Oleum Hippoglossi; Oleum Jecoris Hippoglossi.

Палтусовый Печёночный Жир

CAS — 8001-46-5.

Pharmacopoeias. In *Br.*
BP 2008 (Halibut-liver Oil). The fixed oil extracted from the fresh or suitably preserved liver of the halibut species belonging to the genus *Hippoglossus*. It contains not less than 30 000 units of vitamin A activity per g. Wt per mL 0.915 to 0.925 g. A pale to golden yellow liquid with a fishy, but not rancid, odour and taste. Practically insoluble in alcohol; miscible with chloroform, with ether and with petroleum spirit. Store in well-filled containers. Protect from light.

Profile

Halibut-liver oil is used as a means of giving vitamins A (p.1971) and D (p.1986); the proportion of vitamin A to vitamin D is usually greater in halibut-liver oil than in cod-liver oil (p.1935). It is usually given in capsules.

Preparations

BP 2008: Halibut-liver Oil Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Pancutan Base; ***Canad.:*** Nutrol A; ***Switz.:*** Halibut.

Multi-ingredient: ***Arg.:*** Eryteal; Klorane Bebe Eryteal; Pancutan; ***Austria:*** Nuri-Kapseln; Vitawund; ***Chile:*** Hipoglos; Mintaglos; Nistaglos; ***Fr.:*** Eryteal†; Preparation H; ***Port.:*** Halibut; ***Switz.:*** A Vogel Capsules polyvitamineses†.

Hetaflur *(BAN, USAN, rINN)*

Cetylamine Hydrofluoride; GA-242; Hétaflur; Hetaflurum; SKF-2208. Hexadecylamine hydrofluoride.

Гетафлур

$C_{16}H_{35}N,HF$ = 261.5.
CAS — 3151-59-5.

Profile

Hetaflur is used as a source of fluoride (see Sodium Fluoride, p.1962) in the prevention of dental caries.

Preparations

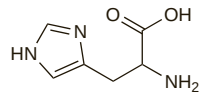
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Israel:*** Elmex†.

Histidine *(USAN, rINN)*

H; His; Histidiini; Histidin; Histidina; Histidinas; L-Histidine; Histidinum; Hisztidin; NSC-137773. L-2-Amino-3-(1*H*-imidazol-4-yl)propionic acid.

Гистидин

$C_6H_9N_3O_2$ = 155.2.
CAS — 71-00-1.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Histidine). Colourless crystals or a white or almost white crystalline powder. Soluble in water; very slightly soluble in alcohol. Protect from light.
USP 31 (Histidine). White, odourless crystals. Soluble in water; very slightly soluble in alcohol; insoluble in ether. pH of a 2% solution in water is between 7.0 and 8.5.

Histidine Hydrochloride

Histidiinihydrokloridimonohydraatti; Histidina, hidrocloruro; Histidine (chlorhydrate d') monohydraté; Histidine Monohydrochloride; Histidin-hydrochlorid monohydrát; Histidinhydrokloridmonohydrat; Histidini hydrochloridum monohydricum; Histidinium Chloride; Histidino hidrochloridas monohidratas; Histydyny monochlorowodorek; Hisztidin-hidroklorid-monohidrát. L-Histidine hydrochloride monohydrate.

$C_6H_9N_3O_2,HCl,H_2O$ = 209.6.
CAS — 645-35-2 (anhydrous histidine hydrochloride).

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Histidine Hydrochloride Monohydrate). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol. A 5% solution in water has a pH of 3.0 to 5.0. Protect from light.

Profile

Histidine is a basic amino acid that is essential for infant growth and which may be essential for some other groups, such as patients with uraemia. Histidine and histidine hydrochloride are used as dietary supplements.

Honey

Clarified Honey; Gereinigter Honig; Honung; Hunaja; Madu; Med; Medus; Mel; Mel Depuratum; Mel Despumatum; Miel; Miel Blanc; Miel purificada; Purified Honey; Strained Honey.

Мёд

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn*. Also in *USNF*.
Ph. Eur. 6.2 (Honey; Mel). It is produced by bees (*Apis mellifera*) from the nectar of plants or from secretions of living parts of plants, which the bees collect, transform by combining with specific substances of their own, deposit, dehydrate, store, and leave in the honey comb to ripen and mature. If the bee has been exposed to treatment to prevent or cure diseases or to any substance intended for preventing, destroying, or controlling any pest, unwanted species of plants or animals, appropriate steps are taken to ensure that the levels of residues are as low as possible. It is an almost white to dark brown, viscous liquid which may be partly crystalline.
USNF 26 (Purified Honey). It is obtained by purification of honey from the comb of the bee, *A. mellifera* and all subspecies of *A. mellifera*. The honey is extracted by centrifugation, pressure, or other suitable procedures. Specific gravity 1.400 and 1.435 at 20°. Store in airtight containers. It is not intended for infants under one year of age unless it is free from *Clostridium* spp.

Profile

Honey, which contains about 70 to 80% of glucose and fructose, is used as a demulcent and sweetening agent, especially in linctuses and cough mixtures (p.1547). Preparations containing honey are used in the management of skin ulcers, wounds, and burns.

Contamination. Honey has been identified as a source of *Clostridium botulinum* spores and thus recommendations have been made that honey should not be given to infants under 1 year because of the risk of causing infant botulism.[1,2]

Honey produced from certain species of *Rhododendron* plants has been found to contain grayanotoxins. Grayanotoxin I is responsible for honey poisoning, manifest as bradycardia, cardiac arrhythmias, hypotension, gastrointestinal disturbances, dizziness, loss of consciousness, blurred vision, chills, cyanosis, sweating, and salivation.[3,4] Convulsions have also been reported.[4]

1. Arnon SS, *et al.* Honey and other environmental risk factors for infant botulism. *J Pediatr* 1979; **94:** 331–6.
2. Tanzi MG, Gabay MP. Association between honey consumption and infant botulism. *Pharmacotherapy* 2002; **22:** 1479–83.
3. Özhan H, *et al.* Cardiac emergencies caused by honey ingestion; a single centre experience. *Emerg Med J* 2004; **21:** 742–4.
4. Dilber E, *et al.* A case of mad honey poisoning presenting with convulsion: intoxication instead of alternative therapy. *Turk J Med Sci* 2002; **32:** 361–2.

Wounds. Anecdotal reports and traditional usage dating back to ancient Egypt suggest that honey may be of some value as a wound dressing (p.1585). Its antibacterial properties are attributed both to high osmolality and the liberation of hydrogen peroxide, but may vary with the source:[1-4] in Europe, some of the best activity has been seen with lime-flower honey.[2] Sterilised manuka honey (p.2337) was reported to heal a leg ulcer infected with meticillin-resistant *Staphylococcus aureus*,[5] although a randomised open-label study found no evidence that dressings impregnated with manuka honey improved the healing of venous leg ulcers at 12 weeks compared with usual care.[6] In a preliminary study, honey obtained from the tea plant (see Xanthine-containing Beverages, p.2415) significantly reduced the incidence of grade 3 and 4 radiation-induced oral mucositis.[7]

A group from India[8] has reported that the properties of honey offer a potentially simple and cheap means of preserving skin grafts in developing countries, with 100% uptake of reconstituted grafts stored for up to 6 weeks and 80% uptake of those stored for 7 to 12 weeks. In comparison with sulfadiazine silver, occlusive honey dressings were also found to be more effective for the treatment of superficial partial thickness thermal burns.[9]

However, concern has been expressed since honey may contain not only chemical contaminants but clostridial spores (see also above), and it has been suggested[2] that to be medically acceptable, honey must be sterile, residue-free, and of measured antibacterial activity.

Sugar has been used similarly to honey in treating wounds (see p.1970).

1. Greenwood D. Honey for superficial wounds and ulcers. *Lancet* 1993; **341:** 90–1.
2. Postmes T, *et al.* Honey for wounds, ulcers, and skin graft preservation. *Lancet* 1993; **341:** 756–7.
3. Molan PC. Re-introducing honey in the management of wounds and ulcers - theory and practice. *Ostomy Wound Manage* 2002; **48:** 28–40.
4. Booth S. Are honey and sugar paste alternatives to topical antiseptics? *J Wound Care* 2004; **13:** 31–3.
5. Natarajan S, *et al.* Healing of an MRSA-colonized, hydroxyurea-induced leg ulcer with honey. *J Dermatol Treat* 2001; **12:** 33–6.
6. Jull A, *et al.* Honey as Adjuvant Leg Ulcer Therapy trial collaborators. Randomized clinical trial of honey-impregnated dressings for venous leg ulcers. *Br J Surg* 2008; **95:** 175–82.
7. Biswal BM, *et al.* Topical application of honey in the management of radiation mucositis: a preliminary study. *Support Care Cancer* 2003; **11:** 242–8.
8. Subrahmanyam M. Storage of skin grafts in honey. *Lancet* 1993; **341:** 63–4.
9. Subrahmanyam M. A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* 1998; **24:** 157–61.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Antibacterial Honey Barrier; ***Ital.:*** Oramil; ***Neth.:*** Melrosum; ***UK:*** Medihoney Antibacterial Wound Gel; Mesitran.

Multi-ingredient: ***Arg.:*** Expectosan Hierbas y Miel; ***Austral.:*** Logicin Natural Lozenges†; ***Braz.:*** Calmatoss†; Elixir de Inhamet†; Expectomel; Melagriao; Melxi†; Peitoral Martel†; ***Canad.:*** Mielocol; ***Chile:*** Fray Ro-

mano; Jarabe Palto Compuesto con Miel Adulto; Jarabe Palto Compuesto con Miel Infantil; Mielax; Mielito; Paltomiel; Paltomiel Plus; Pulmosina; ***Fr.:*** Feromiel; Taido; ***Indon.:*** Pectum; Sirec; ***Irl.:*** Venos Honey & Lemon; ***Ital.:*** Alvear con Ginseng; Apiserum con Telergon 1; Bebimix; Bioton; Fon Wan Eleuthero†; Fon Wan Ginsenergy; Liozim; Nepiros; Nerex; Nutrigel†; Pollingel Ginseng†; ***Mex.:*** Guayalin-Plus†; ***NZ:*** Lemsip Dry Cough†; Robitussin Honey Cough; ***Pol.:*** Babicum; ***Rus.:*** Bronchicum Husten (Бронхикум Сироп от Кашля); ***S.Afr.:*** Choats Extract of Lettuce Cough Mixture; Enzian Anaemodoron Drops; ***Switz.:*** Neo-Angin au miel et citron; ***UK:*** Adult Meltus for Chesty Coughs & Catarrh; Beehive Balsam; Buttercup Syrup (Honey and Lemon flavour); Herb and Honey Cough Elixir; Honey & Molasses; Jackson's Lemon Linctus; Jackson's Troublesome Coughs; Lemsip Cough & Cold Dry Cough; Lockets; Lockets Medicated Linctus; M & M; Meltus Expectorant; Meltus Honey & Lemon; Potters Children's Cough Pastilles; Potters Gees Linctus; Regina Royal Five; Sanderson's Throat Specific; Throaties Pastilles; Venos Honey & Lemon; Zubes Honey & Lemon; ***Venez.:*** Jengimiel; Jengimiel Sabila; Perebron con Miel†.

Invert Sugar

Azúcar invertido.

CAS — 8013-17-0.

ATC — C05BB03.

ATC Vet — QC05BB03.

Pharmacopoeias. *Br.* and *US* include preparations of invert sugar.

Profile

Invert sugar is an equimolecular mixture of glucose and fructose which may be prepared by the hydrolysis of sucrose with a suitable mineral acid such as hydrochloric acid. Invert sugar has similar actions and uses to those of glucose (p.1945) and fructose (p.1945). It has been used as a 10% solution as an alternative to glucose in parenteral nutrition but, as with fructose, such use cannot be recommended.

A syrup of invert sugar is used as a stabilising agent; when mixed with suitable proportions of sucrose-based syrup it will help to prevent crystallisation of the sucrose.

Preparations

BP 2008: Invert Syrup;
USP 31: Invert Sugar Injection; Multiple Electrolytes and Invert Sugar Injection Type 1; Multiple Electrolytes and Invert Sugar Injection Type 2; Multiple Electrolytes and Invert Sugar Injection Type 3.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***S.Afr.:*** Emex; ***USA:*** Travert.

Iron

Eisen; Fer; Ferro; Ferrum; Hierro; Ijzer; Järn; Rauta; Železo; Železo.

Fe = 55.845.

CAS — 7439-89-6.

Pharmacopoeias. *Eur.* (see p.vii) includes a form for homoeopathic preparations.
Ph. Eur. 6.2 (Iron for Homoeopathic Preparations; Ferrum ad Praeparationes Homoeopathicae). A fine, blackish-grey powder, without metallic lustre, obtained by reduction or sublimation. Practically insoluble in water and in alcohol; it dissolves with heating in dilute mineral acids.

Adverse Effects

The astringent action of **oral** iron preparations sometimes produces gastrointestinal irritation and abdominal pain with nausea and vomiting. These irritant adverse effects are usually related to the amount of elemental iron taken rather than the type of preparation. Other gastrointestinal effects may include either diarrhoea or constipation. Adverse effects can be reduced by giving it with or after food (rather than on an empty stomach) or by beginning therapy with a small dose and increasing gradually. Modified-release products are claimed to produce fewer adverse effects but this may only reflect the lower availability of iron from these preparations. Oral liquid preparations containing iron salts may blacken the teeth and should be drunk through a straw. The faeces of patients taking iron salts may be coloured black.

The adverse effects associated with iron given **parenterally** are described under iron dextran (see p.1951).

Since absorbed iron is conserved by the body, **iron overload**, with increased storage of iron in various tissues (haemosiderosis), may occur as a result of excessive or mistaken therapy, especially parenteral therapy. Patients with pre-existing iron storage or absorption diseases are also at risk.

Acute iron **overdosage** can be divided into four stages.

- In the first phase, which occurs up to 6 hours after oral ingestion, gastrointestinal toxicity, notably vomiting and diarrhoea, predominates. Other effects may include cardiovascular disorders such as hypotension, metabolic changes including acidosis and hyperglycaemia, and CNS depression ranging from lethargy to coma. Patients with only mild to moderate poisoning do not generally progress past this first phase.
- The second phase, which is not always seen, may occur at 6 to 24 hours after ingestion and is characterised by a temporary remission or clinical stabilisation.
- In the third phase, 12 to 48 hours after ingestion, gastrointestinal toxicity recurs together with shock, metabolic acidosis, severe lethargy or coma, hepatic necrosis and jaundice, hypoglycaemia, coagulation disorders, oliguria or renal failure, and possible myocardial dysfunction.
- The fourth phase may occur several weeks after ingestion and is characterised by gastrointestinal obstruction and possibly late hepatic damage.

Relatively small amounts of iron may produce symptoms of toxicity. It has been stated that more than the equivalent of 20 mg/kg of iron could lead to some symptoms of toxicity and that in a young child the equivalent of about 60 mg/kg of iron should be regarded as extremely dangerous. Estimates of acute lethal dosages have ranged from the equivalent of 150 mg/kg of iron upwards. Serum-iron concentrations have also been used as an indication of the severity of overdosage: a peak concentration of 5 micrograms/mL or more is reportedly associated with severe poisoning in many patients.

Effects on the cardiovascular system. For a suggestion that iron overload may contribute to ischaemic heart disease, see Effects in Non-deficient Subjects, below.

Effects on growth. Iron supplementation in iron-replete children has been reported to adversely affect their growth—see Effects in Non-deficient Subjects, below.

Iron overload. Because the body lacks a mechanism for the excretion of excess iron, abnormally high absorption or repeated blood transfusion will result in iron overload (p.1442), leading eventually to haemochromatosis. The consequences of haemochromatosis include pigment deposition in skin and other organs, mild liver dysfunction, endocrine dysfunction (failure of the adolescent growth spurt, hypogonadism, sometimes diabetes and hypothyroidism), and heart disease (pericarditis, heart failure, and arrhythmias). If unchecked, the iron build-up can lead to death, mainly through heart failure or arrhythmia. Where iron overload is due to increased absorption, phlebotomy is the treatment of choice; however, if phlebotomy is not tolerated or in patients who are transfusion-dependent (as in β-thalassaemia—see p.1045) treatment with iron chelators such as desferrioxamine is used to retard accumulation.

Treatment of Adverse Effects

In treating acute iron poisoning, speed is essential to reduce absorption of iron from the gastrointestinal tract. Activated charcoal is ineffective, but gastric lavage should be considered in those who have ingested the equivalent of more than 60 mg/kg of elemental iron within 1 hour of presentation. Serum-iron concentrations may be an aid to estimating the severity of poisoning. Although these do not correlate well with symptoms, the UK Poisons Information Service considers that concentrations taken about 4 hours after ingestion generally indicate the severity of poisoning as follows:

- less than 3 micrograms/mL, mild poisoning
- 3 to 5 micrograms/mL, moderate poisoning
- 5 micrograms/mL or more, severe poisoning

In patients with moderate poisoning, or severe asymptomatic poisoning, the measurement should be repeated after a further 2 hours, and chelation therapy with desferrioxamine (p.1441) should be considered if the concentration is rising. In patients with severe symptomatic poisoning, chelation therapy should be considered straight away.

Other measures include the symptomatic management and therapy of metabolic and cardiovascular disorders.

◊ General references.

1. Proudfoot AT, *et al.* Management of acute iron poisoning. *Med Toxicol* 1986; **i:** 83–100.
2. Mann KV, *et al.* Management of acute iron overdose. *Clin Pharm* 1989; **8:** 428–40.
3. Mills KC, Curry SC. Acute iron poisoning. *Emerg Med Clin North Am* 1994; **12:** 397–413.
4. Fine JS. Iron poisoning. *Curr Probl Pediatr* 2000; **30:** 71–90.

Overdosage. References highlighting the specific problem of iron overdose in children.[1-4] Child-resistant packaging and warning labels may be helpful in reducing the problem.

1. Anonymous. Iron-containing drugs and supplements: accidental poisoning. *WHO Drug Inf* 1995; **9:** 159–60.
2. Fitzpatrick R, Murray V. Iron toxicity: dietary supplements. *Pharm J* 1996; **256:** 666.
3. Committee on Safety of Medicines/Medicines Control Agency. Oral iron supplements: accidental overdose may be fatal in children. *Current Problems* 2001; **27:** 14. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007456&RevisionSelectionMethod=LatestReleased (accessed 08/11/05)
4. Singhi SC, *et al.* Acute iron poisoning: clinical picture, intensive care needs and outcome. *Indian Pediatr* 2003; **40:** 1177–82.

Overdosage in pregnancy. Limited data on the treatment of iron overdose in pregnancy from the UK National Teratology Information Service, suggested that treatment with desferrioxamine should not be withheld if clinically indicated.[1-3] Most pregnancies had a normal outcome. A literature review[4] of iron overdose in pregnant women found that women with peak serum-iron concentrations greater than or equal to 4 micrograms/mL were more frequently symptomatic, but that there was no relationship between peak iron level and frequency of spontaneous abortion, preterm delivery, congenital anomalies, or perinatal or maternal death. However, women with stage 3 iron toxicity, defined as those manifesting with hepatic, renal, or cardiac failure, were more likely to spontaneously abort, deliver preterm, or die.

1. McElhatton PR, *et al.* The consequences of iron overdose and its treatment with desferrioxamine in pregnancy. *Hum Exp Toxicol* 1991; **10:** 251–9.
2. McElhatton PR, *et al.* Outcome of pregnancy following deliberate iron overdose by the mother. *Hum Exp Toxicol* 1993; **12:** 579.
3. McElhatton PR, *et al.* The outcome of pregnancy following iron overdose by the mother. *Br J Clin Pharmacol* 1998; **45:** 212P–213P.
4. Tran T, *et al.* Intentional iron overdose in pregnancy—management and outcome. *J Emerg Med* 2000; **18:** 225–8.

Precautions

Iron compounds should not be given to patients receiving repeated blood transfusions or to patients with anaemias not produced by iron deficiency unless iron deficiency is also present. Oral and parenteral iron therapy should not be used together. Care should be taken in patients with iron-storage or iron-absorption diseases such as haemochromatosis, haemoglobinopathies, or existing gastrointestinal diseases such as inflammatory bowel disease, intestinal strictures and diverticulae.

Liquid preparations containing iron salts should be well diluted with water and swallowed through a straw to prevent discoloration of the teeth.

Effects in non-deficient subjects. There has been concern about the potential consequences of iron supplementation in individuals and groups who are not actually iron-deficient. Apart from the suggestion that certain populations may be at somewhat increased risk of microbial *infection* after supplementation (see Infections, below), there is some evidence that supplementation in children without iron deficiency may *retard their growth*.[1,2] It has also been proposed that iron may be associated with *ischaemic heart disease*, by modifying low-density lipoprotein in ways which increase its atherogenic potential and by sensitising the myocardium to ischaemic injury.[3,4] However, conclusions of a cohort study[5] and a systematic review[6] did not support any correlation between iron status and coronary heart disease. There is some suggestion that an excess of iron may be *carcinogenic*;[7,8] conclusive studies are lacking.

1. Idjradinata P, *et al.* Adverse effect of iron supplementation on weight gain of iron-replete young children. *Lancet* 1994; **343:** 1252–4.
2. Dewey KG, *et al.* Iron supplementation affects growth and morbidity of breast-fed infants: results of a randomized trial in Sweden and Honduras. *J Nutr* 2002; **132:** 3249–55.
3. Burt MJ, *et al.* Iron and coronary heart disease: iron's role is undecided. *BMJ* 1993; **307:** 575–6.
4. Sullivan JL. Iron and coronary heart disease: iron makes myocardium vulnerable to ischaemia. *BMJ* 1993; **307:** 1066–7.
5. Sempos CT, *et al.* Serum ferritin and death from all causes and cardiovascular disease: the NHANES II Mortality Study. *Ann Epidemiol* 2000; **10:** 441–8.