2. Wiesner DM. Betel-nut withdrawal. *Med J Aust* 1987; **146:** 453.
3. López-Vilchez MA, *et al.* Areca-nut abuse and neonatal withdrawal syndrome. Abstract: *Pediatrics* 2006; **117:** 203. Full version: http://pediatrics.aappublications.org/cgi/content/full/117/1/e129 (accessed 10/04/08)
4. Sullivan RJ, *et al.* Effects of chewing betel nut (Areca catechu) on the symptoms of people with schizophrenia in Palau, Micronesia. *Br J Psychiatry* 2000; **177:** 174–8.
5. Deahl MP. Psychostimulant properties of betel nuts. *BMJ* 1987; **294:** 841.

Aristolochia

Serpentaria.

NOTE. *Aristolochia clematitis* has also been known as asarabacca (p.2261).

Pharmacopoeias. *Chin.* allows various species of *Aristolochia*.

Profile

Aristolochia spp. (birthworts) including *A. clematitis* and *A. ringens (A. brasiliensis)* have been used in herbal medicine.

Serpentary (serpentaria) is the dried rhizome and roots of *Aristolochia serpentaria* (Virginian snakeroot) and of *A. reticulata* (Texan snakeroot) (Aristolochiaceae). Snakeroot is also used as a common name to describe poisonous *Eupatorium* spp. Preparations of serpentary have been used as bitters. The active ingredient is aristolochic acid, which has been tried in a number of inflammatory disorders, mainly in folk medicine; the sodium salt of aristolochic acid has also been used. However, there is concern over such use since aristolochic acid has been reported to be carcinogenic and nephrotoxic.

Chinese medicine has employed various species of *Aristolochia* including *A. contorta*, *A. debilis* (but see under Adverse Effects, below), and *A. manshuriensis*. The terms Mu Tong and Fangji have been used for *Aristolochia* spp. in traditional medicine.

Adverse effects. Progressive interstitial fibrosis of the kidney related to a slimming regimen containing Chinese herbs had been reported in 70 patients in Belgium by 1993; 30 of these patients had terminal renal failure.[1] Renal failure has also been reported[2] in 2 patients in the UK after ingestion of Chinese herbal medicines that were later found to contain aristolochic acid, a known nephrotoxin;[3] one of these patients subsequently developed invasive urothelial carcinoma.[4] Inadvertent ingestion of aristolochic acid can originate as a result of the substitution of *Aristolochia* spp. (probably *A. manshuriensis*) for other innocuous herbal substances;[2,5] the Belgian cases were probably as a result of substitution of *A. fangchi* extracts for *Stephania tetrandra*.[1] As a result of these cases, the UK MCA issued a permanent ban on *Aristolochia* preparations in 1999. Similar bans have been made in several other countries;[3] in 2004, the Chinese regulatory authority also banned the use of *A. fangchi* and *A. debilis* in traditional medicine formulations. Examination of 39 patients in Belgium with nephropathy associated with *A. fangchi* ingestion had revealed 18 cases of urothelial carcinoma and evidence of mild to moderate dysplasia in 19 patients.[6] There had appeared to be a higher risk of carcinoma with total doses of *A. fangchi* in excess of 200 g.

Aristolochic acid has been proposed as the cause of endemic (Balkan) nephropathy,[7] which is confined to a very specific rural geographical distribution and first described in the 1950s. Data supporting this hypothesis included findings of DNA damage linked to aristolochic acid in kidney samples from affected patients, as well as renal failure in horses who had grazed in the local fields. *Aristolochia clematitis* is endemic to the region and has been found in fields cultivated for wheat grain. It is possible that the local population could be exposed to toxic amounts of aristolochic acid over time from bread made with grain contaminated with *A. clematitis* seeds.

1. Vanhaelen M, *et al.* Identification of aristolochic acid in Chinese herbs. *Lancet* 1994; **343:** 174.
2. Lord GM, *et al.* Nephropathy caused by Chinese herbs in the UK. *Lancet* 1999; **354:** 481–2.
3. Cosyns JP. Aristolochic acid and 'Chinese herbs nephropathy': a review of the evidence to date. *Drug Safety* 2003; **26:** 33–48.
4. Lord GM, *et al.* Urothelial malignant disease and Chinese herbal nephropathy. *Lancet* 2001; **358:** 1515–6.
5. But PP, Ma S-c. Chinese-herb nephropathy. *Lancet* 1999; **354:** 1731–2.
6. Nortier JL, *et al.* Urothelial carcinoma associated with the use of a chinese herb (Aristolochia fangchi). *N Engl J Med* 2000; **342:** 1686–92.
7. Grollman AP, *et al.* Aristolochic acid and the etiology of endemic (Balkan) nephropathy. *Proc Natl Acad Sci U S A* 2007; **104:** 12129–34.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Euserpina Cellulite.

Multi-ingredient: ***S.Afr.:*** Borstol Cough Remedy.

Arnica

Árnica; Arnica, fleur d' (arnica flower); Arnicae Anthodium; Arnicae flos (arnica flower); Arnikablomma (arnica flower); Arnikinkukka (arnica flower); Arnikový květ (arnica flower); Arnikų žiedai (arnica flower); Hegyi árnika virág (arnica flower); Koszyczek arniki (arnica flower); Leopard's Bane; Mountain Tobacco; Wolf's Bane; Wolfsbane.

NOTE. Wolfsbane is also used as a common name for aconite (p.2246).

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

Ph. Eur. 6.2 (Arnica Flower; Arnica Flos). It consists of the whole or partially broken, dried flowerheads of *Arnica montana*. It contains not less than 0.4% w/w of total sesquiterpene lactones expressed as dihydrohelenalin tiglate, calculated with reference to the dried drug. It has an aromatic odour. Protect from light.

Profile

Arnica is generally used in the form of the flowerheads of *Arnica montana* (Compositae).

Arnica flower is irritant to mucous membranes and when ingested has produced severe symptoms including gastrointestinal and nervous system disturbances, both tachycardia and bradycardia, and collapse. Tincture of arnica may cause dermatitis when applied to the skin of sensitive persons.

Preparations of arnica flower and arnica root are used as astringents for topical application to unbroken skin in conditions such as sprains and bruises; such preparations are not considered suitable for internal use. Arnica flowers are the source of arnica oil, which has been used similarly.

Herbal preparations containing arnica are available for oral use.

Homoeopathy. Arnica has been used in homoeopathic medicines under the following names: Arnica montana; Arnica, Flos; Arnica montana e flore; Arnica montana ex herba; Arnica, Planta tota; Arnica montana ex planta tota; Arn. mont. Some homoeopathic preparations are available for oral use.

◊ References.

1. Leivers K. Unravelling the confusion around arnica's herbal and homoeopathic use. *Pharm J* 2005; **275:** 289–91.
2. Kouzi SA, Nuzum DS. Arnica for bruising and swelling. *Am J Health-Syst Pharm* 2007; **64:** 2434–43.

Preparations

Ph. Eur.: Arnica Tincture.

Proprietary Preparations (details are given in Part 3)

Arg.: Herbaccion Desinflamante†; ***Austral.:*** Sports Ice Bruising Relief; ***Belg.:*** Arnican; ***Chile:*** Arnikaderm; ***Fr.:*** Arnican; Pharmadose teinture d'arnica; ***Ger.:*** Arnikatinktur; Arthrosenex AR; Doc; Enelbin-Salbe; Hyzum N†; Vasotonin†; ***Mex.:*** Balsamo Nordin; Estimul; ***Port.:*** Arnigel; ***Singapore:*** SinEccH; ***UK:*** Arnicare; Atrogel.

Multi-ingredient: ***Arg.:*** Fluido; ***Austral.:*** Joint & Muscle Cream; Percutane; ***Austria:*** Arnicet; Asthmatee EF-EM-ES; Berggeist; Cional; Dynexan; Heparin Comp; Rheuma; Sportino Akut†; ***Belg.:*** Älgi-Cool; Purigel Crisp; Purigel NF; ***Braz.:*** Dermol†; Traumed†; ***Chile:*** Lefkaflam; Matikomp; ***Cz.:*** Arnidol; Heparin-Gel†; ***Fr.:*** Arnicadol; Creme Rap; Decramp; Dermocica; Evarose; Lelong Contusions†; ***Ger.:*** Arnikamill†; Cefawell†; Combudoron; Dolo-cyl; Essaven Sport†; Gothaplast Rheumamed AC; Heparin Comp†; Heparin Kombi-Gel†; Heusin†; Lindofluid N; Retterspitz Ausserlich; Retterspitz Quick; Rhoival†; Sportino Akut; Stullmaton†; Trauma-cyl; Varicylum-S; Venengel†; Vitosal†; ***Hong Kong:*** New Patecs A; ***Ital.:*** Flebolider; Flodolor; Venalta; ***Malaysia:*** Arnica Comp†; ***Mex.:*** Reudol; ***Pol.:*** Arcalen; Arnisol; Dentosept; Dentosept A; Emorect; Escalar; Prostapol; Reumobonisol; Stomatosol; Uroprost; Venoforton; ***S.Afr.:*** Arnica Massage Oil; Combudoron; Dynexan; Lotio Pruni Comp cum Cupro; Muscle Rub; Wecesin; ***Spain:*** Arnicon†; Encialina†; ***Switz.:*** Combudoron; Eubucal†; Euceta avec camomille et arnica; Fortacet; GU Eau†; Onguent aux herbes Keller; Perskindol Cool Arnica; Topaceta; Wecesin†; ***UK:*** Hansaplast Herbal Heat Plaster; Profelan; ***Venez.:*** Andantol Jalea; Biomicovo†; Gelsem.

Arsenic Trioxide *(USAN)*

Acidum Arsenicosum Anhydricum; Arseni Trioxydum; Arsenic; Arsenic Oxide; Arsénico, trióxido de; Arsenicum Album; Arsénieux, anhydride; Arsenii trioxidum; Arsenious Acid; Arsenous Oxide; White Arsenic. Diarsenic trioxide.

As_2O_3 = 197.8.

CAS — 1327-53-3 (arsenic trioxide); 7784-45-4 (arsenic triiodide).

ATC — L01XX27.

ATC Vet — QL01XX27.

Pharmacopoeias. In *Jpn.*

Eur. (see p.vii) includes a form for homoeopathic preparations.

Ph. Eur. 6.2 (Arsenious Trioxide for Homoeopathic Preparations; Arsenii Trioxidum ad Praeparationes Homoeopathicae). A white or almost white powder. Practically insoluble to sparingly soluble in water; it dissolves in solutions of alkali hydroxides and carbonates.

Adverse Effects

The toxicity of arsenic compounds varies according to chemical composition, solubility, and valency. Inorganic arsenic compounds are much more toxic than organic compounds and elemental arsenic is the least toxic. Toxicity increases with increasing solubility, and trivalent (arsenite) compounds are more toxic than pentavalent (arsenate) compounds. Arsenic exerts its effects through a variety of pathophysiological mechanisms such as induction of oxidative stress and binding to sulphydryl groups in enzymes, and it has the potential to affect most of the major organ systems in the body; it also induces alteration in gene expression.

Acute poisoning. Estimates of lethal and toxic oral doses vary: the lethal dose of arsenic trioxide has been reported to be around 100 to 300 mg; a dose of 1 mg/kg of arsenic may be lethal in children; acute toxic doses of arsenic compounds have been reported to range from 1 mg to 10 g. Symptoms of acute poisoning occur within 30 minutes to several hours after ingestion and food delays the onset.

Early features of acute arsenic poisoning following ingestion involve the gastrointestinal tract with common symptoms of a metallic or garlic taste, a burning sensation in the mouth, dysphagia, abdominal pain, severe nausea, projectile vomiting, haemorrhagic gastritis, and profuse 'rice-water' diarrhoea leading to hypovolaemic shock; the breath may have an odour of garlic. In the absence of adequate treatment, death can occur within 24 hours of a severely toxic dose. Absorption of arsenic may produce multisystem toxicity days or weeks later, which could include cardiomyopathy, anaemia, leucopenia, skin disorders, acute respiratory distress syndrome, hepatitis, renal failure, encephalopathy, and peripheral polyneuropathy.

Arsenic compounds are irritant and corrosive when inhaled or in contact with the skin or eyes; acute systemic effects may occur after inhalation or skin contact.

Chronic poisoning. Arsenic is widely distributed in the environment: the smelting industry (non-ferrous metals) is a major industrial source of arsenic contamination in the soil, water, and air; mining residues and arsenical pesticides and wood preservatives also contribute to soil and water contamination. Seafood is a source of organic arsenic. Occupational exposure is a potential cause of chronic arsenic toxicity but in the general population, food and drinking water is usually the source of arsenic.

Chronic arsenic poisoning or occupational exposure typically produces varied skin disorders appearing over 1 to 10 years, particularly hyperkeratosis, especially affecting the palms and soles, and changes in skin pigmentation. Transverse white lines (Mee's lines) may appear in the nails several weeks after absorption. Gastrointestinal disturbances may occur, although are less likely with chronic exposure. Hypertension, cardiovascular disorders, and diabetes mellitus have been associated with chronic arsenic poisoning. Jaundice may occur as a result of hepatomegaly and portal hypertension may eventually develop. Encephalopathy and peripheral neuropathies may also occur. Arsenic is toxic to the bone marrow and produces a wide range of blood disorders including leucopenia and aplastic anaemia. Chronic exposure to arsenic has been associated with neoplasms of the skin, lungs, bladder, liver, and kidney. Chronic inhalation of arsenic salts may result in perforation of the nasal septum.

Adverse effects of therapeutic use. Reported adverse effects of arsenic trioxide therapy in patients with acute promyelocytic leukaemia (APL) include leucocytosis, neutropenia, raised liver enzyme values, gastrointestinal disturbances, fatigue, oedema, hyperglycaemia, hypokalaemia, dyspnoea, cough, skin rashes, pruritus, pyrexia, headaches, paraesthesia, and dizziness. Prolongation of the QT interval and other cardiac arrhythmias have occurred. The so-called 'leukocyte activation syndrome' ('APL differentiation syndrome') similar to one that develops with tretinoin therapy (see Retinoic Acid Syndrome, p.1618) has occurred in some patients. Sudden death has been reported in a few patients.

◊ References,[1-8] including discussion of epidemic toxicity due to arsenic-contaminated drinking water.[4,6-8]

1. Health and Safety Executive. Inorganic arsenic compounds. *Toxicity Review 16*. London: HMSO, 1986.
2. Shannon RL, Strayer DS. Arsenic-induced skin toxicity. *Hum Toxicol* 1989; **8:** 99–104.
3. Gebel T. Confounding variables in the environmental toxicology of arsenic. *Toxicology* 2000; **144:** 155–62.
4. WHO. Arsenic and arsenic compounds. *Environmental Health Criteria 224*. Geneva: WHO, 2001. Also available at: http://www.inchem.org/documents/ehc/ehc/ehc224.htm (accessed 11/04/08)
5. Borak J, Hosgood HD. Seafood arsenic: implications for human risk assessment. *Regul Toxicol Pharmacol* 2007; **47:** 204–12.
6. Flora SJ, *et al.* Arsenic induced oxidative stress and the role of antioxidant supplementation during chelation: a review. *J Environ Biol* 2007; **28** (2 suppl): 333–47.
7. Islam LN, *et al.* Association of respiratory complications and elevated serum immunoglobulins with drinking water arsenic toxicity in human. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 2007; **42:** 1807–14.
8. Guha Mazumder DN. Arsenic and non-malignant lung disease. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 2007; **42:** 1859–67.

Adulteration. Arsenical compounds have reportedly been used to "cut" cocaine and symptoms of arsenic poisoning may occur in cocaine abusers.[1] Toxicity due to the presence of arsenic in various ethnic remedies has also been reported.[2-4]

1. Lombard J, *et al.* Arsenic intoxication in a cocaine abuser. *N Engl J Med* 1989; **320:** 869.
2. Kew J, *et al.* Arsenic and mercury intoxication due to Indian ethnic remedies. *BMJ* 1993; **306:** 506–7.
3. Ernst E, Thompson Coon J. Heavy metals in traditional Chinese medicines: a systematic review. *Clin Pharmacol Ther* 2001; **70:** 497–504.
4. Ernst E. Heavy metals in traditional Indian remedies. *Eur J Clin Pharmacol* 2002; **57:** 891–6.

Treatment of leukaemia. References[1-5] to and a review[6] of adverse effects in patients receiving arsenic trioxide for the treatment of acute promyelocytic leukaemia, including a report of sudden death occurring in 3 patients in a dose-finding study.[5]

1. Huang SY, *et al.* Acute and chronic arsenic poisoning associated with treatment of acute promyelocytic leukaemia. *Br J Haematol* 1998; **103:** 1092–5.
2. Huang CH, *et al.* Complete atrioventricular block after arsenic trioxide treatment in an acute promyelocytic leukemic patient. *Pacing Clin Electrophysiol* 1999; **22:** 965–7.
3. Camacho LH, *et al.* Leukocytosis and the retinoic acid syndrome in patients with acute promyelocytic leukemia treated with arsenic trioxide. *J Clin Oncol* 2000; **18:** 2620–5.
4. Ohnishi K, *et al.* Prolongation of the QT interval and ventricular tachycardia in patients treated with arsenic trioxide for acute promyelocytic leukemia. *Ann Intern Med* 2000; **133:** 881–5.
5. Westervelt P, *et al.* Sudden death among patients with acute promyelocytic leukemia treated with arsenic trioxide. *Blood* 2001; **98:** 266–71.
6. Rust DM, Soignet SL. Risk/benefit profile of arsenic trioxide. *Oncologist* 2001; **6** (suppl 2): 29–32.

Treatment of Adverse Effects

Acute poisoning due to the ingestion of arsenic compounds should be treated by immediate gastric lavage if the patient presents within 1 hour and has not already vomited. Activated charcoal has been used to reduce absorption but is unlikely to be of benefit unless a significant amount of arsenic has been ingested. Intravenous replacement of fluids and electrolytes should be undertaken as necessary to correct dehydration and electrolyte imbalance; pressor agents may be required.

Chelation therapy should start immediately the cause of arsenic poisoning is suspected. The therapy of choice for acute poisoning is unithiol (p.1468) given intravenously in cases of gastrointestinal toxicity. Dimercaprol (p.1444) given intramuscularly is the second choice therapy if unithiol is unavailable. Oral therapy with unithiol or succimer (p.1466) should be substituted when gastrointestinal disturbances are no longer a problem. Oral penicillamine (p.1456) has also been used, including in conjunction with dimercaprol in severely ill patients, but its use in arsenic poisoning has been superseded by unithiol and succimer.

Patients suffering from chronic arsenic poisoning should be removed from the source of contamination as soon as possible. Initiation of oral chelation therapy with unithiol or succimer will depend on the patient's clinical condition and laboratory results of arsenic in urine, hair, and nails.

Chelation therapy should be continued until arsenic concentrations in urine have fallen to acceptable levels, although the therapeutic end-points of chelation therapy are poorly defined.

If renal failure occurs haemodialysis may be required.

Poisoning. The treatment of 3 patients who had ingested massive doses of arsenic has been described.[1,2] An adult survived after ingesting 54 g of arsenic trioxide:[1] in addition to standard supportive measures, attempts to remove the arsenic from his gastrointestinal tract included lavage, endoscopic removal, manual removal after gastrotomy, and cleansing enemas, plus chelation therapy. Of 2 siblings who ingested solubilised inorganic arsenic in a pesticide solution,[2] one child (aged 4 months) was estimated to have ingested 428 mg/kg arsenic and died despite aggressive attempts at removal of the arsenic, including chelation therapy, extracorporeal membrane oxygenation, exchange transfusion, and haemodialysis. The other child, aged 2 years, was estimated to have ingested 14.6 mg/kg arsenic, and survived following standard chelation therapy.

1. Dueñas-Laita A, *et al.* Acute arsenic poisoning. *Lancet* 2005; **365:** 1982.
2. Lai MW, *et al.* Acute arsenic poisoning in two siblings. *Pediatrics* 2005; **116:** 249–57.

Precautions

Patients receiving arsenic trioxide for acute promyelocytic leukaemia should have their ECG, blood sugar, electrolytes, blood count, and coagulation monitored at least twice weekly during induction and at least weekly during consolidation. More frequent monitoring may be needed in clinically unstable patients. Arsenic trioxide should be used with caution in renal impairment since renal excretion is the main route of elimination.

Pharmacokinetics

Water-soluble arsenic acids and their salts are more rapidly absorbed from the gastrointestinal tract than poorly soluble arsenicals such as arsenic trioxide. The absorption of arsenic trioxide is dependent upon the physical form of the compound and coarsely powdered material may be eliminated in the faeces before significant dissolution and absorption can occur. Soluble arsenic salts may also be absorbed following inhalation and through skin.

Once absorbed, arsenic is stored mainly in the liver, kidneys, heart, and lungs, with smaller amounts in the muscles and nervous tissue. About 2 weeks after ingestion, arsenic is deposited in the hair and nails and remains fixed to the keratin for years. It is also deposited in the bones and skin.

Although pentavalent arsenic is reduced to some degree *in vivo* to the more toxic trivalent form, trivalent arsenic is slowly and extensively oxidised to pentavalent arsenic. Both forms are methylated and excreted in the urine, mainly as dimethylarsinic acid, with smaller amounts appearing as monomethylarsonic acid and inorganic arsenic compounds. Although about 60% of a dose may be eliminated in the urine within 8 days, small amounts may continue to be excreted for several weeks after a single dose. Less significant amounts of arsenic are excreted in the faeces and sweat and via the lungs and skin. It is also distributed into breast milk and readily crosses the placenta.

Uses and Administration

Arsenic trioxide is used for induction of remission and consolidation in acute promyelocytic leukaemia (see below). It is given as an intravenous infusion over 1 to 2 hours to patients who are refractory to, or who have relapsed from, conventional therapy with retinoids and antineoplastics; if acute vasomotor reactions occur, the rate of infusion may be slowed and up to 4 hours may be taken. For induction, a dose of 150 micrograms/kg is given once daily until remission occurs; no more than 50 doses should be given (in the USA, the maximum number of induction doses allowed is 60). Treatment for consolidation must begin 3 to 4 weeks after completion of induction (or 3 to 6 weeks in the USA). The dose for consolidation is 150 micrograms/kg once daily given for 25 doses spread over a period of up to 5 weeks; the regimen suggested in the UK is to give the daily dose for 5 days each week followed by 2 days without dosing.

Arsenic trioxide is used in certain Asian herbal remedies. Arsenic anhydride has also been used.

Arsenic trioxide has been widely used as a constituent of weedkillers and sheepdips and as a rodenticide.

Arsenic trioxide and arsenic triiodide were formerly used internally as solutions or externally as ointments in the treatment of various skin diseases, but such use is generally no longer recommended. Externally, arsenic trioxide has a caustic action.

Homoeopathy. Arsenic trioxide has been used in homoeopathic medicines under the following names: Arsenious trioxide; Arsenici trioxidum; Arsenicum album; Acidum arsenicosum; Ars. alb.

Acute myeloid leukaemias. The use of arsenic trioxide in the management of patients with acute promyelocytic leukaemia (p.652) has been reviewed.[1-4] Remission was achieved in patients who had relapsed despite conventional therapy with retinoids and antineoplastics.[5,6] Arsenic trioxide is also being investigated for postremission therapy and in conjunction with transplantation.[4] Treatment was also successful in newly-diagnosed patients but severe liver toxicity occurred in some cases.[5]

For references to adverse effects occurring in patients receiving arsenic trioxide for acute promyelocytic leukaemia, see under Adverse Effects, above.

1. Soignet SL. Clinical experience of arsenic trioxide in relapsed acute promyelocytic leukemia. *Oncologist* 2001; **6** (suppl 2): 11–6.
2. Murgo AJ. Clinical trials of arsenic trioxide in hematologic and solid tumors: overview of the National Cancer Institute Cooperative Research and Development Studies. *Oncologist* 2001; **6** (suppl 2): 22–8.
3. Slack JL, *et al.* Advances in the management of acute promyelocytic leukemia and other hematologic malignancies with arsenic trioxide. *Oncologist* 2002; **7** (suppl 1): 1–13.
4. Douer D, Tallman MS. Arsenic trioxide: new clinical experience with an old medication in hematologic malignancies. *J Clin Oncol* 2005; **23:** 2396–2410.
5. Niu C, *et al.* Studies on treatment of acute promyelocytic leukemia with arsenic trioxide: remission induction, follow-up, and molecular monitoring in 11 newly diagnosed and 47 relapsed acute promyelocytic leukemia patients. *Blood* 1999; **94:** 3315–24.
6. Soignet SL, *et al.* United States multicenter study of arsenic trioxide in relapsed acute promyelocytic leukemia. *J Clin Oncol* 2001; **19:** 3852–60.

Multiple myeloma. Arsenic trioxide is under investigation for the treatment of relapsed or refractory multiple myeloma (p.658).

References.

1. Munshi NC. Arsenic trioxide: an emerging therapy for multiple myeloma. *Oncologist* 2001; **6** (suppl 2): 17–21.
2. Munshi NC, *et al.* Clinical activity of arsenic trioxide for the treatment of multiple myeloma. *Leukemia* 2002; **16:** 1835–7.
3. Bahlis NJ, *et al.* Feasibility and correlates of arsenic trioxide combined with ascorbic acid-mediated depletion of intracellular glutathione for the treatment of relapsed/refractory multiple myeloma. *Clin Cancer Res* 2002; **8:** 3658–68.
4. Berenson JR, Yeh HS. Arsenic compounds in the treatment of multiple myeloma: a new role for a historical remedy. *Clin Lymphoma Myeloma* 2006; **7:** 192–8.

Myelodysplastic syndromes. The use of arsenic trioxide for the treatment of myelodysplastic syndromes (p.654) is also under investigation.

References.

1. List A, *et al.* Opportunities for Trisenox (arsenic trioxide) in the treatment of myelodysplastic syndromes. *Leukemia* 2003; **17:** 1499–1507.
2. Vey N. Arsenic trioxide for the treatment of myelodysplastic syndromes. *Expert Opin Pharmacother* 2004; **5:** 613–21.
3. Schiller GJ, *et al.* Phase II multicenter study of arsenic trioxide in patients with myelodysplastic syndromes. *J Clin Oncol* 2006; **24:** 2456–64.
4. Vey N, *et al.* Arsenic trioxide in patients with myelodysplastic syndromes: a phase II multicenter study. *J Clin Oncol* 2006; **24:** 2465–71.
5. Sekeres MA. New data with arsenic trioxide in leukemias and myelodysplastic syndromes. *Clin Lymphoma Myeloma* 2007; **8** (suppl 1): S7–S12.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Trisenox; ***Belg.:*** Trisenox; ***Cz.:*** Trisenox; ***Fr.:*** Trisenox; ***Gr.:*** Trisenox; ***Ital.:*** Trisenox; ***Jpn:*** Trisenox; ***Neth.:*** Trisenox; ***Spain:*** Trisenox; ***UK:*** Trisenox; ***USA:*** Trisenox.

Multi-ingredient: ***Ital.:*** Pasta Arsenicale.

Arsine

Arsenic Trihydride; Arsina; Hydrogen Arsenide.

AsH_3 = 77.95.

CAS — 7784-42-1.

Profile

Arsine is a heavy colourless gas with a garlic-like odour, which has no clinical uses but is an environmental or occupational hazard. It is highly toxic and causes severe haemolysis which may result in acute renal failure. It is potentially toxic below the odour threshold of 0.5 ppm and dangerously toxic after exposure to as little as 3 ppm; there may be a latent period of up to 24 hours following exposure before symptoms develop. Symptoms of arsine gas poisoning include generalised weakness, muscle cramps, thirst, headache, abdominal pain, nausea, vomiting, anorexia, jaundice, bronze skin coloration, haemolytic anaemia, haematuria, oliguria, and anuria. Pulmonary oedema, ECG abnormalities, and neurological disorders have also been reported. Treatment involves exchange transfusions and haemodialysis; dimercaprol and other chelating agents have been used but are of no value in the acute stage and do not prevent haemolysis.

◊ References.

1. Fowler BA, Weissberg JB. Arsine poisoning. *N Engl J Med* 1974; **291:** 1171–4.
2. Hesdorffer CS, *et al.* Arsine gas poisoning: the importance of exchange transfusions in severe cases. *Br J Ind Med* 1986; **43:** 353–5.
3. Rael LT, *et al.* The effects of sulfur, thiol, and thiol inhibitor compounds on arsine-induced toxicity in the human erythrocyte membrane. *Toxicol Sci* 2000; **55:** 468–77.

Asafetida

Asafétida; Asafoetida; Asant; Devil's Dung; Gum Asafetida.

Pharmacopoeias. In *Chin.*

Profile

Asafetida is an oleo-gum resin obtained from various species of *Ferula* (Umbelliferae). It has been used as a carminative and antispasmodic. It was also formerly used as an expectorant. It is used in cooking and is an ingredient of certain foods.

◊ References.

1. Kelly KJ, *et al.* Methemoglobinemia in an infant treated with the folk remedy glycerited asafoetida. *Pediatrics* 1984; **73:** 717–19.

Preparations

Proprietary Preparations (details are given in Part 3)
S.Afr.: Duiwelsdrekdruppels.

Multi-ingredient: ***India:*** Tummy Ease; ***S.Afr.:*** Entressdruppels HM; Stuidruppels; ***Thai.:*** Flatulence; ***UK:*** Daily Tension & Strain Relief.

Asarabacca

Ásaro europeo; Hazelwort; Rhizoma Asari; Wild Nard.

NOTE. Asarabacca has also been used as a common name for *Aristolochia clematitis* (see Aristolochia, p.2260).

Profile

Asarabacca is the dried rhizome, roots, and leaves of *Asarum europaeum* (Aristolochiaceae), which is an ingredient of snuffs. It is also an irritant emetic and has been used in rodent poisons. Asarabacca is an ingredient of preparations given for respiratory disorders.

Homoeopathy. Asarabacca has been used in homoeopathic medicines under the following names: Asarum; Asarum europaeum; Asar. eur.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Escarol†.

Asbestos

Amianto; Asbesto.

Profile

The name asbestos is applied to several naturally occurring and widely distributed fibrous mineral silicates of the serpentine and amphibole groups. They include amosite (brown asbestos), anthophyllite, chrysotile (white asbestos), and crocidolite (blue asbestos).

Asbestos has properties of heat resistance, insulation, and reinforcement and has been used extensively for heat or electrical insulation, fire protection, in friction materials, and in the construction industry in a wide variety of materials including cement, pipes, and tiles.

When inhaled, asbestos fibres can cause asbestosis (pulmonary fibrosis), lung cancer, and mesothelioma of the pleura and peri-