life-threatening haemorrhage. Propranolol may also have a role in patients with portal hypertensive gastropathy. In a controlled study, propranolol reduced the incidence of recurrent bleeding from portal hypertensive gastropathy in patients with cirrhosis.[34]

Prophylaxis of a first bleed in patients with portal hypertension is controversial since about 70% of patients who have varices will never bleed, but should probably be given to patients with cirrhosis and varices thought to be at high risk of bleeding. A reliable system that will identify those at high risk of haemorrhage has yet to be devised. The NIEC (North Italian Endoscopic Club) system is probably the best so far,[35,36] and is based on size of the varices, presence of red wale marks on the varices, and Child-Pugh class; amendments to improve the traditional index have been suggested.[36] Sclerotherapy had been considered as a method of prophylaxis, but its value has not been clearly established. Studies show that beta blockers decrease the incidence of a first bleed[27,37] and are probably the treatment of choice if prophylaxis is to be given. Banding ligation may be a suitable alternative for patients who are unable to take beta blockers.[38] Others consider banding ligation to be the standard therapy for prophylaxis.[9] A meta-analysis[39] of 9 randomised controlled studies concluded that variceal banding ligation was superior to beta blockers in preventing a first variceal bleed, whereas a systematic review[40] of 16 randomised controlled studies found both treatments to be effective and suggested that the estimated effect of banding ligation in some studies may be biased and was associated with shorter duration of follow-up.

It is postulated that a reduction in portal pressure to below 12 mmHg is necessary to reduce the incidence of variceal bleeding and that treatment with beta blockers alone does not achieve this. More effective drugs are being sought, and isosorbide mononitrate[9,41,42] (as adjunctive therapy with a beta blocker) and clonidine[43] have been investigated for the prophylaxis of a first bleed and prevention of recurrent haemorrhage in patients with portal hypertension.

1. Williams SGJ, Westaby D. Management of variceal haemorrhage. *BMJ* 1994; **308:** 1213–17.
2. Roberts LR, Kamath PS. Pathophysiology and treatment of variceal hemorrhage. *Mayo Clin Proc* 1996; **71:** 973–83.
3. Sung JJY. Non-surgical treatment of variceal haemorrhage. *Br J Hosp Med* 1997; **57:** 162–6.
4. Stanely AJ, Haynes PC. Portal hypertension and variceal haemorrhage. *Lancet* 1997; **350:** 1235–9.
5. McCormack G, McCormick PA. A practical guide to the management of oesophageal varices. *Drugs* 1999; **57:** 327–35.
6. Dagher L, *et al.* Management of oesophageal varices. *Hosp Med* 2000; **61:** 711–17.
7. Anonymous. Early management of bleeding oesophageal varices. *Drug Ther Bull* 2000; **38:** 37–40.
8. Krige JEJ, Beckingham IJ. ABC of diseases of liver, pancreas, and biliary system. Portal hypertension—1: varices. *BMJ* 2001; **322:** 348–51.
9. Sharara AI, Rockey DC. Gastroesophageal variceal hemorrhage. *N Engl J Med* 2001; **345:** 669–81.
10. Anonymous. Portal hypertensive gastropathy. *Lancet* 1991; **338:** 1045–6.
11. D'Amico G, *et al.* Emergency sclerotherapy versus medical interventions for bleeding oesophageal varices in cirrhotic patients. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 08/02/06).
12. Abraldes JG, *et al.* Medical management of variceal bleeding in patients with cirrhosis. *Can J Gastroenterol* 2004; **18:** 109–13.
13. Bañares R, *et al.* Endoscopic treatment versus endoscopic plus pharmacologic treatment for acute variceal bleeding: a meta-analysis. *Hepatology* 2002; **35:** 609–15.
14. Escorsell À, *et al.* Multicenter randomized controlled trial of terlipressin versus sclerotherapy in the treatment of acute variceal bleeding: the TEST study. *Hepatology* 2000; **32:** 471–6.
15. Ioannou G, *et al.* Terlipressin for acute esophageal variceal hemorrhage. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 08/02/06).
16. Erstad BL. Octreotide for acute variceal bleeding. *Ann Pharmacother* 2001; **35:** 618–26.
17. Corley DA, *et al.* Octreotide for acute esophageal variceal bleeding: a meta-analysis. *Gastroenterology* 2001; **120:** 946–54.
18. Gøtzsche PC, Hróbjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2005 (accessed 08/02/06).
19. van Buuren HR, ter Borg PC. Transjugular intrahepatic portosystemic shunt (TIPS): indications and long-term patency. *Scand J Gastroenterol* 2003; **38** (Suppl 239): 100–104.
20. Bernard B, *et al.* Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. *Hepatology* 1999; **29:** 1655–61.
21. Hou M-C, *et al.* Antibiotic prophylaxis after endoscopic therapy prevents rebleeding in acute variceal hemorrhage: a randomized trial. *Hepatology* 2004; **39:** 746–53.
22. Laine L, Cook D. Endoscopic ligation compared with sclerotherapy for treatment of esophageal variceal bleeding: a meta-analysis. *Ann Intern Med* 1995; **123:** 280–7.
23. Wright AS, Rikkers LF. Current management of portal hypertension. *J Gastrointest Surg* 2005; **9:** 992–1005.
24. Nijhawan S, Rai RR. Does post-ligation oesophageal ulcer healing require treatment? *Lancet* 1994; **343:** 116–17.
25. Bosch J, Garcia-Pagan JC. Prevention of variceal rebleeding. *Lancet* 2003; **361:** 952–4.
26. Bernard B, *et al.* Beta-adrenergic antagonists in the prevention of gastrointestinal rebleeding in patients with cirrhosis: a meta-analysis. *Hepatology* 1997; **25:** 63–70.
27. Talwalkar JA, Kamath PS. An evidence-based medicine approach to beta-blocker therapy in patients with cirrhosis. *Am J Med* 2004; **116:** 759–66.
28. Villanueva C, *et al.* Nadolol plus isosorbide mononitrate compared with sclerotherapy for the prevention of variceal rebleeding. *N Engl J Med* 1996; **334:** 1624–9.
29. Groszmann RJ, Garcia-Tsao G. Endoscopic variceal banding vs. pharmacological therapy for the prevention of recurrent variceal hemorrhage: what makes the difference? *Gastroenterology* 2002; **123:** 1388–91.
30. Jenkins SA, *et al.* Randomised trial of octreotide for long term management of cirrhosis after variceal haemorrhage. *BMJ* 1997; **315:** 1338–41.
31. Sanyal AJ, *et al.* Transjugular intrahepatic portosystemic shunts compared with endoscopic sclerotherapy for the prevention of recurrent variceal hemorrhage: a randomized, controlled trial. *Ann Intern Med* 1997; **126:** 849–57.
32. Cello JP, *et al.* Endoscopic sclerotherapy compared with percutaneous transjugular intrahepatic portosystemic shunt after initial sclerotherapy in patients with acute variceal hemorrhage: a randomized, controlled trial. *Ann Intern Med* 1997; **126:** 858–65.
33. Rössle M, *et al.* Randomised trial of transjugular-intrahepatic-portosystemic shunt versus endoscopy plus propranolol for prevention of variceal rebleeding. *Lancet* 1997; **349:** 1043–9.
34. Pérez-Ayuso RM, *et al.* Propranolol in prevention of recurrent bleeding from severe portal hypertensive gastropathy in cirrhosis. *Lancet* 1991; **337:** 1431–4.
35. The North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices: a prospective multicenter study. *N Engl J Med* 1988; **319:** 983–9.
36. Merkel C, *et al.* Prognostic indicators of risk for first variceal bleeding in cirrhosis: a multicenter study in 711 patients to validate and improve the North Italian Endoscopic Club (NIEC) index. *Am J Gastroenterol* 2000; **95:** 2915–20.
37. Pagliaro L, *et al.* Prevention of first bleeding in cirrhosis: a meta-analysis of randomised trials of nonsurgical treatment. *Ann Intern Med* 1992; **117:** 59–70.
38. Burroughs AK, Patch D. Primary prevention of bleeding from esophageal varices. *N Engl J Med* 1999; **340:** 1033–5.
39. Tripathi D, *et al.* Variceal band ligation versus beta-blockers for primary prevention of variceal bleeding: a meta-analysis. *Eur J Gastroenterol Hepatol* 2007; **19:** 835–45.
40. Gluud LL, *et al.* Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. *Am J Gastroenterol* 2007; **102:** 2842–8.
41. Angelico M, *et al.* Isosorbide-5-mononitrate versus propranolol in the prevention of first bleeding in cirrhosis. *Gastroenterology* 1993; **104:** 1460–5.
42. Merkel C, *et al.* Randomised trial of nadolol alone or with isosorbide mononitrate for primary prophylaxis of variceal bleeding in cirrhosis. *Lancet* 1996; **348:** 1677–81.
43. Blendis LM. Clonidine for portal hypertension: a sympathetic solution? *Ann Intern Med* 1992; **116:** 515–17.

Varicose veins. Varicose veins are tortuous, protruding veins in the legs, that occur when weak vein walls and valve incompetence result in venous reflux and dilatation. Symptoms associated with varicose veins include heaviness, tension, aching, and itching of the legs. Complications include oedema, thrombophlebitis, deep venous thrombosis, lipodermatosclerosis, and venous ulceration. Risk factors for varicose veins include increasing age, pregnancy, and occupations that involve prolonged standing.[1]

The management of varicose veins has been reviewed.[1-3] Conservative management using compression hosiery may be effective for relief of symptoms in some patients but longer-term compliance is poor.[3] Surgery or sclerotherapy are other treatment options, depending on the veins affected. Surgical treatment, which is the gold standard for treatment of more severe varicose veins, may involve ligation of the affected vein, stripping of the affected stem vein, or avulsions of the varicosities.[3] In sclerotherapy, which may be the treatment of choice for thread veins,[2] a sclerosant is injected into the affected vein where it irritates and damages the lining of the vein causing local thrombosis, fibrosis, and stenosis. Detergent sclerosants include monoethanolamine oleate, sodium tetradecyl sulfate, lauromacrogol 400, and sodium morrhuate; osmotic sclerosants include hypertonic sodium chloride solutions, and hypertonic mixtures of sodium chloride and glucose; caustic sclerosants include chromated glycerol, and a mixture of iodine and sodium iodide. Graduated compression dressings are usually applied after sclerotherapy to minimise the time taken for the surrounding tissue to absorb the damaged segment of vein. Compression may also help to reduce complications of sclerotherapy including hyperpigmentation, oedema, aching, thrombophlebitis, and deep venous thrombosis. A systematic review[4] of randomised controlled trials of injection sclerotherapy failed to determine its place in the overall management of varicose veins, since the type of sclerosant, formulation, local pressure dressing, or degree and length of compression do not appear to have a significant effect on efficacy. However, the evidence supports its current place in practice, which is in the treatment of recurrent varicose veins following surgery, and thread veins. In another systematic review,[5] the use of surgery or sclerotherapy for the management of primary varicose veins was compared. There was a tendency for better early outcomes with sclerotherapy whereas surgery produced more long-term benefits. However, there was insufficient evidence to recommend the use of one form of treatment over the other, and the extent of the varicose veins ultimately governs the choice.

New methods of treatment being tried include foam sclerotherapy, in which a detergent-like sclerosant is mixed with air to create a foam,[2] ambulatory phlebectomy, endovenous laser therapy, and radiofrequency ablation.[3,6]

1. London NJ, Nash R. ABC of arterial and venous disease: varicose veins. *BMJ* 2000; **320:** 1391–4.
2. Rabe E, *et al.* German Society of Phlebology. Guidelines for sclerotherapy of varicose veins (ICD 10: I83.0, I83.1, I83.2, and I83.9). *Dermatol Surg* 2004; **30:** 687–93.
3. Beale RJ, Gough MJ. Treatment options for primary varicose veins—a review. *Eur J Vasc Endovasc Surg* 2005; **30:** 83–95.
4. Tisi PV, *et al.* Injection sclerotherapy for varicose veins. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 04/06/08).
5. Rigby KA, *et al.* Surgery versus sclerotherapy for the treatment of varicose veins. Available in the Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 09/02/06).
6. Sadick NS. Advances in the treatment of varicose veins: ambulatory phlebectomy, foam sclerotherapy, endovascular laser, and radiofrequency closure. *Dermatol Clin* 2005; **23:** 443–55.

Preparations

BP 2008: Ethanolamine Oleate Injection.

Proprietary Preparations (details are given in Part 3)
Braz.: Ethamolin; ***Jpn:*** Oldamin; ***USA:*** Ethamolin.

Monosodium Glutamate

Chinese Seasoning; E621; Glutamato monosódico; MSG; Natrii Glutamas; Sodium Glutamate. Sodium hydrogen L-(+)-2-aminoglutarate monohydrate.

$C_5H_8NNaO_4,H_2O$ = 187.1.
CAS — 142-47-2 (anhydrous monosodium glutamate).

Pharmacopoeias. In *Chin.* Also in *USNF.*
USNF 26 (Monosodium Glutamate). White, practically odourless, free-flowing crystals or crystalline powder. It may have either a slightly sweet or slightly salty taste. Freely soluble in water; sparingly soluble in alcohol. pH of a 5% solution in water is between 6.7 and 7.2. Store in airtight containers.

Profile

Monosodium glutamate is widely used as a flavour enhancer and imparts a meaty flavour.

In susceptible individuals, ingestion of foods containing monosodium glutamate may cause MSG symptom complex, a condition characterised by burning sensations, or numbness, in the back of the neck and arms, tingling or warmth or weakness in the face, back and neck, facial pressure, chest pain, headache, nausea, drowsiness or weakness. In patients with asthma, who may be predisposed to develop this condition, bronchospasm may occur. The symptoms tend to occur within an hour of eating 3 g or more of monosodium glutamate on an empty stomach.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Chile:*** Glutacyl Vitaminado; ***Thai.:*** Hemo-Cyto-Serum.

Motherwort

Agripalma; Agripaume, herbe de; Hjärtstilla; Leonuri cardiacae herba; Leonuri Herba; Leonurus; Motherwort Herb; Nukula; Srdečníková nať; Sukatžolių žolė.

Pharmacopoeias. In *Eur.* (see p.vii). *Chin.* includes the fruit.
Ph. Eur. 6.2 (Motherwort). The whole or cut, dried, flowering aerial parts of *Leonurus cardiaca*. It contains not less than 0.2% of flavonoids, expressed as hyperoside ($C_{21}H_{20}O_{12}$ = 464.4) calculated with reference to the dried drug. Protect from light.

Profile

Motherwort is given in herbal medicine for nervous and cardiac disorders; it is also used in products promoted for mild hyperthyroidism.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Pacifenity†; Valerian†; ***Austria:*** Thyreogutt; ***Canad.:*** Thunas Tab for Menstrual Pain†; ***Fr.:*** Biocarde; ***Ger.:*** Biovital Aktiv†; Biovital Classic; Mutellon; Oxacant N†; Oxacant-sedativ; ***Hung.:*** Biovital†; ***Pol.:*** Biovital N; Klimax†; Lumewal; Nervinolum; Nerwobonisol; ***Switz.:*** Tisane pour le coeur et la circulation; ***UK:*** Menopause Relief; Modern Herbals Stress; Period Pain Relief; Prementaid; Quiet Life; SuNerven; Wellwoman.

Moxaverine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de moxaverina; Meteverine Hydrochloride; Moxavérine, Chlorhydrate de; Moxaverini Hydrochloridum. 1-Benzyl-3-ethyl-6,7-dimethoxyisoquinoline hydrochloride.

Моксаверина Гидрохлорид

$C_{20}H_{21}NO_2,HCl$ = 343.8.
CAS — 10539-19-2 (moxaverine); 1163-37-7 (moxaverine hydrochloride).
ATC — A03AD30.
ATC Vet — QA03AD30.

Profile

Moxaverine hydrochloride has a similar structure to papaverine (p.2191) and has been given by mouth and injection as an antispasmodic and in vascular disorders. The base is also used as an antispasmodic.

Doses of moxaverine hydrochloride of up to 300 mg three times daily by mouth have been suggested for the treatment of vasospastic disorders; it has also been given by intravenous infusion.

Much lower doses have been recommended for the treatment of gastrointestinal and biliary-tract spasm.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Certonal†; Kollateral.

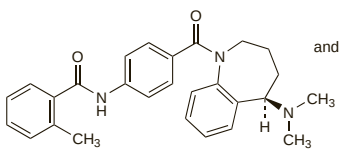
Multi-ingredient: ***Austria:*** Hedonin.

Mozavaptan *(rINN)* ⊗

Manavaptan; Mozavaptán; Mozavaptanum; OPC-31260. *N*-(4-{[(5*RS*)-5-(Dimethylamino)-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-yl]carbonyl}phenyl)-2-methylbenzamide.

Мозаваптан

$C_{27}H_{29}N_3O_2$ = 427.5.
CAS — 137975-06-5.



and enantiomer

Profile
Mozavaptan is a selective vasopressin V_2-receptor antagonist used for the treatment of hyponatraemia in cancer-related syndrome of inappropriate antidiuretic hormone secretion.

Mulungu

Profile
The bark of the mulungu tree, *Erythrina verna* (*E. mulungu*) Fabaceae, has traditionally been used in South America as a sedative and as a hypotensive.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Anevrase†; Calmapax; Elixir de Passiflora†; Passaneuro; Passicalm†; Passiflora Composta†; Passilex†; Sedalin†; Xarope Sao Joao†.

Mumps Skin Test Antigen

Parotiditis, prueba cutánea contra el antígeno de la.

Pharmacopoeias. In *US*.
USP 31 (Mumps Skin Test Antigen). A sterile suspension of formaldehyde-inactivated mumps virus prepared from the extra-embryonic fluid of virus-infected chick embryos, concentrated and purified by differential centrifugation, and diluted with isotonic sodium chloride solution. It contains a preservative and glycine as a stabilising agent. Each mL contains not less than 20 complement-fixing units. It should be stored at 2° to 8°. The expiry date is not later than 18 months after date of manufacture or of release from manufacturer's cold storage.

Profile
Recovery from mumps produces skin hypersensitivity to mumps virus. Mumps skin test antigen, has been used with other antigens to assess the status of cell-mediated immunity. A positive reaction may indicate previous infection with mumps virus but it is not considered to be very reliable. It should not be given to patients hypersensitive to egg protein.

Preparations

USP 31: Mumps Skin Test Antigen.

Proprietary Preparations (details are given in Part 3)
USA: MSTA†.

Muramidase Hydrochloride

N-Acetylmuramide Glycanohydrolase Hydrochloride; E1105 (muramidase); Globulin G_1 Hydrochloride; Lysozyme Hydrochloride; Muramidasa, hidrocloruro de.

CAS — 9001-63-2 (muramidase); 9066-59-5 (muramidase hydrochloride).
ATC — D06BB07; J05AX02.
ATC Vet — QD06BB07; QJ05AX02.

Pharmacopoeias. In *Jpn*.

Profile
Muramidase is a mucopolysaccharidase normally present in saliva and other tissues and secretions. It is active against Gram-positive bacteria, possibly by transforming the insoluble polysaccharides of the cell wall to soluble mucopeptides. It is also thought to be active against some viruses and some Gram-negative bacteria.

Muramidase has been given, usually as the hydrochloride, to patients with herpes zoster and other painful viral infections, and for mouth and respiratory-tract disorders. It has been used with antibacterials in an attempt to enhance their activity. Sensitivity reactions have been reported.

Adverse effects. A report[1] of a toxic epidermal necrolysis-type drug eruption in a patient who took an oral cold preparation containing muramidase chloride, which was considered to be the probable cause. The patient's condition improved after intravenous corticosteroid therapy.

1. Kobayashi M, *et al*. A case of toxic epidermal necrolysis-type drug eruption induced by oral lysozyme chloride. *J Dermatol* 2000; **27:** 401–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Murazyme; ***Braz.:*** Murazyme†; ***Hong Kong:*** CP-Lyso; Eurozyme; Flemizyme; Jemizym†; Leftose; Lysosmin; Neuzym; ***Ital.:*** Immunozima†; ***Jpn:*** Leftose; Neuzym; ***Malaysia:*** Leftose†; Neuzym; Noflux; ***Singapore:*** Leftose; Lyzyme; Neuflo; Neuzyme; ***Thai.:*** Leftose.

Multi-ingredient: ***Arg.:*** Bim†; Gammanova†; ***Braz.:*** Colpistar; Tricomax; Trinotrex†; ***Cz.:*** Laryprontt†; ***Fr.:*** Cantalene; Glossithiase; Hexalyse; Lyso-6; Lysopaine; ***Ger.:*** Frubienzym; ***Gr.:*** Lyso-6; Lysopaine; Sopain-Plus; ***Hong Kong:*** Hexalyse; Quadezyme; ***Ital.:*** Narlisim; ***Port.:*** Narizima; ***Rus.:*** Hexalyse (Гексализ); Lysobact (Лизобакт); ***Singapore:*** Biotene; ***Spain:*** Egarone†; Espectral†; Lizipaina; Normo Nar†; Pulmotropic; Rino Dexa; Trofalgon; ***Switz.:*** Arbid-top; Gem; Lyso-6†; Lysopaine; Mebucasol f; Sangerol; ***Thai.:*** Siduol; ***UK:*** Biotene Dry Mouth; BioXtra†; ***USA:*** Biotene with Calcium.

Poisonous Mushrooms or Toadstools

Champignons vénéneux; Giftpilze; Setas venenosas.

CAS — 23109-05-9 (α-amanitin); 21150-22-1 (β-amanitin); 21150-23-2 (γ-amanitin); 58919-61-2 (coprine); 16568-02-8 (gyromitrin); 2552-55-8 (ibotenic acid); 60-34-4 (methylhydrazine); 300-54-9 (muscarine); 2763-96-4 (muscimol); 37338-80-0 (orellanine); 17466-45-4 (phalloidin); 28227-92-1 (phalloin); 39412-56-1 (phallolysin).

Classification
This monograph describes poisonous mushrooms often known as toadstools, their toxins, toxic effects, and the treatment of those effects. Their only use is in homoeopathic medicine (see below). *Amanita muscaria* and *Psilocybe* spp. are abused for their psychoactive properties (see also Psilocin, p.2375).

Mushrooms can be classified into 8 groups according to their principal toxins and toxic effects:

- *Group I.* Most deaths due to mushroom poisoning follow the ingestion of mushrooms containing cyclopeptides and among these mushrooms *Amanita phalloides* ('death cap') has been reported to be responsible for 90% of all mushroom fatalities. The cyclopeptides are a group of heat-stable cyclic polypeptides with molecular weights ranging from 800 to 1100 and include the amatoxins (α-, β-, γ-amanitin) and phallotoxins (phalloidin, phaloin, phallolysin). Other mushrooms containing cyclopeptides include *A. verna* ('deadly agaric', 'fool's mushroom'), *A. virosa*, ('destroying angel') and *A. bisporigera* ('white destroying angel'), and *Galerina autumnalis*, *G. marginata*, and *G. venenata*.
- *Group II.* Although *A. muscaria* ('fly agaric') and *A. pantherina* ('panther cap', 'false blusher') may contain small amounts of muscarine, the antimuscarinic effects of the hallucinogenic agent muscimol and the insecticidal agent ibotenic acid usually predominate.
- *Group III.* Many species of *Gyromitra* contain toxins known as gyromitrins that decompose to release methylhydrazine (monomethylhydrazine; MMH) an inhibitor of the coenzyme pyridoxal phosphate.
- *Group IV.* Mushrooms whose principal toxin is muscarine include many of the *Clitocybe* and *Inocybe* spp. *A. muscaria* and *A. pantherina* (see above) may also contain small amounts.
- *Group V. Coprinus atramentarius* ('ink cap') contains the compound coprine, one of whose metabolites is an inhibitor of acetaldehyde dehydrogenase and it may therefore produce 'disulfiram-like' symptoms after drinking alcohol.
- *Group VI.* Mushrooms that may contain the hallucinogenic indoles psilocin and psilocybine include species of *Psilocybe*, *Panaeolus*, *Gymnopilus*, *Stropharia*, and *Conocybe*.
- *Group VII.* Many mushrooms that only act as gastrointestinal irritants and do not produce systemic effects are included in this group.
- *Group VIII.* A further group has sometimes been used to classify some species of *Cortinarius* that contain a renal toxin thought by some to be orellanine, but whose exact nature remains to be determined.

Adverse Effects
The clinical course of poisoning due to mushrooms is related to their principal toxins:

- *Group I.* Initial symptoms may occur 6 to 24 hours after ingestion of mushrooms containing cyclopeptides, and usually consist of gastrointestinal effects such as abdominal pain, nausea, severe vomiting, and profuse diarrhoea similar to that in cholera. The patient may then appear to recover and be symptom-free for 2 to 3 days, although liver-enzyme values may be increasing. After this phase, the more serious toxic effects of the amatoxins become apparent and there are signs of hepatic, renal, cardiac, and CNS toxicity. Symptoms include jaundice, oliguria, anuria, hypoglycaemia, coagulopathies, circulatory collapse, convulsions, and coma. The mortality rate is high in this third phase, with death usually being due to hepatic failure following hepatic necrosis. Up to 90% of untreated patients may die, though the rate can be as low as 15 to 30% after treatment.
- *Group II.* The adverse effects of mushrooms containing ibotenic acid and muscimol usually occur within 2 hours of ingestion. Symptoms may include ataxia, euphoria, delirium, and hallucinations associated with other antimuscarinic effects. Fatalities are rare.
- *Group III.* Patients who have ingested mushrooms containing gyromitrins usually develop symptoms of poisoning within 6 to 24 hours. These consist initially of nausea, vomiting, abdominal pain, and muscle cramps, headache, dizziness and fatigue. Delirium, convulsions, coma, methaemoglobinaemia and haemolysis may also occur. Occasionally jaundice and hepatic necrosis lead to hepatic failure and death. Up to 40% of patients die.
- *Group IV.* Symptoms typical of 'cholinergic crisis' (see Adverse Effects of Neostigmine, p.631) may appear about 30 minutes to 2 hours after ingestion of mushrooms containing muscarine. These include bradycardia, bronchospasm, salivation, perspiration, lachrymation, rhinorrhoea, involuntary urination and defaecation, and diarrhoea. Miosis, hypotension, and cardiac arrhythmias may also occur. Rarely death may follow due to cardiac arrest or respiratory-tract obstruction.
- *Group V.* Since one of the metabolites of coprine is an acetaldehyde dehydrogenase inhibitor, drinking alcohol, even up to several days after ingestion of mushrooms containing this compound, will produce symptoms similar to those of the 'disulfiram-alcohol' interaction (see Disulfiram, Adverse Effects, p.2296). Fatalities are rare.
- *Group VI.* The adverse effects of ingestion of mushrooms containing psilocin and psilocybine are similar to those described under lysergide (p.2335). Symptoms usually occur within about 30 minutes to 2 hours. Fatalities are rare.
- *Group VII.* Generally no treatment is required for adverse gastrointestinal effects seen with this group of mushrooms.
- *Group VIII.* There may be a delay of as long as 14 to 20 days before symptoms of poisoning due to *Cortinarius* appear. Patients will develop an intense thirst. Other symptoms usually include nausea, vomiting, diarrhoea, and anorexia. Muscle aching and spasms and a feeling of coldness may also occur. In severe cases renal failure may lead to death. It has been reported that up to 15% of patients die.

Pregnancy. α-Amanitine does not appear to cross the placental barrier, even during the acute phase of intoxication.[1]

1. Belliardo F, *et al*. Amatoxins do not cross the placental barrier. *Lancet* 1983; **i:** 1381.

Treatment of Adverse Effects
As there are no specific antidotes for the majority of cases of mushroom poisoning and which species is involved is often unknown, treatment consists primarily of symptomatic and supportive measures. The stomach may be emptied by gastric lavage if the patient has not already vomited spontaneously. However, if presentation is delayed (because of the slow onset of symptoms seen with some types of mushrooms) measures to empty the stomach are unlikely to be productive. Activated charcoal may be of use in binding toxins in the gastrointestinal tract and preventing absorption. Determining the interval between ingestion and the onset of symptoms often helps to identify the type of mushrooms ingested. If possible specimens of the mushrooms or a sample of the stomach contents should be sent to an expert mycologist for identification. Particular attention should be paid to intravenous replacement of fluids and electrolytes especially if vomiting and diarrhoea are severe. If the ingestion of hepatotoxic or nephrotoxic mushrooms is suspected liver and renal function should be monitored.

Since some mushrooms contain a wide range of toxins and patients may have ingested more than one species, specific therapy should only be instituted following positive identification.

- *Group I.* There is little clinical evidence to support the efficacy of specific agents or treatments for the management of cyclopeptide poisoning. Drugs such as benzylpenicillin, silymarin or silibinin have been given to try to protect the liver against the hepatotoxic effects of the amatoxins. Exchange transfusions, haemodialysis, or charcoal haemoperfusion have been tried to facilitate amatoxin removal. The removal of bile via a duodenal tube left *in situ* has been suggested to reduce enterohepatic circulation of amatoxins. Forced diuresis has also been advocated. Liver transplantation may be required for progressive hepatic failure. A radio-immunoassay for the detection of amatoxins is available in some countries to confirm a diagnosis of cyclopeptide poisoning.