The best-studied treatment for PBC is ursodeoxycholic acid, which is thought to replace toxic endogenous bile acids, stimulate bile acid secretion, and exert local immunosuppressive and cytoprotective effects.[1,4,5,7-9] The value of ursodeoxycholic acid is controversial: its reported therapeutic benefits in terms of delaying disease progression and the need for liver transplantation[5,10] have not been confirmed by meta-analysis or systematic review.[11,12] Both of these were, however, criticised[13,14] on the grounds that most of the studies included had follow-up periods of only 2 years. In consequence, some do not recommend its use,[12,15] but others still believe it to be the treatment of choice.[1,7,13,14,16] Its advocates consider that it appears to be efficacious for about 10 years and improves long-term survival by delaying the progression of hepatic fibrosis, development of oesophageal varices, and the need for liver transplantation. However, it is not effective in the presence of extensive fibrosis or cirrhosis in advanced disease.[13,14,16]

Both penicillamine and azathioprine have been used in PBC, but trials have failed to show any benefit from treatment[5-7] and their use has declined. A systematic review[17] identified a significant increase in the occurrence of adverse effects with penicillamine and concluded that its use could not be supported for patients with PBC. Corticosteroids, colchicine, ciclosporin, and chlorambucil have also been tried, but toxicity has restricted their use.[5,7] They may be of benefit[2,4,6,7] when used with ursodeoxycholic acid, although some guidelines[5] do not recommend their use. A systematic review[18] of studies with methotrexate concluded that it tended to increase mortality or the need for liver transplantation and should not therefore be used in patients with PBC outside clinical trials. Budesonide[7] and bezafibrate[1,7] have also been tried.

Symptomatic treatment includes the use of bile acid sequestrants, such as colestyramine, to treat both pruritus and hypercholesterolaemia. Ursodeoxycholic acid may also improve pruritus in up to 40% of patients, and rifampicin, phenobarbital, and opioid antagonists are used as second-line therapies.[1,4,5,8] Vitamin D and calcium supplementation will prevent osteomalacia; supplementation with vitamins A, E, and K may also be necessary.[1,4,5,8] Liver transplantation is recommended for liver failure, although PBC can recur in the allograft.[5,13,14,16]

1. Nishio A, *et al.* Primary biliary cirrhosis: lessons learned from an organ-specific disease. *Clin Exp Med* 2001; **1:** 165–78.
2. Kaplan MM. Primary biliary cirrhosis: past, present, and future. *Gastroenterology* 2002; **123:** 1392–4.
3. Mason A, Nair S. Primary biliary cirrhosis: new thoughts on pathophysiology and treatment. *Curr Gastroenterol Rep* 2002; **4:** 45–51.
4. Poupon R, Poupon RE. Treatment of primary biliary cirrhosis. *Baillieres Best Pract Res Clin Gastroenterol* 2000; **14:** 615–28.
5. Heathcote EJ. Management of primary biliary cirrhosis. *Hepatology* 2000; **31:** 1005–13.
6. Heathcote EJ. Evidence-based therapy of primary biliary cirrhosis. *Eur J Gastroenterol Hepatol* 1999; **11:** 607–15.
7. Holtmeier J, Leuschner U. Medical treatment of primary biliary cirrhosis and primary sclerosing cholangitis. *Digestion* 2001; **64:** 137–50.
8. Prince MI, Jones DE. Primary biliary cirrhosis: new perspectives in diagnosis and treatment. *Postgrad Med J* 2000; **76:** 199–206.
9. Lindor K. Ursodeoxycholic acid for the treatment of primary biliary cirrhosis. *N Engl J Med* 2007; **357:** 1524–9.
10. Lindor KD, *et al.* Ursodeoxycholic acid for primary biliary cirrhosis. *Lancet* 2000; **355:** 657–8.
11. Gluud C, Christensen E. Ursodeoxycholic acid for primary biliary cirrhosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2001 (accessed 04/04/06).
12. Goulis J, *et al.* Randomised controlled trials of ursodeoxycholic-acid therapy for primary biliary cirrhosis: a meta-analysis. *Lancet* 1999; **354:** 1053–60.
13. Talwalkar JA, Lindor KD. Primary biliary cirrhosis. *Lancet* 2003; **362:** 53–61.
14. Kaplan MM, Gershwin ME. Primary biliary cirrhosis. *N Engl J Med* 2005; **353:** 1261–73. Correction. *ibid.* 2006; **354:** 313.
15. Anonymous. Ursodeoxycholic acid for primary biliary cirrhosis. *Drug Ther Bull* 1999; **37:** 30–2.
16. Oo YH, Neuberger J. Options for treatment of primary biliary cirrhosis. *Drugs* 2004; **64:** 2261–71.
17. Gong Y, *et al.* -Penicillamine for primary biliary cirrhosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 04/04/06).
18. Gong Y, Gluud C. Methotrexate for primary biliary cirrhosis. Available in the Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2005 (accessed 04/04/06).

Gallstones. Gallstones (cholelithiasis) occur when mechanisms for the solubilisation of cholesterol or bilirubin fail or are overcome. They may be divided into those formed of pure cholesterol, which are usually solitary; pigment stones, largely made up of bilirubin or its derivatives; and mixed stones of cholesterol, bile pigment, and calcium salts, which form the great majority of cases seen in the West.

Gallstones are generally more common in women than in men. The prevalence also increases with age and obesity, although rapid weight loss as a result of dieting or surgery is associated with an increased risk.

As many as two-thirds of patients with gallstones are asymptomatic. Symptoms usually relate to the site of the stone although biliary colic is often present regardless of whether the stone is in the gallbladder or biliary tract. If the stone blocks the exit from the gallbladder, inflammation and bacterial infection may follow (acute cholecystitis), sometimes leading to perforation and subsequent peritonitis. Less commonly, obstruction of the common bile duct by gallstones (choledocholithiasis) may lead to cholestasis and jaundice; infection of the bile ducts and septicaemia may follow. Pancreatitis may also be associated with gallstone disease, and there may be an increased risk of developing malignant neoplasms of the gallbladder.

Treatment. Asymptomatic gallstones discovered during other investigations should not be treated, and even mildly symptomatic patients may be managed with analgesics and subsequent observation. Potent analgesics such as morphine may be needed in more severe cases (see Biliary and Renal Colic, p.5). In symptomatic patients the preferred treatment for gallstones is surgical removal of the gallbladder; laparoscopic cholecystectomy causes less postoperative morbidity than open surgery, and has largely replaced other methods of treatment.

In patients unsuited to, or unwilling to undergo, surgery for gallbladder stones, drug therapy, alone or with lithotripsy, may be considered.

Exogenous bile acids have been tried in an attempt to dissolve the cholesterol component of gallstones. Ursodeoxycholic acid is more effective and is associated with fewer adverse effects than chenodeoxycholic acid. Combination therapy has also been tried but this is no more effective than ursodeoxycholic acid alone. Dissolution of gallstones is slow but can be achieved in about one-third of cases with the best results seen with small stones. However, about half of all successfully treated patients will develop further gallstones within 10 years. Studies of prophylactic bile acid therapy have mostly yielded disappointing results, although such therapy may be of benefit in patients on very-low-calorie diets, after surgery for weight loss, and in those receiving treatment with octreotide.

Somewhat larger stones may respond to extracorporeal shock-wave lithotripsy, or fluoroscopically guided laser lithotripsy, which may be more effective. Oral bile acids should then be given to dissolve the stone fragments.

Another method that has been used is the direct instillation of a solvent (usually methyl *tert*-butyl ether) into the gallbladder, which dissolves stones within a matter of hours, and is effective against almost all cholesterol-based stones regardless of size and number. Care is required to avoid overflow of the solvent into the common bile duct or the duodenum, where it can cause inflammation. Other solvents, such as ethyl propionate have been investigated as potentially less toxic alternatives, and edetic acid has been suggested as a possible solvent for non-cholesterol gallstones. As with all non-surgical methods, recurrence is likely.

Patients with **stones in the common bile duct** or **acute cholecystitis** require prompt therapy because of the risk of serious complications; endoscopic sphincterotomy and physical retrieval of the stones with a basket or balloon appears to be the preferred treatment, with open surgery as an alternative. A biliary stent to allow bile flow around the stone has been used as a temporary measure in patients with stones too large to remove by endoscopic sphincterotomy. Lithotripsy or infusion of a solvent such as monoctanoin or methyl *tert*-butyl ether are possible alternatives in patients unfit for surgery.

In patients who develop cholecystitis or cholangitis antibacterial therapy may be required (see Biliary-tract Infections, p.164).

References.

1. Johnston DE, Kaplan MM. Pathogenesis and treatment of gallstones. *N Engl J Med* 1993; **328:** 412–21.
2. Ransohoff DF, Gracie WA. Treatment of gallstones. *Ann Intern Med* 1993; **119:** 606–19.
3. May GR, *et al.* Efficacy of bile acid therapy for gallstone dissolution: a meta-analysis of randomized trials. *Aliment Pharmacol Ther* 1993; **7:** 139–48.
4. Hofmann AF, *et al.* Pathogenesis and treatment of gallstones. *N Engl J Med* 1993; **328:** 1854–5.
5. Anonymous. Managing patients with gallstones. *Drug Ther Bull* 1994; **32:** 33–5.
6. Lanzini A, Northfield TC. Pharmacological treatment of gallstones: practical guidelines. *Drugs* 1994; **47:** 458–70.
7. Tait N, Little JM. The treatment of gall stones. *BMJ* 1995; **311:** 99–105.
8. Jakobs R, *et al.* Fluoroscopically guided laser lithotripsy versus extracorporeal shock wave lithotripsy for retained bile duct stones: a prospective randomised study. *Gut* 1997; **40:** 678–82.
9. Toouli J, Wright TA. Gallstones. *Med J Aust* 1998; **169:** 166–71.
10. Bateson MC. Gallbladder disease. *BMJ* 1999; **318:** 1745–8.
11. Ahmed A, *et al.* Management of gallstones and their complications. *Am Fam Physician* 2000; **61:** 1673–80.
12. Bellows CF, *et al.* Management of gallstones. *Am Fam Physician* 2005; **72:** 637–42.
13. Portincasa P, *et al.* Cholesterol gallstone disease. *Lancet* 2006; **368:** 230–9.
14. Caddy GR, Tham TCK. Symptoms, diagnosis and endoscopic management of common bile duct stones. *Best Pract Res Clin Gastroenterol* 2006; **20:** 1085–1101.

Preparations

BP 2008: Ursodeoxycholic Acid Capsules; Ursodeoxycholic Acid Tablets; ***USP 31:*** Ursodiol Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Dexo; Solutrat; UDCA; Ursidesox; Ursomax; Urzac; ***Austral.:*** Ursofalk; ***Austria:*** Ursofalk; ***Belg.:*** Ursochol; Ursofalk; ***Braz.:*** Ursacol; ***Canad.:*** Urso; ***Chile:*** Solvobil; Ursofalk; ***Cz.:*** Ursochol; Ursofalk; Ursosan; ***Fin.:*** Adursal; ***Fr.:*** Delursan; Ursolvan; ***Ger.:*** Cholit-Ursan; Cholofalk; UDC; Urso†; Ursochol; Ursofalk; ***Gr.:*** Ursofalk; ***Hong Kong:*** Ursofalk; Ursosan; ***Hung.:*** Ursofalk; ***India:*** Udiliv; ***Indon.:*** Estazor; Pramur; Urdafalk; Urdahex; ***Irl.:*** Ursofalk; ***Israel:*** Ursofalk; Ursolit; ***Ital.:*** Benursil†; Biliepar; Coledos†; Desocol; Desoxil; Deursil; Dissolursil; Epasol†; Fraurs; Galmax†; Lentorsil†; Litoff; Liturso; Tauro; Tudcabil†; Urdes; Ursacol; Ursilon; Ursobil; Ursodamor; Ursodexil†; Ursodiol; Ursofalk†; Ursoflor; Ursolac†; Ursolisin; Ursoprogé†; ***Jpn:*** Urso; Ursosan†; ***Malaysia:*** Ursofalk; ***Mex.:*** Ursofalk; ***Neth.:*** Ursochol; Ursofalk; ***Norw.:*** Ursofalk; ***NZ:*** Actigall; Ursofalk; ***Philipp.:*** Ursofalk; ***Pol.:*** Proursan; Ursocam; Ursofalk; Ursopol; ***Port.:*** Destolit; Ursofalk; ***Rus.:*** Ursosan (Урсосан); ***S.Afr.:*** Ursotan†; ***Singapore:*** Ursofalk; ***Spain:*** Ursobilane; Ursochol; ***Swed.:*** Ursofalk; ***Switz.:*** De-ursil; Ursochol; Ursofalk; ***Thai.:*** Udihep; Ursofalk; Ursolin; ***Turk.:*** Ursofalk; ***UK:*** Destolit; Urdox; Ursofalk; Ursogal; ***USA:*** Actigall; Urso.

Multi-ingredient: ***Austria:*** Lithofalk†; ***Ger.:*** Lithofalk; Urso Mix†; ***Gr.:*** Lithiofalk†; ***Ital.:*** Bilenor; ***Jpn:*** Cabe 2; Eki Cabe.

Urtica

Brännässleblad (nettle leaf); Brennessel; Dilgėlių lapai (nettle leaf); Kopřivový list (nettle leaf); Liść pokrzywy (nettle leaf); Nokkosenlehti (nettle leaf); Ortie; Ortie dioïque; Ortie, feuille d' (nettle leaf); Ortiga; Pokrzywa zwyczajna; Stinging Nettle; Urtica dioica; Urticae folium (nettle leaf).

Pharmacopoeias. In *Ger.* and *US* (both specify the root and rhizome of *Urtica dioica*).
Eur. (see p.vii) includes the leaf of *Urtica* spp. and also a form of *Urtica dioica* for homoeopathic preparations.
Br. includes a form of *Urtica urens* for homeopathic preparations.
Ph. Eur. 6.2 (Nettle Leaf; Urticae Folium). The whole or cut dried leaves of *Urtica dioica*, *Urtica urens*, or a mixture of the 2 species. It contains a minimum of 0.3% for the sum of caffeoylmalic acid and chlorogenic acid expressed as chlorogenic acid ($C_{16}H_{18}O_9$ = 354.3), calculated on the dried basis.
Ph. Eur. 6.2 (Common Stinging Nettle for Homoeopathic Preparations). The whole, fresh, flowering plant of *Urtica dioica*. Protect from light.
BP 2008 (Urtica Urens Herb for Homeopathic Preparations). Fresh leaves and flowers of *Urtica urens*. The plant produces an itchy, burning sensation.
USP 31 (Stinging Nettle). The dried roots and rhizomes of *Urtica dioica* (Urticaceae), and may contain *Urtica urens*, known in commerce as dwarf nettle, as a minor component. It contains not less than 0.8% of total amino acids, not less than 0.05% of sitosterol, and not less than 0.003% scopoletin ($C_{10}H_8O_4$ = 192.2), calculated on the dried basis. Store in airtight containers. Protect from light.

Profile

Urtica (*Urtica dioica*) has been used in herbal medicine, mainly for urinary-tract and rheumatic disorders. *Urtica urens* has been used similarly.

Homoeopathy. Urtica has been used in homoeopathic medicines under the following names: Common stinging nettle; Urtica dioica; Urtica urens; Urt. u.

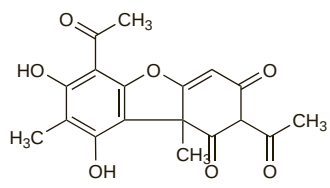
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Uro-POS; ***Braz.:*** Imuno Max; ***Cz.:*** Koprivovy Caj, Koprivova Nat; Zihlava†; ***Ger.:*** Arthrodynat N†; Asendra†; Azuprostat Urtica†; Bazoton; Flexal Brennessel; Hox Alpha; Natu-lind; Natu-prosta; Pro-Sabona Uno†; Prosta-Truw; Prostaforton; Prostagalen; Prostaherb N; Prostamed Urtica; Prostaneurin†; Prostata; Prostawern; Rheuma-Hek; Rheuma-Kapseln; Rheuma-Stada†; Serless†; Uro-POS; Urol pros; Urticaprostat uno†; Urtipret†; Urtivit; utk; ***Pol.:*** Prostaherb N; Urtix; ***Switz.:*** Valverde Prostate capsules.

Multi-ingredient: ***Austral.:*** Cough Relief†; Extralife Flow-Care; Haemo-Red Formula; Infant Tonic†; Irontona; Urapro†; Vitatona; ***Austria:*** Anaemodoron; Berggeist; Florissamin†; Florissamol†; Menodoron; Mentopin; Prostagutt; Prostatonin; Species Carvi comp†; ***Braz.:*** Prostem Plus; ***Canad.:*** Allercept†; Ultra Quercitin; ***Cz.:*** Abfuhr-Heilkrautertee†; Diabeticka Cajova Smes-Megadiabetin; Nephrosal†; Perospir†; Prostakan Forte; Prostatonin†; Pulmoran; Species Urologicae Planta; Stoffwechseltee N†; ***Fr.:*** Fitacnol†; ***Ger.:*** Combudoron; Presselin Nieren-Blasen K 3†; Prostagutt forte; Prostatin F†; Uvirgan N†; Vollmers praparierter gruner N; Winar†; ***Hong Kong:*** Calmiderm; ***Ital.:*** Biothymus DS; Pluvio; Prostaplant; Sebacnol†; Shamday Antiforfora†; ***Malaysia:*** Cleansa Plus†; Prostakan†; ***Mex.:*** Prosgutt; ***Pol.:*** Alliofil; Herbaton; Immunofort; Naturapia Prostata; Nefrobonisol; Seboren; Urofort; ***Rus.:*** Herbion Urtica (Гербион Уртика); Prostagutt Forte (Простагут Форте); ***S.Afr.:*** Combudoron; Enzian Anaemodoron Drops; Menodoron; ***Spain:*** Natusor Artilane†; ***Switz.:*** Combudoron; Prostagutt-F; Prostatonin; The a l'avoine sauvage de Vollmer; Tisane Diuretique; Tisane pour les problemes de prostate; ***UK:*** Sinose.

Usnea Barbata

Barba de capuchino.
CAS — 125-46-2 (usnic acid).



(usnic acid)

Profile

Usnea barbata is a lichen. It contains usnic acid, which is reported to have antimicrobial activity. *Usnea barbata* extract, usnic acid, and copper usnate have been used in topical preparations.

Adverse effects. Two patients developed severe hepatotoxicity believed to be associated with usnic acid contained in a multi-