M.p. 81° to 83°. Soluble 1 in 100 of water at 25°, 1 in 20 of water at 80°, 1 in 20 of glycerol; freely soluble in alcohol, in chloroform, in ether, and in solutions of fixed alkali hydroxides. Its solutions are acid to litmus. Store in airtight containers. Protect from light.

Profile
Vanillin is used as a flavour and in perfumery.

Preparations
BP 2008: Tolu-flavour Solution.

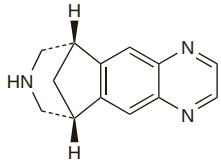
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Pulmex; Pulmex Baby; ***Turk.:*** Musilaks.

Varenicline *(BAN, rINN)*

Vareniclina; Varénicline; Vareniclinum. 7,8,9,10-Tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline.

Варениклин

$C_{13}H_{13}N_3$ = 211.3.
CAS — 249296-44-4.
ATC — N07BA03.
ATC Vet — QN07BA03.



Varenicline Tartrate *(BANM, USAN, rINNM)*

CP-526555-18; Tartrato de vareniclina; Varénicline, Tartrate de; Vareniclini Tartras.

Варениклина Тартрат

$C_{13}H_{13}N_3,C_4H_6O_6$ = 361.3.
CAS — 375815-87-5.
ATC — N07BA03.
ATC Vet — QN07BA03.

Adverse Effects and Precautions
The most common adverse effect of varenicline is nausea; other adverse effects also commonly reported are headache, dizziness, somnolence, fatigue, sleep disturbances, increased appetite, and gastrointestinal disturbances including vomiting, constipation, and flatulence. There have been reports of neuropsychiatric symptoms as well as exacerbation of pre-existing psychiatric illness in patients who have taken varenicline. Patients should be monitored for such symptoms, including suicidal ideation or behaviour, agitation, depression, or other changes in behaviour.

Dizziness and somnolence may affect the performance of skilled tasks such as driving.

Pharmacokinetics
Varenicline is well absorbed from the gastrointestinal tract, reaching peak plasma concentrations within 3 to 4 hours; bioavailability is high. Steady state concentrations are reached within 4 days of multiple oral dosing. Metabolism is minimal and about 92% of a dose is excreted unchanged in the urine; the elimination half-life is about 24 hours.

◊ References.

1. Faessel HM, *et al.* Single-dose pharmacokinetics of varenicline, a selective nicotinic receptor partial agonist, in healthy smokers and nonsmokers. *J Clin Pharmacol* 2006; **46:** 991–8.
2. Burstein AH, *et al.* Pharmacokinetics, safety, and tolerability after single and multiple oral doses of varenicline in elderly smokers. *J Clin Pharmacol* 2006; **46:** 1234–40.
3. Burstein AH, *et al.* Pharmacokinetics, safety, and tolerability after single and multiple oral doses of varenicline in elderly smokers. *J Clin Pharmacol* 2006; **46:** 1234–40.
4. Faessel HM, *et al.* Multiple-dose pharmacokinetics of the selective nicotinic receptor partial agonist, varenicline, in healthy smokers. *J Clin Pharmacol* 2006; **46:** 1439–48.

Uses and Administration
Varenicline is a selective nicotinic receptor partial agonist that is used as an aid for smoking cessation.

Varenicline is given orally as the tartrate with doses expressed in terms of the equivalent amount of varenicline; 1.71 mg of varenicline tartrate is equivalent to about 1 mg of varenicline. An initial dose equivalent to 500 micrograms varenicline is given once daily for the first 3 days, increasing to 500 micrograms twice daily for the next 4 days. The dose from the eighth day for the remainder of the course is 1 mg twice daily. The dose may be reduced to 500 micrograms twice daily if adverse effects are intolerable. Patients are advised to set a date to stop smoking and start varenicline 1 to 2 weeks before. Treatment is normally given for 12 weeks; in patients who successfully stop smoking, a further 12 weeks of treatment has been recommended to reduce the risk of relapse. For doses in renal impairment, see below.

◊ Reviews.

1. Zierler-Brown SL, Kyle JA. Oral varenicline for smoking cessation. *Ann Pharmacother* 2007; **41:** 95–9.
2. Potts LA, Garwood CL. Varenicline: the newest agent for smoking cessation. *Am J Health-Syst Pharm* 2007; **64:** 1381–4.
3. Hays JT, *et al.* Efficacy and safety of varenicline for smoking cessation. *Am J Med* 2008; **121** (suppl 1): S32–S42.
4. Anonymous. Varenicline for smoking cessation. *Drug Ther Bull* 2008; **46:** 33–6.

Administration in renal impairment. In patients with severe renal impairment (creatinine clearance less than 30 mL/minute) licensed product information recommends a starting dose of 500 micrograms daily increased if necessary after 3 days to a maximum dose of 500 micrograms twice daily (in the USA) or 1 mg once daily (in the UK). In patients with end-stage renal disease undergoing haemodialysis, a maximum dose of 500 micrograms once daily may be given provided that this is well tolerated. No dosage adjustment is considered to be needed in patients with lesser degrees of impairment.

Smoking cessation. Varenicline is an α4β2 nicotinic acetylcholine receptor partial agonist that is used as an aid for smoking cessation (p.2354). Results from 2 randomised controlled studies[1,2] show greater efficacy than placebo as well as favourable results compared with bupropion, a standard treatment for smoking cessation. However, these studies also showed that nausea was reported in almost 30% of participants in the varenicline group; abnormal dreams were also a problem. A further 12 weeks of treatment with varenicline improved abstinence at 24 weeks in patients who stopped smoking in the first 12 weeks of treatment; after stopping all treatment, the reduced relapse rate was maintained in this group up to 28 weeks later (i.e. 1 year from the start of treatment).[3]

1. Gonzales D, *et al.* Varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 47–55.
2. Jorenby DE, *et al.* Efficacy of varenicline, an α4β2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 56–63. Correction. *ibid.*; 1355.
3. Tonstad S, *et al.* Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA* 2006; **296:** 64–71.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Champix; ***Braz.:*** Champix; ***Cz.:*** Champix; ***Fr.:*** Champix; ***Gr.:*** Champix; ***Hung.:*** Champix; ***NZ:*** Champix; ***Port.:*** Champix; ***UK:*** Champix; ***USA:*** Chantix.

Vascular Endothelial Growth Factor

Сосудистого Эндотелиального Фактора Роста; Фактор Роста Эндотелия Сосудов

Profile
Vascular endothelial growth factor is a family of structurally related proteins involved in angiogenesis and vasculogenesis. VEGF-A, the first member of the family to be discovered and still often referred to as simply VEGF, is thought to provide most of the angiogenic effect of this family. Other members described to date include: VEGF-B, VEGF-C, VEGF-D, VEGF-E, and placental growth factor.

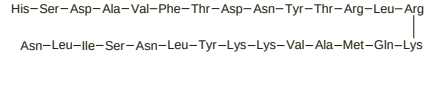
A gene therapy product supplying the gene for vascular endothelial growth factor D via an adenoviral vector is under investigation for the prevention of stenosis in synthetic grafts used in haemodialysis.

Vasoactive Intestinal Peptide

Péptido vasoactivo intestinal; PIV; Vasoactive Intestinal Polypeptide; VIP.

Вазоактивный Пептид Кишечника

CAS — 37221-79-7.



Aviptadil *(BAN, rINN)*

Aviptadilum; Vasoactive Intestinal Octacosapeptide (Swine).

Авиптадил

$C_{147}H_{238}N_{44}O_{42}S$ = 3325.8.
CAS — 40077-57-4.

Profile
Vasoactive intestinal peptide acts as a hormone and neurotransmitter in various parts of the body; it is a potent relaxant of smooth muscle and has vasodilator and bronchodilator properties as well as stimulating the gastrointestinal tract to increased secretion. It is available as a synthetic analogue, aviptadil. It has been tried in the management of acute oesophageal food impaction, and for the treatment of acute respiratory distress syndrome, pulmonary arterial hypertension, acute lung injury, and chronic thromboembolic pulmonary hypertension. Aviptadil has been tried as a combination product with phentolamine for erectile dysfunction (p.2179).

◊ Vasoactive intestinal peptide has potential therapeutic applications in immunological disorders since it appears to inhibit inflammatory responses; it modulates the function of inflammatory cells via specific receptors affecting both innate and adaptive immunity.[1] It also appears to have endogenous neuroprotective properties within the CNS, possibly through influencing the expression and secretion of glial-cell derived neuroprotective factors. Consequently, it may have therapeutic potential in neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, and stroke.[2]

1. Delgado M, *et al.* The significance of vasoactive intestinal peptide in immunomodulation. *Pharmacol Rev* 2004; **56:** 249–90.
2. Dejda A, *et al.* Neuroprotective potential of three neuropeptides PACAP, VIP and PHI. *Pharmacol Rep* 2005; **57:** 307–20.

Preparations
Proprietary Preparations (details are given in Part 3)
NZ: Invicorp.

Vasopressin *(rINNM)*

ADH; Antidiuretic Hormone; Beta-Hypophamine; Vasopresina; Vasopressiini; Vasopressine; Vasopressinum; Vazopresin.

Вазопрессин

CAS — 11000-17-2 (vasopressin injection).
ATC — H01BA01.
ATC Vet — QH01BA01.

NOTE. Vasopressin Injection is *rINN*.

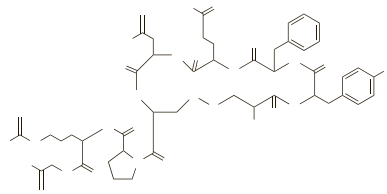
Pharmacopoeias. In *US*, which includes both argipressin and lypressin in this title.
An injection is included in *Jpn*.
USP 31 (Vasopressin). A polypeptide hormone having the properties of causing the contraction of vascular and other smooth muscles, and of antidiuresis. It is prepared by synthesis or obtained from the posterior lobe of the pituitary of healthy, domestic animals used for food by humans. Its vasopressor activity is not less than 300 USP units/mg. Store in airtight containers at 2° to 8°.

Argipressin *(BAN, rINN)*

[8-Arginine]vasopressin; Argipresina; Argipressine; Argipressinum; AVP. Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH_2 cyclic (1→6) disulphide.

Аргипрессин

$C_{46}H_{65}N_{15}O_{12}S_2$ = 1084.2.
CAS — 113-79-1.
ATC — H01BA06.
ATC Vet — QH01BA06.



Description. Argipressin is a form of vasopressin obtained from most mammals including man but excluding pig. It is usually prepared synthetically. Lypressin (see below) is vasopressin from pig.

Argipressin Tannate *(BANM, USAN, rINNM)*

8-L-Arginine-vasopressin Tannate; Argipressine, Tannate d'; Argipressini Tannatum; CI-107; Tanato de argipresina. Tannins compound with argipressin.

Аргипрессина Таннат

ATC — H01BA06.
ATC Vet — QH01BA06.

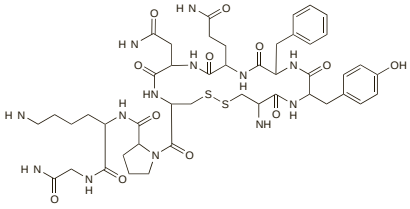
Units
8.2 units of argipressin for bioassay are contained in approximately 20 micrograms of synthetic peptide acetate (with human albumin 5 mg and citric acid) in one ampoule of the first International Standard (1978).

Lypressin *(BAN, USAN, rINN)*

L-8; Lipresina; Lipressina; Lipresszin; LVP; Lypressiini; Lypressine; Lypressinum. [8-Lysine]vasopressin; Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Lys-Gly-NH_2 cyclic (1→6) disulphide.

Липрессин

$C_{46}H_{65}N_{13}O_{12}S_2$ = 1056.2.
CAS — 50-57-7.
ATC — H01BA03.
ATC Vet — QH01BA03.



Description. Lypressin is the form of vasopressin present in the posterior pituitary of pigs.

Pharmacopoeias. *US* includes Lypressin Nasal Solution.

Incompatibility. Vasopressin was shown to be physically compatible (when injected at the Y-site in an intravenous tubing set) when tested in intravenous fluids with other drugs commonly used in cardiac arrest.[1] However, tests of vasopressin with drugs commonly used in septic shock showed physical incompatibility with phenytoin (when mixed in infusion bags).[2] Precipitation has also been reported[3] with vasopressin and furosemide together in intravenous fluids (tested at the Y-site).

1. Feddema S, *et al.* Physical compatibility of vasopressin with medications commonly used in cardiac arrest. *Am J Health-Syst Pharm* 2003; **60:** 1271–2.
2. Barker B, *et al.* Visual compatibility of vasopressin with other injectable drugs. *Am J Health-Syst Pharm* 2005; **62:** 1969, 1975–6.
3. Faria CE, *et al.* Visual compatibility of furosemide with phenylephrine and vasopressin. *Am J Health-Syst Pharm* 2006; **63:** 906–8.

Units

7.7 units of lypressin are contained in about 23.4 micrograms of synthetic peptide (with albumin 5 mg and citric acid) in one ampoule of the first International Standard (1978).

Adverse Effects

Large parenteral doses of vasopressin may give rise to marked pallor, pounding headache, vertigo, sweating, tremor, nausea, vomiting, diarrhoea, eructation, cramp, and a desire to defaecate; some of these effects may also occur after large intranasal doses of lypressin. In women, vasopressin may cause uterine cramps of a menstrual character. Hyponatraemia with water retention and signs of water intoxication can occur.

Hypersensitivity reactions have occurred and include urticaria and bronchoconstriction. Anaphylactic shock and cardiac arrest have been reported.

Vasopressin may constrict coronary arteries. Chest pain, myocardial ischaemia, and infarction have occurred following injection, and fatalities have been reported. Other cardiovascular effects include occasional reports of arrhythmias and bradycardia, as well as hypertension. Peripheral vasoconstriction has resulted in gangrene, and thrombosis as well as local irritation at the injection site may occur.

Nasal congestion, irritation, and ulceration have been reported occasionally after intranasal use, usually as lypressin; systemic effects at usual intranasal doses are mostly reported to be mild.

Effects on the heart. Arrhythmias, including ventricular tachycardia and fibrillation,[1] torsade de pointes,[2-4] and asystole[5] are among the adverse effects of vasopressin. Paradoxical bradycardia and hypotension have also been reported.[6]

1. Kelly KJ, *et al.* Vasopressin provocation of ventricular dysrhythmia. *Ann Intern Med* 1980; **92:** 205–6.
2. Eden E, *et al.* Ventricular arrhythmia induced by vasopressin: torsade de pointes related to vasopressin-induced bradycardia. *Mt Sinai J Med* 1983; **50:** 49–51.
3. Stein LB, *et al.* Fatal torsade de pointes occurring in a patient receiving intravenous vasopressin and nitroglycerin. *J Clin Gastroenterol* 1992; **15:** 171–4.
4. Faigel DO, *et al.* Torsade de pointes complicating the treatment of bleeding esophageal varices: association with neuroleptics, vasopressin, and electrolyte imbalance. *Am J Gastroenterol* 1995; **90:** 822–4.
5. Fitz JD. Vasopressin induction of ventricular ectopy. *Arch Intern Med* 1982; **142:** 644.
6. Kraft W, *et al.* Paradoxical hypotension and bradycardia after intravenous arginine vasopressin. *J Clin Pharmacol* 1998; **38:** 283–6.

Ischaemia. Reports of ischaemia and infarction associated with vasopressin.[1-10]

1. Greenwald RA, *et al.* Local gangrene: a complication of peripheral Pitressin therapy for bleeding esophageal varices. *Gastroenterology* 1978; **74:** 744–6.
2. Colombani P. Upper extremity gangrene secondary to superior mesenteric artery infusion of vasopressin. *Dig Dis Sci* 1982; **27:** 367–9.
3. Lambert M, *et al.* Reversible ischemic colitis after intravenous vasopressin therapy. *JAMA* 1982; **247:** 666–7.
4. Anderson JR, Johnston GW. Development of cutaneous gangrene during continuous peripheral infusion of vasopressin. *BMJ* 1983; **287:** 1657–8.
5. Reddy KR, *et al.* Bilateral nipple necrosis after intravenous vasopressin therapy. *Arch Intern Med* 1984; **144:** 835–6.
6. Brearly S, *et al.* A lethal complication of peripheral vein vasopressin infusion. *Hepatogastroenterology* 1985; **32:** 224–5.
7. Sweren BS, Bohlman ME. Gastric and splenic infarction: a complication of intraarterial vasopressin infusion. *Cardiovasc Intervent Radiol* 1989; **12:** 207–9.
8. Maceyko RF, *et al.* Vasopressin-associated cutaneous infarcts, alopecia, and neuropathy. *J Am Acad Dermatol* 1994; **31:** 111–13.
9. Lin RY, *et al.* Vasopressin-induced amber-like skin necrosis. *Dermatology* 1997; **195:** 271–3.
10. Dunser MW, *et al.* Ischemic skin lesions as a complication of continuous vasopressin infusion in catecholamine-resistant vasodilatory shock: incidence and risk factors. *Crit Care Med* 2003; **31:** 1394–8.

Treatment of Adverse Effects

The antidiuretic effects on water retention and sodium imbalance may be treated by water restriction and a temporary withdrawal of vasopressin. Severe cases may require osmotic diuresis alone or with furosemide.

Extravasation. Localised intravenous and intra-arterial guanethidine was used in the treatment of a patient with extravasation of vasopressin.[1] The intra-arterial use of guanethidine was considered to have helped to avoid necrotic changes.

1. Crocker MC. Intravascular guanethidine in the treatment of extravasated vasopressin. *N Engl J Med* 1981; **304:** 1430.

Precautions

Vasopressin should not be used in patients with chronic nephritis with nitrogen retention. It should be avoided or given only with extreme care, and in small doses, to patients with vascular disease, especially of the coronary arteries.

It should be given with care to patients with conditions which might be aggravated by water retention including asthma, epilepsy, migraine, and heart failure. Fluid intake should be adjusted to avoid hyponatraemia and water intoxication. Care is also required in hypertension or other conditions that may be exacerbated by a rise in blood pressure. Nasal absorption of vasopressin may be impaired in patients with rhinitis.

Abuse. Vasopressin or its analogues have been abused as so-called 'smart drugs' for their supposed effect on memory recall and cognition.

Resistance. Antibodies to vasopressin were detected in 6 of 28 patients being treated for diabetes insipidus, all of whom had a decrease in antidiuretic effect with previously effective argipressin or lypressin therapy;[1] desmopressin and chlorpropamide remained effective in these patients. There have been reports of patients with diabetes insipidus of pregnancy unresponsive to argipressin but responsive to desmopressin.[2] This was probably due to excessive placental production of vasopressinase, an enzyme which degrades argipressin.

1. Vokes TJ, *et al.* Antibodies to vasopressin in patients with diabetes insipidus: implications for diagnosis and therapy. *Ann Intern Med* 1988; **108:** 190–5.
2. Shah SV, Thakur V. Vasopressinase and diabetes insipidus of pregnancy. *Ann Intern Med* 1988; **109:** 435–6.

Interactions

The antidiuretic effects of vasopressins might be expected to be enhanced in some patients receiving chlorpropamide, clofibrate, carbamazepine, fludrocortisone, urea, or tricyclic antidepressants. Lithium, heparin, demeclocycline, noradrenaline, and alcohol may decrease the antidiuretic effect. Ganglion-blocking drugs may increase sensitivity to the pressor effects of vasopressins.

Cimetidine. A report of severe bradycardia and heart block leading to asystole in a patient given combined vasopressin and cimetidine therapy.[1]

1. Nikolic G, Singh JB. Cimetidine, vasopressin and chronotropic incompetence. *Med J Aust* 1982; **2:** 435–6.

Uses and Administration

Vasopressin is secreted by the hypothalamus and stored in the posterior lobe of the pituitary gland. It may be prepared from the gland of mammals or by synthesis. Vasopressin has a direct antidiuretic action on the kidney, increasing tubular reabsorption of water. It also constricts peripheral blood vessels and causes contraction of the smooth muscle of the intestine, gallbladder, and urinary bladder. It has practically no oxytocic activity.

Vasopressin, which is usually given parenterally or intranasally in the synthetic forms of argipressin or lypressin, is used in the treatment of cranial diabetes insipidus due to a deficiency in antidiuretic hormone. It is ineffective in nephrogenic diabetes insipidus. Argipressin has also been used in the prevention and treatment of postoperative abdominal distension, and was formerly given to remove gas in abdominal visualisation procedures. Argipressin or lypressin are used in the treatment of bleeding oesophageal varices. Argipressin may have a role in cardiopulmonary resuscitation and shock due to vasodilatation.

In the treatment of cranial diabetes insipidus to control polyuria, argipressin may be given subcutaneously or intramuscularly; the dose in the UK is 5 to 20 units every 4 hours. In the USA, 5 to 10 units given 2 or 3 times daily or more has been used. Alternatively, argipressin or lypressin has been given as a nasal spray; dosage should be individually adjusted as required. A long-acting oily suspension of vasopressin tannate was formerly used by intramuscular injection in diabetes insipidus.

In the initial control of variceal bleeding argipressin is given in an initial dose of 20 units in 100 mL of glucose 5% infused intravenously over 15 minutes. Lypressin has also been given for bleeding oesophageal varices. Doses for children are given under Administration in Children, below.

Vasopressin has also been used as a vasoconstrictor in local anaesthetic injections.

Administration. Results[1] suggesting that although intravenous argipressin produced much higher plasma concentrations than intranasal, the latter evoked a greater CNS response.

1. Pietrowsky R, *et al.* Brain potential changes after intranasal vs intravenous administration of vasopressin: evidence for a direct nose-brain pathway for peptide effects in humans. *Biol Psychiatry* 1996; **39:** 332–40.

Administration in children. Although not licensed in the UK for use in children, the *BNFC* includes a dose for adjunctive treatment of acute massive haemorrhage of the gastrointestinal tract or oesophageal varices in patients aged from 1 month to 18 years. An initial dose of 0.3 units/kg (up to 20 units) is given intravenously over 20 to 30 minutes, followed by a continuous infusion of 0.3 units/kg per hour adjusted according to response to a maximum of 1 unit/kg per hour. If the bleeding stops the infusion is continued at the same dose for 12 hours, then gradually withdrawn over 24 to 48 hours; the maximum duration of treatment should be 72 hours.

Vasopressin given by continuous intravenous infusion in an average dose of 9 milliunits/kg per hour was safe and effective in 5 children who had diabetes insipidus as a manifestation of severe brain injury.[1] A dose of 1.5 to 3 milliunits/kg per hour has also been used safely for postoperative diabetes insipidus in 2 children aged 3 years and under.[2] Similar initial doses of argipressin were used in 3 comatose children with cranial diabetes insipidus,[3] while a published algorithm for the management of acute cranial diabetes insipidus has recommended an initial dose of vasopressin of 0.25 to 1 milliunits/kg per hour, subsequently titrated to achieve an appropriate output and specific gravity of urine, and a serum sodium value of between 140 and 145 mmol/litre.[4]

1. Ralston C, Butt W. Continuous vasopressin replacement in diabetes insipidus. *Arch Dis Child* 1990; **65:** 896–7.
2. McDonald JA, *et al.* Treatment of the young child with postoperative central diabetes insipidus. *Am J Dis Child* 1989; **143:** 201–4.
3. Lee Y-J, *et al.* Continuous infusion of vasopressin in comatose children with neurogenic diabetes insipidus. *J Pediatr Endocrinol Metab* 1995; **8:** 257–62.
4. Lugo N, *et al.* Diagnosis and management algorithm of acute onset of central diabetes insipidus in critically ill children. *J Pediatr Endocrinol Metab* 1997; **10:** 633–9.

Advanced cardiac life support. Vasopressin (as argipressin) may be used as an alternative to adrenaline in cardiopulmonary resuscitation (see p.1156). In a preliminary study argipressin 40 units by intravenous injection appeared to be of value in the treatment of cardiac arrest due to ventricular fibrillation.[1] Spontaneous circulation returned in 16 of 20 patients so treated; 14 were successfully resuscitated on arrival in hospital and 8 survived to be discharged. In comparison, of 20 patients treated with 1 mg of adrenaline intravenously only 7 were resuscitated and 3 survived till discharge. However, a larger study[2] found no difference between vasopressin and adrenaline in the rates of survival to hospital admission for patients with ventricular fibrillation or pulseless electrical activity, although vasopressin was associated with a higher rate of hospital admission and discharge among patients with asystole. It also found that two doses of vasopressin followed by a single dose of adrenaline resulted in a better survival rate than three doses of adrenaline. Another large study[3] of patients who experienced cardiac arrest while in hospital and were treated with either vasopressin 40 units or adrenaline 1 mg, found no difference in survival to discharge from hospital. A systematic review[4] of 5 trials, including these 3, found no clear advantage for the use of vasopressin over adrenaline in the treatment of cardiac arrest.

1. Lindner KH, *et al.* Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation. *Lancet* 1997; **349:** 535–7.
2. Wenzel V, *et al.* A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *N Engl J Med* 2004; **350:** 105–13.
3. Stiell IG, *et al.* Vasopressin versus epinephrine for inhospital cardiac arrest: a randomised controlled trial. *Lancet* 2001; **358:** 105–9.
4. Aung K, Htay T. Vasopressin for cardiac arrest: a systematic review and meta-analysis. *Arch Intern Med* 2005; **165:** 17–24.

Diabetes insipidus. For a discussion of diabetes insipidus and its management, including reference to the use of vasopressin analogues (particularly desmopressin), see p.2179.

Haemorrhagic disorders. There are reports of vasopressin being used in the management of various haemorrhagic disorders including blood loss in abortion and caesarean section[1,2] and haemoptysis.[3,4] Infusion of vasopressin into the superior or inferior mesenteric artery has been used in the management of lower gastrointestinal bleeding, but modern embolisation techniques may be associated with fewer complications.[5] For the use of va-