mydriatic effect can last several hours. Solutions containing 2.5% or more may cause intense irritation and a local anaesthetic other than butacaine (which is incompatible) should be instilled into the eye a few minutes beforehand.

Ocular solutions containing lower concentrations (usually 0.12% phenylephrine hydrochloride) are used as a **conjunctival decongestant** (see Conjunctivitis, p.564).

Phenylephrine has been used parenterally in the treatment of hypotensive states, such as those encountered during circulatory failure or spinal anaesthesia. Phenylephrine has also been used in orthostatic hypotension (see under Fludrocortisone, p.1530). For **hypotension**, an initial dose of phenylephrine hydrochloride 2 to 5 mg may be given as a 1% solution subcutaneously or intramuscularly with further doses of 1 to 10 mg if necessary, according to response. A dose of 100 to 500 micrograms by slow intravenous injection as a 0.1% solution, repeated as necessary after at least 15 minutes, has also been used. In severe hypotensive states, 10 mg in 500 mL of glucose 5% or sodium chloride 0.9% has been infused intravenously, initially at a rate of up to 180 micrograms/minute, reduced, according to the response, to 30 to 60 micrograms/minute.

For children's doses, see Administration in Children, below.

Phenylephrine hydrochloride has been given by intravenous injection to stop **paroxysmal supraventricular tachycardia** but other drugs are preferred (see Cardiac Arrhythmias, p.1160). The initial dose is usually not greater than 500 micrograms given as a 0.1% solution with subsequent doses gradually increased in increments of 100 to 200 micrograms up to 1 mg if necessary.

Phenylephrine hydrochloride has been used for its vasoconstrictor action as an **adjunct** to local anaesthetics.

Phenylephrine has also been used as the acid tartrate to prolong the bronchodilator effects of isoprenaline when given by inhalation. However, isoprenaline is now little used by this route.

Phenylephrine tannate has also been used.

Administration in children. Phenylephrine hydrochloride is used for the symptomatic relief of **nasal congestion**; however, over-the-counter cough and cold preparations containing sympathomimetic decongestants (including phenylephrine) should be used with caution in children and generally avoided in those under 2 years of age (see p.1547). In the USA, the following doses have been used in children:

- 2 to 6 years: 2 or 3 drops of a 0.125% or 0.16% solution into each nostril every four hours as needed
- 6 to 12 years: 2 or 3 drops, or 1 or 2 sprays, of a 0.25% solution may be instilled into each nostril every four hours as needed.

In the UK, oral preparations for nasal congestion associated with colds and hay fever are not licensed in children under 12 years of age.

Phenylephrine is used for **mydriasis** in diagnostic or therapeutic procedures. Solutions containing 2.5% are used in children as the 10% strength is contra-indicated owing to the risk of systemic effects.

For acute **hypotension**, the *BNFC* states that phenylephrine hydrochloride may be given subcutaneously or intramuscularly in the following doses:

- 1 to 12 years: 100 micrograms/kg every 1 to 2 hours as needed (to a maximum dose of 5 mg)
- 12 to 18 years: 2 to 5 mg, followed if necessary by further doses of 1 to 10 mg (maximum initial dose 5 mg)

Although the intravenous route is not licensed in the UK for such use in children, intravenous injection is preferred to the other parenteral routes; the *BNFC* recommends the following doses given as a 0.1% solution:

- 1 to 12 years: 5 to 20 micrograms/kg (maximum 500 micrograms), repeated as needed after at least 15 minutes.
- 12 to 18 years: 100 to 500 micrograms, repeated as needed after at least 15 minutes

For intravenous infusion, the solution is diluted with glucose 5% or sodium chloride 0.9% to a concentration of 20 micrograms/mL and given as a continuous infusion via a central venous catheter. The *BNFC* gives the following doses:

- 1 to 16 years: 100 to 500 nanograms/kg per minute, adjusted according to response
- 16 to 18 years: initially up to 180 micrograms/minute, reduced to 30 to 60 micrograms/minute according to response

Faecal incontinence. Topical application of phenylephrine gel has been shown to increase resting anal tone[1] and has been investigated in patients with faecal incontinence.[2] Although application of a 10% gel did not appear to be of clinical benefit in a double-blind crossover study in 36 patients with faecal incontinence caused by internal sphincter dysfunction,[3] continence was improved in another small study in patients with ileoanal pouches.[4]

1. Cheetham MJ, *et al.* Topical phenylephrine increases anal canal resting pressure in patients with faecal incontinence. *Gut* 2001; **48:** 356–9.
2. Cheetham M, *et al.* Drug treatment for faecal incontinence in adults. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 04/01/07).
3. Carapeti EA, *et al.* Randomized controlled trial of topical phenylephrine in the treatment of faecal incontinence. *Br J Surg* 2000; **87:** 38–42.
4. Carapeti EA, *et al.* Randomized, controlled trial of topical phenylephrine for fecal incontinence in patients after ileoanal pouch construction. *Dis Colon Rectum* 2000; **43:** 1059–63.

Nasal congestion. A meta-analysis concluded that there was insufficient evidence that phenylephrine 10 mg was an effective oral decongestant.[1]

1. Hatton RC, *et al* Efficacy and safety of oral phenylephrine: systematic review and meta-analysis. *Ann Pharmacother* 2007; **41:** 381–90.

Priapism. Alpha agonists, including phenylephrine, may be used in the management of priapism (see under Metaraminol, p.1333). For reference to phenylephrine in low dosage and dilute solution being given by intracavernosal injection to reverse priapism, see under Alprostadil, p.2184.

Preparations

BP 2008: Phenylephrine Eye Drops; Phenylephrine Injection;
USP 31: Antipyrine, Benzocaine, and Phenylephrine Hydrochloride Otic Solution; Isoproterenol Hydrochloride and Phenylephrine Bitartrate Inhalation Aerosol; Phenylephrine Hydrochloride Injection; Phenylephrine Hydrochloride Nasal Jelly; Phenylephrine Hydrochloride Nasal Solution; Phenylephrine Hydrochloride Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Fadalefrina; Mydfrin†; Poen Efrina; Prefrin; Qura Nasal; ***Austral.:*** Actifed PE; Albalon Relief; Isopto Frin†; Neo-Synephrine; Nyal Decongestant; Nyal Sinus Relief†; Prefrin; Sudafed PE; Visopt†; ***Austria:*** Visadron; ***Belg.:*** Spraydil; Visadron; ***Braz.:*** Denason; ***Canad.:*** Ak-Dilate†; Dionephrine; Mydfrin; Neo-Synephrine; Prefrin; Triaminic Thin Strips Nasal Congestion; Triaminic Toddler Congestion; ***Chile:*** Mydfrin; ***Cz.:*** Humex Nosni; Neo-Synephrine; Visadron†; ***Fin.:*** Oftan Metaoksedrin†; ***Fr.:*** Auristan†; Neosynephrine; ***Ger.:*** Neo-Mydrial†; Neosynephrin-POS; Otriven Baby; Visadron; ***Hong Kong:*** Mydfrin; Prefrin; ***India:*** Drosyn; Pupiletto†; ***Irl.:*** Isopto Frin†; ***Israel:*** Af-Taf; Efrin; Neo-Synephrine; Prefrin†; ***Ital.:*** Isonefrine; Neo-Synephrine; Ribex Nasale†; Visadron†; ***Malaysia:*** Analux†; Isopto Frin†; Mydfrin; Prefrin†; ***Mex.:*** Dilufrin; Lefrine; Nefrin; Rinolan; Weiscalina†; ***Neth.:*** Boradrine; Visadron; ***NZ:*** Albalon Relief†; Isopto Frin†; Neosynephrine; Prefrin; ***Philipp.:*** Mydfrin; ***Port.:*** Davinefrina; Neo-Sinefrina; VibrocilFen; Visadron; ***Rus.:*** Irifrin (Ирифрин); Nazol Baby (Назол Бэби); Nazol Kids (Назол Кидс); ***S.Afr.:*** I-Glo; Naphensyl; Prefrin; ***Singapore:*** Isopto Frin†; Mydfrin; Prefrin†; ***Spain:*** ADA; Analux†; Boraline; Disneumon Mentol; Disneumon Pernasal; Mirazul; Rin Up†; Visadron; Vistafrin; ***Switz.:*** Gouttes nasales†; Rexophtal N; Spray nasal pour enfants; ***Turk.:*** Mydfrin; ***UK:*** Boots Decongestant Capsules; Fenox; Non-Drowsy Sudafed Congestion Relief; ***USA:*** AH-chew D; Ak-Dilate; Children's Nostril; Lusonal; Medicone†; Mydfrin; Nasop; Neo-Synephrine; Neofrin; Nostril; Ocu-Phrin; Pedia Care Childrens Decongestant; Phenoptic†; Phenyl-T; Prefrin†; Pretz-D†; Rectacaine; Relief; Rhinall; Sinex; Sudafed PE; Triaminic Infant Thin Strips Decongestant; Triaminic Thin Strips Cold; Tronolane.

Multi-ingredient: numerous preparations are listed in Part 3.

Used as an adjunct in: ***Braz.:*** Anestesico.

Phenylpropanolamine *(BAN, rINN)*

Fenilpropanolamina; Fennylpropanolamin; Fenyylipropanoliamiini; (±)-Norephedrine; Phénylpropanolamine; Phenylpropanolaminum. (1*RS*,2*SR*)-2-Amino-1-phenylpropan-1-ol.

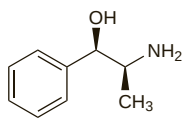
Фенилпропаноламин

$C_9H_{13}NO$ = 151.2.

CAS — 14838-15-4.

ATC — R01BA01.

ATC Vet — QG04BX91; QR01BA01.



(+)-Form

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of phenylpropanolamine: Pseudocaine.

Phenylpropanolamine Hydrochloride

(BANM, rINNM)

Fenilpropanolamin-hidroklorid; Fenilpropanolamino hidrochloridas; Fenylpropanolamin hydrochlorid; Fenylpropanolaminhydroklorid; Fenyylipropanoliamiinihydrokloridi; Hidrocloruro de fenilpropanolamina; Mydriatin; Phénylpropanolamine, chlorhydrate de; Phenylpropanolamini Hydrochloridum; Phenylpropanolamini hydrochloridum.

Фенилпропаноламина Гидрохлорид

$C_9H_{13}NO,HCl$ = 187.7.

CAS — 154-41-6.

ATC — R01BA01.

ATC Vet — QG04BX91; QR01BA01.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
US also includes phenylpropanolamine bitartrate.
Ph. Eur. 6.2 (Phenylpropanolamine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water and in alcohol; practically insoluble in dichloromethane.
USP 31 (Phenylpropanolamine Hydrochloride). A white crystalline powder, having a slight aromatic odour. Soluble 1 in 1.1 of water, 1 in 7.4 of alcohol, and 1 in 4100 of chloroform; insoluble in ether. pH of a 3% solution in water is between 4.2 and 5.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Ephedrine, p.1558.

Severe hypertensive episodes have followed phenylpropanolamine ingestion (see below). As with other indirect-acting sympathomimetics, tolerance to the therapeutic effects of phenylpropanolamine has been reported with prolonged use.

◊ An extensive and detailed review[1] of adverse effects attributed to phenylpropanolamine noted in 1990 that many of the adverse drug reactions reported in Europe described an alteration of mental status whereas those in North America were more often compatible with hypertension. The author suggested that this might be due to a difference in the isomers present in phenylpropanolamine preparations, based on earlier reports that *d*-norpseudoephedrine, the most potent of several isomeric forms as a stimulant of the CNS, was present in European preparations of phenylpropanolamine. However, later investigation suggests that currently the racemic mixture (±)-norephedrine (*d*,*l*-norephedrine) is the isomeric form present in commercial preparations in both Europe and the USA.[2]

The original review[1] concentrated on North American cases. The majority of products available were decongestants or cough or cold remedies; a small number were promoted as diet aids.

The data suggested that over-the-counter (OTC) products were more likely to be associated with an adverse reaction than a prescription medication; this may be because such OTC products were more likely to be overused and to be considered innocuous by the patient. It was also likely that drug interactions (below) rather than 'true overdosages' were involved in many of the adverse events, particularly as many OTC preparations contain other ingredients. (See also Abuse under Ephedrine, p.1558, for further discussion about the consequences of use of OTC preparations containing sympathomimetics, including phenylpropanolamine.)

The adverse reactions varied widely ranging from headache and elevated blood pressure to cardiopulmonary arrest, intracranial haemorrhage, and death. Mild reactions included blurred vision, dizziness, anxiety, agitation, tremor, confusion, and hypersensitivity reaction. Severe reactions included hypertensive crisis with hypertensive encephalopathy, seizures, arrhythmias, psychosis, and acute tubular necrosis. One unifying theme of many of the severe cases was that high blood pressure or symptoms suggestive of this were the presenting feature; an acute, persistent, severe headache was also noted in many cases.

It was pointed out that overall phenylpropanolamine was relatively safe. Although billions of doses were consumed annually, few cases of adverse drug reactions had been reported.

It was believed that certain groups may be at particular risk of adverse reactions to phenylpropanolamine: persons with elevated blood pressure, overweight persons (who are likely to be both hypertensive and to use diet aids), patients with eating disorders (who tend to abuse substances including diet aids), and the elderly (who may be multiple drug takers and likely to be hypertensive and at risk already of a stroke).

Subsequently, after a large case-control study in the USA which found an increased risk of haemorrhagic stroke associated with the use of preparations containing phenylpropanolamine (and in particular in women who used phenylpropanolamine as an appetite suppressant),[3] the FDA took steps to remove phenylpropanolamine from all drug products in the USA and requested that it no longer be marketed. Products containing phenylpropanolamine have also been withdrawn in some other countries. However, this study and the FDA decision have been criticised[4-6] notably on the basis that there was no evidence of an increased risk with the amount of phenylpropanolamine normally present in decongestant preparations and the study may have been subject to confounding. The UK CSM[7] considered that the evidence