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17. Maheshwari A, *et al*. Resistance to recombinant human granulocyte colony-stimulating factor in neonatal alloimmune neutropenia associated with anti-human neutrophil antigen-2a (NB1) antibodies. Abstract: *Pediatrics* 2002; **109:** 698. Full version: http://pediatrics.aappublications.org/cgi/content/full/109/4/e64 (accessed 27/10/05)

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Filgen; Neupogen; Neutrofil; Neutromax; ***Austral.:*** Neulasta; Neupogen; ***Austria:*** Neulasta; Neupogen; ***Belg.:*** Neulasta; Neupogen; ***Braz.:*** Filgrastine; Granulen; Granulokine; Leucin; Neulastim; ***Canad.:*** Neulasta; Neupogen; ***Chile:*** Neupogen; Neutromax; ***Cz.:*** Neulasta; Neupogen; Neupopeg; ***Denm.:*** Neulasta; Neupogen; ***Fin.:*** Neulasta; Neupogen; ***Fr.:*** Neulasta; Neupogen; ***Ger.:*** Neulasta; Neupogen; ***Gr.:*** Granulokine; Neulasta; ***Hong Kong:*** Neupogen; ***Hung.:*** Neulasta; Neupogen; ***India:*** Neupogen; ***Indon.:*** Neulastim; Neupogen; ***Irl.:*** Neulasta; Neupogen; ***Israel:*** Neupogen; ***Ital.:*** Granulokine; Neulasta; Neupogen; Neupopeg; ***Jpn:*** Gran; ***Malaysia:*** Neupogen; Peglasta; ***Mex.:*** Filatil; Neulastim; Neupogen; ***Neth.:*** Neulasta; Neupogen; Neupopeg; ***Norw.:*** Neulasta; Neupogen; ***NZ:*** Neupogen; ***Philipp.:*** Granulokine; ***Pol.:*** Neulasta; Neupogen; ***Port.:*** Neulasta; Neupogen; Neupopeg; ***Rus.:*** Neupogen (Нейпоген); ***S.Afr.:*** Neupogen; ***Singapore:*** Neulastim; Neupogen; ***Spain:*** Neulasta; Neupogen; ***Swed.:*** Neulasta; Neupogen; ***Switz.:*** Neulasta; Neupogen; ***Thai.:*** Neupogen; Neutromax; ***Turk.:*** Neupogen; ***UK:*** Neulasta; Neupogen; ***USA:*** Neulasta; Neupogen; ***Venez.:*** Neupogen.

Gelatin ⊗

Gelatina; Gélatine; Liivate; Modifiye Jelatin; Želatina; Želatyna; Zselatin.

ATC — B02BC01 (absorbable gelatin sponge); B05AA06 (gelatin).

ATC Vet — QB02BC01 (absorbable gelatin sponge); QB05AA06 (gelatin).

Grades. Gelling grades of gelatin are usually graded by gel strength, expressed as 'Bloom value', 'Bloom strength', or 'Bloom rating'.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *Viet.* Also in *USNF*.

The gelatin described in some pharmacopoeias is not necessarily suitable for preparations for parenteral use or for other special purposes.

Ph. Eur. 6.2 (Gelatin). A purified protein obtained either by partial acid hydrolysis (type A), by partial alkaline hydrolysis (type B), or by enzymatic hydrolysis of collagen from animals (including fish and poultry); it may also be a mixture of different types. The hydrolysis leads to gelling and non-gelling product grades. Gelling grades are characterised by the gel strength (Bloom value). It is not suitable for parenteral use or for other special purposes.

A faintly yellow or light yellowish-brown solid, usually occurring as translucent sheets, shreds, powder, or granules.

Gelling grades of gelatin swell in cold water and on heating give a colloidal solution which on subsequent cooling forms a more or less firm gel. Gelatin is practically insoluble in common organic solvents. Different gelatins form aqueous solutions that vary in clarity and colour. A 1% solution in water at about 55° has a pH of 3.8 to 7.6. Protect from heat and moisture.

USNF 26 (Gelatin). It is obtained by the partial hydrolysis of collagen derived from the skin, white connective tissue, and bones of animals. Gelatin derived from an acid-treated precursor is known as Type A, and gelatin derived from an alkali-treated precursor is known as Type B.

Faintly yellow or amber sheets, flakes, or shreds, or a coarse to fine powder, the colour varying in depth according to the particle size. A solution has a slight, characteristic, bouillon-like odour. It is stable in air when dry, but is subject to microbial decomposition when moist or in solution. Gelatin swells and softens when immersed in cold water, gradually absorbing 5 to 10 times its weight of water. Soluble in hot water, in 6N acetic acid, and in a hot mixture of glycerol and water; insoluble in alcohol, in chloroform, in ether, and in fixed and volatile oils.

Incompatibility. A white precipitate was formed immediately when vancomycin injection was infused through a giving set containing modified fluid gelatin solution.[1]

1. Taylor A, Hornbrey P. Incompatibility of vancomycin and gelatin plasma expanders. *Pharm J* 1991; **246:** 466.

Adverse Effects

Hypersensitivity reactions including anaphylactic reactions have occurred after the infusion of gelatin or its derivatives. Rapid infusion of gelatin derivatives may directly stimulate the release of histamine and other vasoactive substances.

For adverse reactions associated with the topical use of gelatin, see Haemostasis under Uses and Administration, below.

Hypersensitivity. Severe anaphylactoid reactions have been reported with infusion of modified fluid gelatin solutions.[1,2] As of June 2006, the Australian Adverse Drug Reactions Advisory Committee (ADRAC)[3] had also received 70 reports of hypotension or hypersensitivity reactions associated with succinylated gelatin. Although severe hypersensitivity reactions to gelatin-based plasma expanders appear to be rare, they may be underreported and fatalities have occurred.[2] The possibility of cross reactivity between succinylated gelatin and polygeline has also been considered; there are a few reports of patients who, after a reaction during clinical use with one plasma expander, have shown a positive skin test result to the other.[4,5] Some hypersensitivity reactions have been attributed to the use of gelatin as an excipient in vaccines[6-8] and other injectable drug products.[9] A haemostatic gelatin sponge put into place at the end of spinal surgery for a disc hernia was thought to be responsible for a delayed hypersensitivity reaction that caused oedema of the soft tissues and subsequent tingling and paresis of the lower limbs; removal of the sponge produced improvement.[10]

For reports of fatal reactions in asthmatic patients given gelatin derivatives, see Polygeline, p.1077.

1. Blanloeil Y, *et al*. Accidents anaphylactoïdes sévères après perfusion d'une gélatine fluide modifiée en solution équilibrée *Therapie* 1983; **38:** 539–46.
2. Walker SR, MacSweeney ST. Plasma expanders used to treat or prevent hypotension can themselves cause hypotension. *Postgrad Med J* 1998; **74:** 492–4.
3. Adverse Drug Reactions Advisory Committee (ADRAC). Problems with colloids in fluid resuscitation. *Aust Adverse Drug React Bull* 2006; **25:** 10. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0606.pdf (accessed 07/12/06)
4. Russell WJ, Fenwick DG. Anaphylaxis to Haemaccel and cross reactivity to Gelofusin . *Anaesth Intensive Care* 2002; **30:** 481–3.
5. Russell WJ, Fenwick DG. Cross-reactivity between Gelofusin and Haemaccel. *Anaesth Intensive Care* 2003; **31:** 121–2.
6. Kelso JM. The gelatin story. *J Allergy Clin Immunol* 1999; **103:** 200–202.
7. Patja A, *et al*. Allergic reactions to measles-mumps-rubella vaccination. Abstract: *Pediatrics* 2001; **107:** 398. Full version: http://pediatrics.aappublications.org/cgi/content/full/107/2/e27 (accessed 27/10/05)
8. Pool V, *et al*. Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after measles-mumps-rubella vaccine in the United States. Abstract: *Pediatrics* 2002; **110:** 1241. Full version: http://pediatrics.aappublications.org/cgi/content/full/110/6/e71 (accessed 27/10/05)
9. Sakaguchi M, *et al*. A case of anaphylaxis to gelatin included in erythropoietin products. *J Allergy Clin Immunol* 1999; **103:** 349–50.
10. Purello-D'Ambrosio F, *et al*. Allergy to gelatin. *Allergy* 2000; **55:** 414–15.

Precautions

When gelatin or its derivatives are used as plasma expanders the precautions under Dextran 70 (p.1060) should be considered. There does not appear to be any interference with blood grouping and cross-matching of blood.

When gelatin is used as an absorbable haemostatic the precautions under Oxidised Cellulose (p.1075) should be considered.

Pharmacokinetics

After infusion of modified fluid gelatin (succinylated gelatin), 75% of the dose is excreted in the urine in 24 hours. The half-life is about 4 hours.

Uses and Administration

Gelatin is a protein that has both clinical and pharmaceutical uses.

Gelatin is used as a haemostatic in surgical procedures as an absorbable film or sponge and can absorb many times its weight of blood. It is also employed as a plasma volume expander similarly to the dextrans in hypovolaemic shock (p.1183). A 4% solution of a modified fluid gelatin (succinylated gelatin) has been infused in doses of 500 to 1000 mL. It may also be used in the form of a gelatin-derived polymer, see Polygeline, p.1077.

Gelatin rods may be employed to temporarily block tear outflow in the diagnosis of dry eye (p.2140).

Gelatin is used in the preparation of pastes, pastilles, suppositories, tablets, and hard and soft capsule shells. It is also used for the microencapsulation of drugs and other industrial materials. It has been used as a vehicle for injections: Pitkin's Menstruum, which consists of gelatin, glucose, and acetic acid, has been used in a modified form for heparin while hydrolysed gelatin has been used for corticotropin. Gelatin is an ingredient of preparations used for the protection of stomas and lesions.

Haemostasis. Gelatin acts as a haemostatic (p.1045) by providing a physical meshwork within which clotting can occur.

Gelatin powder may be applied dry to wound beds and may be most useful when mixed with saline or thrombin and applied to bone. Gelatin sponge can be applied dry or soaked in saline or thrombin solutions. When applied to skin wounds the gelatin liquefies within 2 to 5 days; when implanted into tissues it is absorbed within 4 to 6 weeks. Adverse reactions include an increased incidence of infection, compression of surrounding tissue due to fluid absorption, granuloma formation, and fibrosis. Generally, gelatin sponges cause little tissue reaction and can be applied to bone, dura, and pleural tissue (but see also Hypersensitivity, above).

References.

1. Larson PO. Topical hemostatic agents for dermatologic surgery. *J Dermatol Surg Oncol* 1988; **14:** 623–32.
2. Schonauer C, *et al*. The use of local agents: bone wax, gelatin, collagen, oxidized cellulose. *Eur Spine J* 2004; **13** (suppl): S89–S96.
3. Gabay M. Absorbable hemostatic agents. *Am J Health-Syst Pharm* 2006; **63:** 1244–53.

Neonatal intraventricular haemorrhage. Plasma volume expansion in preterm neonates has been thought to help prevent neonatal intraventricular haemorrhage (p.1050). However, a study using plasma or gelatin as plasma volume expanders,[1,2] found no evidence of a decreased risk of such haemorrhage or subsequent death or disability.

1. The Northern Neonatal Nursing Initiative Trial Group. A randomized trial comparing the effect of prophylactic intravenous fresh frozen plasma, gelatin or glucose on early mortality and morbidity in preterm babies. *Eur J Pediatr* 1996; **155:** 580–8.
2. Northern Neonatal Nursing Initiative Trial Group. Randomised trial of prophylactic early fresh-frozen plasma or gelatin or glucose in preterm babies: outcome at 2 years. *Lancet* 1996; **348:** 229–32.

Preparations

USP 31: Absorbable Gelatin Film; Absorbable Gelatin Sponge.

Proprietary Preparations (details are given in Part 3)
Arg.: Gelafundin; Geloplasma; Infukoll; ***Austral.:*** Gelfilm†; Gelfoam; Gelofusine; ***Austria:*** Gelofusin; ***Belg.:*** Gelfoam†; Gelofusine†; ***Braz.:*** Colagenan; Gelfoam; ***Canad.:*** Gelfilm; Gelfoam; ***Chile:*** Gelfoam; Gelofusine; Geloplasma; ***Cz.:*** Gelofusine; Geloplasma; ***Fin.:*** Gelofusine; ***Fr.:*** Bloxang; Gel-Phan; Gelodiet; Gelofusine†; Hydrocoll; ***Ger.:*** Gelafundin; Gelafusal; Gelaspon; Gelastypt; Spongostan; stypro; Thomaegelin†; ***Gr.:*** Gelofusine; ***Hong Kong:*** Gelfoam†; Gelofusine; ***Hung.:*** Gelaspon†; Gelofusine; ***India:*** Seraccel†; ***Indon.:*** Gelafundin; ***Israel:*** Gelfoam; ***Ital.:*** Cutanplast; Eufusin; Gelofusine; Spongostan; ***Malaysia:*** Gelfoam; ***Neth.:*** Gelfilm†; Gelfoam†; Gelofusine; Geloplasma; Willospon†; ***NZ:*** Gelfilm; Gelfoam; Gelofusine; ***Philipp.:*** Gelfoam; ***Pol.:*** Gelofusine; ***Port.:*** Gelafundina; Gelofusine; ***S.Afr.:*** Gelofusine; ***Singapore:*** Gelfoam; Gelofusine†; ***Switz.:*** Physiogel; ***Thai.:*** Gelafundin; Gelofusine; ***Turk.:*** Gelofusin; ***UK:*** Gelofusine; Geloplasma; Volplex; ***USA:*** Gelfilm; Gelfoam; ***Venez.:*** Gelfoam; Gelofusine.

Multi-ingredient: ***Arg.:*** Megaplus; Mucobase; ***Austral.:*** Orabase; Orahesive†; Stomahesive†; ***Austria:*** Gelacet; ***Canad.:*** Orabase†; Orahesive†; Tegasorb; ***Fr.:*** Plasmion; Rectopanbiline; ***Ger.:*** Gelacet N†; ***Irl.:*** Orabase; ***Israel:*** Orabase†; ***Ital.:*** Solecin; ***Mex.:*** Gelafundin; ***NZ:*** Orabase; Stomahesive; ***Port.:*** Dagragel; Varihesive†; ***S.Afr.:*** Granuflex; Orabase; ***Switz.:*** Gelacet†; ***UK:*** Orabase; Orahesive; Stomahesive; ***USA:*** Dome-Paste.

Haemoglobin ⊗

Hemoglobina.

Hemoglobin Glutamer *(rINN)* ⊗

Haemoglobin Glutamer; Hemoglobina glutámero; Hémoglobine Glutamère; Hemoglobinum Glutamerum.

Гемоглобин Глутамер

ATC — B05AA10 (bovine).

ATC Vet — QB05AA10 (bovine); QB05AA90.

NOTE. The species of origin and average molecular mass should be indicated (e.g. hemoglobin glutamer-250 (bovine) indicates a polymerised haemoglobin of bovine origin with an average mass of 250 kD).