of subgroups of patients at risk may have been missed. Aprotinin has also been used to reduce transfusion requirements during orthopaedic surgery.[20]

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Pancreatitis. Aprotinin has been tried in the management of pancreatitis (p.2361) because of the postulated role of proteolytic enzymes in this condition. However, results have been largely disappointing.

Preparations

BP 2008: Aprotinin Injection;
USP 31: Aprotinin Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Quagu-Test; Rivilina; ***Austral.:*** Trasylol†; ***Austria:*** Pantinol†; Trasylol†; ***Belg.:*** Trasylol†; ***Braz.:*** Trasylol†; ***Canad.:*** Trasylol†; ***Chile:*** Trasylol†; ***Cz.:*** Antilysin†; Gordox†; Trasylol†; ***Denm.:*** Trasylol†; ***Fin.:*** Trasylol†; ***Fr.:*** Trasylol†; ***Ger.:*** Trasylol†; ***Gr.:*** Trasylol†; ***Hong Kong:*** Trasylol†; ***Hung.:*** Gordox†; Trasylol†; ***Indon.:*** Trasylol; ***Israel:*** Protosol; ***Malaysia:*** Trasylol†; ***Mex.:*** Protinin†; Trasylol†; ***Neth.:*** Trasylol†; ***NZ:*** Trasylol†; ***Pol.:*** Traskolan†; Trasylol†; ***Rus.:*** Aprotex (Апротекс); Contrykal (Контрикал); Gordox (Гордокс); Trasylol (Трасилол)†; ***S.Afr.:*** Trasylol†; ***Singapore:*** Trasylol†; ***Spain:*** Trasylol†; ***Swed.:*** Trasylol†; ***Switz.:*** Trasylol†; ***Thai.:*** Trasylol†; ***Turk.:*** Trasylol†; ***UK:*** Trasylol†; ***USA:*** Trasylol†; ***Venez.:*** Trasylol†.

Multi-ingredient: ***Arg.:*** Beriplast P; Lacrimax; Maxus; Optilac; Tissucol; Tissucol Duo Quick†; ***Austral.:*** Tisseel Duo; ***Austria:*** Beriplast; TachoComb; Tissucol; Tissucol Duo Quick; ***Belg.:*** Tissucol Duo; ***Braz.:*** Beriplast P; Tissucol†; ***Canad.:*** Tisseel; ***Chile:*** Beriplast P; ***Cz.:*** TachoComb†; Tissucol; ***Denm.:*** Tisseel Duo Quick; ***Fin.:*** Tisseel Duo Quick; ***Fr.:*** Beriplast; Tissucol; ***Ger.:*** Beriplast; TachoComb†; Tissucol Duo S; Tissucol-Kit; ***Gr.:*** Beriplast P; ***Hong Kong:*** Beriplast P; TachoComb; Tisseel; ***Hung.:*** Beriplast P; TachoComb†; Tissucol-Kit; ***Indon.:*** Beriplast; ***Israel:*** Beriplast; Tisseel; ***Ital.:*** Beriplast; Tissucol; ***Mex.:*** Beriplast P; Tissucol†; ***Neth.:*** Beriplast P; Tissucol; Tissucol Duo; ***Pol.:*** Beriplast; ***Port.:*** Tissucol Duo; ***Rus.:*** TachoComb (ТахоКомб); ***Spain:*** Beriplast P Combi; Tissucol Duo; ***Swed.:*** Tisseel Duo Quick; ***Switz.:*** Beriplast P; Tissucol; Tissucol Duo S; ***Thai.:*** TachoComb†; ***Turk.:*** Beriplast P; Tisseel VH; ***UK:*** Tisseel.

Batroxobin *(rINN)*

Batroxobina; Batroxobine; Batroxobinum.

Батроксобин

CAS — 9039-61-6 (batroxobin); 9001-13-2 (haemocoagulase).
ATC — B02BX03.
ATC Vet — QB02BX03.

Profile

Batroxobin is an enzyme obtained from the venom of the viper *Bothrops atrox*. It has also been obtained from *Bothrops moojeni* and a similar preparation is derived from *Bothrops jararaca*.

Batroxobin is reported to act on fibrinogen to produce a fibrin monomer that can be converted by thrombin to a fibrin clot. It is used both as a haemostatic and, in larger doses, to induce a hypofibrinogen state in the management of thromboembolic disorders. When used as a haemostatic it is usually given with a factor-X activator; such a combined preparation is known as haemocoagulase (hemocoagulase). Batroxobin has been given parenterally or by local application.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Defibrase; Reptilase; ***Fr.:*** Reptilase†; ***India:*** Reptilase; ***Ital.:*** Botropase†; ***Port.:*** Reptilase†.

Blood ⊗

Sangre.

Pharmacopoeias. Many pharmacopoeias have monographs, including *US*.

USP 31 (Whole Blood). It is blood that has been collected from suitable human donors under rigid aseptic precautions for transfusion or for further processing into one or more of its components for transfusion. It contains a citrate-based anticoagulant (Anticoagulant Citrate Dextrose Solution, Anticoagulant Citrate Phosphate Dextrose Solution, or Anticoagulant Citrate Phosphate Dextrose Adenine Solution).

Whole blood must be tested for syphilis, hepatitis B virus, human T-cell lymphotropic virus (HTLV) type I and type II, hepatitis C, and HIV. It should also be tested for blood group and rhesus factors, and for unexpected antibodies to red cell antigens.

One unit (dose) of whole blood contains a minimum of 50 g of haemoglobin. One unit of whole blood filtered for removal of leucocytes (Whole Blood, Leukocytes Reduced), contains less than 5×10^6 residual leucocytes.

Whole blood is stored in the original container or transferred to an equivalent one using a technique that does not compromise sterility. It should be stored at 1° to 6°, unless platelets are to be prepared, in which case the blood is stored for no longer than 8 hours after collection at room temperature.

Whole blood collected in Anticoagulant Citrate Dextrose Solution, Anticoagulant Citrate Phosphate Dextrose Solution, or in Anticoagulant Citrate Phosphate Dextrose-Dextrose Solution may be stored for up to 21 days at 1° to 6° after the blood has been drawn. Whole blood collected in Anticoagulant Citrate Phosphate Dextrose Adenine Solution may be stored for up to 35 days at 1° to 6°. If the hermetic seal of the container is broken during collection, preparation, or further processing, the expiry date is not later than 24 hours after the seal is broken (when blood is stored at 1° to 6°), but not to exceed the original expiry date of the unit.

It is a deep red, opaque liquid from which the corpuscles readily settle upon standing for 24 to 48 hours, leaving a clear, yellowish or pinkish supernatant layer of plasma.

The USP 31 gives the names ACD Whole Blood, CPD Whole Blood, CPDA-1 Whole Blood, and Heparin Whole Blood, which specify the anticoagulant used.

Adverse Effects

The rapid transfusion of large volumes of whole blood may overload the circulation and cause pulmonary oedema. Transfusion of very large volumes of citrated blood can lead to hypocalcaemia, although this is not usually a problem unless there is hepatic impairment or hypothermia. Hyperkalaemia may occur but on its own is rarely clinically significant. Hypothermia may result from rapid transfusion of large volumes of cooled blood and may, combined with hypocalcaemia, hyperkalaemia, and resultant acidosis, lead to cardiac toxicity. Disseminated intravascular coagulation may also occur in patients receiving large-volume transfusions. Repeated transfusions of blood, as in thalassaemia, may lead to iron overload.

The transfusion of incompatible blood causes haemolysis, possibly with renal failure. Pyrexia, rigors, and urticaria may be due to antibodies towards a number of blood components. Severe allergic reactions and anaphylaxis can occur. Delayed reactions may occur more than 24 hours after transfusion in patients in whom previous transfusion or pregnancy has induced sensitisation; these reactions are usually mild and manifest as fever, chills, fall in haemoglobin concentration, and haemoglobinuria.

Transmission of infections. The use of blood, blood components, or blood products has been associated with the transmission of viruses, most notably hepatitis B virus and HIV; other reports of transmission include CMV, hepatitis C and possibly other hepatitis viruses, HTLV-I and -II, and the agent causing Creutzfeldt-Jakob disease. Transmission of bacterial and parasitic diseases is also possible including syphilis, Chagas' disease, and malaria.

The main methods of minimising the risk of transmission of infection are by rigorous selection of blood donors and by microbiological screening tests. Contamination during collection and processing is minimised by using closed systems and by strict aseptic technique. Treatment of blood products with heat or chemicals can inactivate some organisms including some viruses, in particular HIV-1, but blood and blood components cannot be treated in either of these ways. Patients receiving multiple transfusions of pooled plasma products are at increased risk of contracting infections and can be offered immunological protection, for example hepatitis B vaccine.

◊ Reviews.

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Creutzfeldt-Jakob disease. While there is no proof that transmission of Creutzfeldt-Jakob disease by blood or blood products has occurred,[1] 3 cases have been reported of possible transmission of variant Creutzfeldt-Jakob disease (vCJD) by blood transfusion.[2-4] It is recognised that there is a need for further assessment of the potential risk of transmission of vCJD by such products.

A number of precautionary measures have been implemented in the UK to minimise transmission of vCJD by blood or tissues:[5]

- plasma is imported from outside the UK for fractionation to manufacture plasma derivatives
- leucocytes are removed from donated blood (leucodepletion) as it was thought that this would remove infectivity. However, *animal* studies have shown that this is not the case and that prion concentration in the blood is likely to be reduced by only about 40%[6]
- plasma is imported for clinical use in patients born after January 1996 (this date was chosen because it was considered that foods infected with bovine spongiform encephalopathy had been largely eliminated from the diet by this time[6])
- donations of blood, platelets, and live bone are not accepted from donors who themselves have received blood components since 1 January 1980, or from any donors who have received intravenous immunoglobulin prepared from UK plasma or who have undergone plasma exchange anywhere in the world

Concern at the risk of transmitting Creutzfeldt-Jakob disease by albumin prepared from placental blood has led to restriction on this source of albumin (see Transmission of Infections under Albumin, p.1052).

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Effects on leucocytes. A study of 50 patients in an intensive care unit found that 45 of them developed leucocytosis after transfusion of packed red blood cells.[1] The leucocytosis, which was accounted for by neutrophils, occurred immediately after transfusion and persisted for 12 hours. A further study[2] of 96 critically ill patients found that leucocytosis commonly occurred in