

omeprazole will be any more effective than H<sub>2</sub> antagonists in preventing recurrence.

AM GHELANI  
S HALE  
H COLEMAN  
H RADZIWNOK  
Research and Development Laboratories,  
Fisons plc, Bakewell Road,  
Loughborough, LE11 0RH,  
C ROBERTSON  
M ATKINSON  
Department of Surgery,  
University Hospital,  
Queen's Medical Centre,  
Nottingham NG7 2UH

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### Elective surgery in a haemophilic patient with high titre inhibitors: use of extracorporeal protein A immunoabsorption

About 12% of congenital haemophiliacs develop IgG factor VIII inhibitors, and in these cases it is difficult or impossible to achieve haemostatic concentrations of factor VIII:c.<sup>1</sup> In emergencies animal factor VIII, high dose human factor VIII, and activated plasma products such as FEIBA have been used with some success.<sup>1</sup> Immune tolerance induction using regular doses of factor VIII can reduce concentrations of inhibitor over a prolonged period<sup>2</sup> but this is impractical if surgery is urgent. In these circumstances plasmapheresis is useful in reducing concentrations of inhibitor.<sup>3</sup> This becomes relatively inefficient, however, at low concentrations of inhibitor and requires replacement treatment

with donor plasma products. These disadvantages are overcome with extracorporeal antibody immunoabsorption in which extensive plasma treatment is feasible without recourse to the use of donor plasma. Patients with Christmas disease with inhibitors have been successfully treated in this way,<sup>4</sup> but as yet there have been no reports in cases of haemophilia A.

A 36 year old haemophilic with 0 IU/dl factor VIII:c, 250 New Oxford U/ml human factor VIII inhibitors, and negative tests for HIV antibodies presented with recurrent dental abscesses. He experienced increasing pain needing prolonged courses of antibiotics and it was felt that he required urgent surgery. Previous minor bleeding had been treated with bed rest alone, but a calf haematoma three years previously had required four months of factor VIII treatment, and a life threatening retroperitoneal haematoma six months previously had been treated with 934 000 U human factor VIII, following which his inhibitors rose to 2890 U/ml. These then fell slowly to 250 U/ml over six months in response to regular factor VIII treatment.

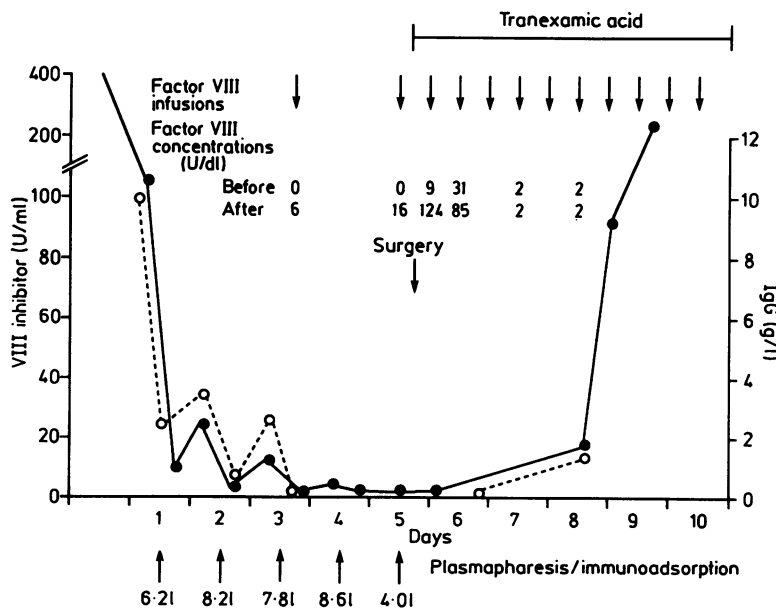
Using venous access via the antecubital vein, over five days, a total of 35 litres of plasma was generated on a Hemonetics V-50 cell separator machine and immunoabsorbed on protein A sepharose columns using a Citem 10 extracorporeal immunoabsorption treatment system (Excorim, Lund, Sweden). The figure shows that serum IgG concentrations and factor VIII inhibitor concentrations fell rapidly with each treatment. With about 30 machine cycles of 200 ml of plasma, the technique was very effective at reducing high concentrations of inhibitor but was less effective at lower concentrations. There were also slight overnight increases in IgG and VIII inhibitor concentrations which were probably explained by the equilibration of extravascular and intravascular IgG. On the fourth day the inhibitor concentrations had fallen to <0.3 IU/ml, but an infusion of human factor VIII calculated to raise the patient's factor VIII concentrations by 200 IU/dl only achieved an increase from 0 to 6 IU/dl. After a further two days of plasmapheresis and immunoabsorption a further infusion of factor VIII increased the

circulating factor VIII concentrations to 124 IU/dl. Oral tranexamic acid 1 g three times a day was started and the patient underwent extraction of four infected teeth including an impacted wisdom tooth. Immunosuppressive and normal human immunoglobulin replacement treatment were not administered. Perioperative haemostasis was normal, and the next day the patient's factor VIII concentrations rose from 31 to 85 U/dl after a further infusion of factor VIII.

On the subsequent two days, similar infusions of factor VIII did not increase factor VIII concentrations and the inhibitor reappeared. To what extent this anamnestic response was modified by the factor VIII infusion on day 3 or the previous desensitisation regimen is uncertain. Factor VIII treatment was continued for a total of seven days and when reviewed three weeks later he had made a full recovery.

Extracorporeal protein A immunoabsorption has been used to remove IgG inhibitors from patients with Christmas disease<sup>4</sup> and to remove HLA antibodies before renal transplantation.<sup>5</sup> A major application of this new technique would be to manage emergency bleeding in haemophiliacs with inhibitors, or to prepare such patients for urgent surgery. Previous workers treating Christmas disease have combined this with immunosuppressive treatment with cyclophosphamide and high dose intravenous immunoglobulin, and have shown long term diminution in factor IX inhibitor concentrations.<sup>4</sup> The case we describe shows that immunoabsorption alone can reduce factor VIII inhibitor to almost undetectable concentrations and that following this, conventional factor VIII support is adequate for surgical procedures. This form of treatment would be particularly applicable in emergency situations where extracorporeal immunoabsorption would avoid the cost and uncertain response to high dose human factor VIII treatment. Our patient was seronegative for HIV, but it should be borne in mind that seropositive patients could be immunocompromised by a period of hypogammaglobulinaemia and should perhaps receive normal IgG replacement treatment at the end of the immunoabsorption procedure.

BJ BOUGHTON  
A PAYNE  
A SERMAN  
C OWEN  
Department of Haematology,  
Queen Elizabeth Hospital,  
Edgbaston, Birmingham B15 2TH



Factor VIII inhibitors (—), serum IgG concentrations (-----), and factor VIII concentrations before and after factor VIII infusions in a patient treated with protein A immunoabsorption.

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