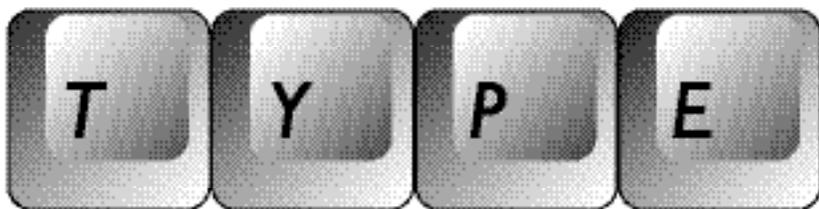


blood

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Indiana Hemophilia & Thrombosis Center, Inc.

Produced for Indiana's primary caregivers and their medical staff by Indiana's Only Federally Recognized Comprehensive Hemophilia Center

at St. Vincent Hospital

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3rd-gen recombinant factor product now available *Baxter's Advate® represents advance in safety in protecting FVIII patients against viral transmission*

The hemophilia community has a long-standing concern regarding the safety of replacement products due to the viral diseases patients have been exposed to through concentrates. These viruses include hepatitis A (HAV), B (HBV), C (HCV), and HIV, among others. Concerns remain regarding the emergence of as yet unidentified viruses that may potentially infect our patient population whenever an infusion product has exposure to human or animal proteins in manufacturing, processing, or final preparation. For this reason, the Medical and Scientific Council (MASAC) of the National Hemophilia Foundation (NHF) has continued to urge clotting factor manufacturers to make all efforts to remove these proteins from all parts of the processes utilized to produce these products to ensure the highest level of safety. The IHTC supports the recommendation of MASAC.

To this end, Baxter BioScience has developed a new generation recombinant factor VIII concentrate to meet this need: Advate®. This new clotting factor product was licensed by the Food and Drug Administration on July 25, 2003. Advate® is licensed to treat or prevent bleeding episodes in patients with factor VIII deficiency. Currently, there are three genetically engineered products on the market aside from Advate®, often referred to as first- and second-generation products, as there are human or animal proteins involved in the manufacturing process, or final preparation. Advate® is a

Patients affiliated with the IHTC's program are informed of all appropriate new product licensures.

third-generation product because there is no added human or animal protein in the manufacturing process, nor are such proteins used as a stabilizer in the product's final preparation.

Studies have been performed prior to licensure and are ongoing. These studies have included 154 unique patients in four controlled clinical studies. More than 20,000

infusions were administered without any evidence of viral transmission or other issues regarding safety or efficacy. Studies have been performed and are continuing in pediatric and adult previously treated patients for the prevention and treatment of bleeding and in the surgical setting. The product has an added viral safety measure, solvent-detergent, to ensure the best possible protection to our patient population.

lation.

Your patients first visit to the IHTC will include:

- Complete disease specific education & supportive literature
- Information on the most current treatments
- Genetic counseling and testing of family members if needed
- Medic alert enrollment or update
- Evaluation of viral status, immunization status and immunizations needed
- Sports recommendations
- Review of available research studies for participation
- Other services available as needed

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Hemophilia and related conditions: conclusion by Amy D. Shapiro, MD

The following is the concluding installment of a 5-part series excerpted from Conn's Current Therapy 2000 on Hemophilia and Related Conditions.

Preventive Care

Male infants born to known or suspected hemophilic carrier mothers should not be circumcised until hemophilia has been excluded. Blood for assay for aPTT and FVIII or IX assay can be obtained from cord blood. When a cord blood sample is not available, venipuncture should be performed from a superficial limb vein in order to lessen the risk of hematoma development requiring replacement therapy. Femoral, arterial, and jugular sites must be avoided.

Routine immunizations, such as DPT or MMR, may be given in the deep subcutaneous tissue or via the usual route when the smallest gauge needle is used and pressure and ice are applied to the site for 3-5 minutes post injection. Hepatitis B vaccine should be given as soon after birth as possible to all infants with hemophilia. The live oral polio attenuated vaccine is contraindicated in any infant when there is an immunocompromised household member (e.g., HIV infected hemophilic). In these instances, the Salk vaccine is utilized. Hepatitis A vaccine should also be administered to unexposed hemophiliacs over two

years of age.

Early infant dental intervention is recommended to teach proper tooth brushing and ensure adequate household water fluoridation. The teeth should be cleaned routinely and anticipated problem areas for causing bleeding discussed. In addition to education about hemophilia, both genetic and psychosocial counseling is important for the family with a newborn with hemophilia, especially for the ~30% for whom there is no previous family experience with the disease. Normal socialization and development is encouraged, and experienced personnel should discuss what minimum limitations are reasonable. An appropriate exercise regimen that excludes contact sports (e.g., tackle football) should be encouraged as a daily routine. Further, the role of such an exercise program for the child and adult following episodes of bleeding is best discussed before the child has a joint bleed.

Important Issues in Hemophilic Bleeding

Early treatment decreases the duration of therapy, predisposition to re-bleeding, morbidity experienced and improves the quality of life. Early signs and symptoms of bleeding may not be notable on physical examination and patient report of pain should be used as a guide for institution of early therapy. Early bleeding episodes may be treated with an approximate 30-40% factor correction.

“Hemophilia and related conditions: conclusion” continued ...

More complicated bleeding episodes or bleeding in areas such as the face, neck, hip, iliopsoas require a higher correction level, 80-100%. Dosage may be calculated using the following formula:

units required = weight (kg) X level desired X volume of distribution

The level desired should be placed into the formula as a whole number (e.g., 40 representing 40%). The volume of distribution for FVIII is ~0.5, and for FIX ~1.0, except in the case of rFIX, where 1.2 is used.

Intervention strategies include on-demand (therapy instituted after a bleeding episode has been experienced/identified) and prophylactic therapy (therapy utilized to prevent bleeding). Prophylactic therapy has been demonstrated to prevent essentially all spontaneous hemarthroses. A decision to undertake a prophylactic regimen should be made in conjunction with the parent/patient and professionals in the comprehensive Hemophilia Treatment Center.

Hip joint or acetabular hemorrhages may result in increased intra-articular pressure. Twice-daily infusion therapy designed to sustain a factor level above 10 units per dl for at least 3 days should be given, along with enforced bed rest. Hip hemarthrosis may be difficult to differentiate from an iliopsoas bleed. The latter limits primary hip extension, whereas hemarthrosis makes any motion of the hip excruciatingly painful. Further, an iliopsoas bleed may lead to decreased sensation over the ipsilateral thigh because of compression of the sacral plexus root of the femoral nerve. Ultrasonography may demonstrate a hematoma in the iliopsoas region. Treatment of the two is similar, although rehabilitation from the hip hemarthrosis is more protracted. Both benefit from physical therapy.

Closed compartment muscle and soft-tissue hemorrhages, often in the upper arm, forearm, wrist, volar hand, and anterior or posterior tibial compartment, may result in impingement on the neurovascular bundle. Swelling and pain proceed tingling, numbness, and loss of distal arterial pulses. Infusion must maintain an adequate hemostatic factor level. Surgical decompression is undertaken only if medical therapy fails to forestall progression, and in consultation with a comprehensive hemophilia treatment center (HTC).

For life-threatening bleeding in a hemophilic, the exigency for immediate infusion is superseded only by resuscitative requirements. The factor level should be maintained >50% in these circumstances. An acutely hemorrhaging hemophilic should be transported, if possible, to

an emergency center that stocks appropriate replacement products. All head injuries must be considered nontrivial unless proved otherwise by observation and CT/MRI imaging. Late bleeding after head trauma can occur up to 3 to 4 weeks following the event. Hence, patients with head and neck injuries should be infused immediately unless convinced the injury is insignificant. Non-hospitalized patients/families should be instructed in neurologic signs and symptoms of central nervous system bleeding, so that repeat infusion, clinical and radiological assessment, and hospitalization occur at the earliest manifestation of bleeding.

Bleeding in the floor of the mouth, pharynx or epiglottic region may result in airway compromise or obstruction, and is treated with an aggressive infusion program and extended clinical follow-up to ensure resolution. Such bleeding may be precipitated by coughing, tonsillitis, oral or otolaryngeal surgery (e.g., extraction of wisdom teeth, tonsillectomy, adenoidectomy), or regional block anesthesia. For surgery and anesthesia, prophylaxis with appropriate infusion therapy prior to the procedure is mandatory.

Continuous infusion regimens to maintain normal circulating factor activity are often utilized in patients post-operatively, in complicated or serious bleeding episodes, or with gastrointestinal lesions, such as ulcer, varices, or hemorrhoids.

Comprehensive Care

Designated hemophilia treatment centers have been established in the United States and many other countries to provide multidisciplinary care of hemophilia and related disorders. The multidisciplinary team provides optimal chronic disease management and lowers associated morbidity and mortality.

The comprehensive hemophilia centers provide voluntary testing for blood-borne viral infections, counseling of patients found seropositive, and access to appropriate care and therapy. Risk reduction counseling and education are essential elements of comprehensive care.

Comprehensive centers are the mainstay for ongoing education of patients and families for management of their bleeding disorder. The centers coordinate home therapy and preventive services and work closely with hemophilia consumer organizations. Further information about hemophilia care, hemophilia centers, and HIV risk reduction and counseling is available through the National Hemophilia Foundation (NHF), 116 W. 32nd St, 11th Floor, N.Y., N.Y. 10001 (800-424-2634), or from Hemophilia of Indiana (317-396-0065).

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Be sure to visit the IHTC's web site at www.ihtc.org.

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