REPORT TO THE GOVERNOR AND GENERAL ASSEMBLY

IOWA HEMOPHILIA ADVISORY COMMITTEE

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EXECUTIVE SUMMARY

There are two divergent populations that will be represented by the Iowa Hemophilia Advisory Committee: 1) those with bleeding disorders (who have problems getting their blood to clot) and 2) those with clotting disorders (whose blood clots excessively or too easily).

The bleeding disorders include hemophilia, von Willebrand disease (vWD) and platelet disorders. Hemophilia is an inherited blood clotting disorder which results in a deficiency of one of the clotting proteins in blood, primarily factor VIII or factor IX. Hemophilia can range from mild to moderate to severe. It is typically expressed in males and carried by females. Approximately 30 percent of cases occur in the absence of a family history. The most common bleeding disorder is von Willebrand's disease, affecting 1 in 100 people. It is transmissible as a dominant or a recessive genetic disorder affecting both males and females. There are three types, ranging in severity from mild to severe. Platelet disorders are not very common and involve defects in different areas of platelet functions. Bleeding is usually mild in nature with prolonged bleeding under the skin and in mucus membranes.

There are a number of clotting disorders. Thrombophilia is a disorder in which the blood clots easily or excessively and increases the risk of blood clot formation in veins. Factor V Leiden mutation, prothrombin gene mutation, protein C deficiency, and protein S deficiency are inherited disorders that cause increases in fibrin production, an important protein involved in clot formation.

By 1970, it became apparent to hematologists treating hemophilia that merely offering effective hemostatic therapy during a bleeding crisis was insufficient to improve patient prognosis. This realization led to the development of a national network of hemophilia treatment centers (HTCs) around the country. The charge to the HTCs is to provide and coordinate comprehensive, multi-disciplinary services, including hematology care, dental care, orthopedic care, physical therapy, psychosocial support, infectious disease care, and financial, vocational and genetic counseling to persons with bleeding disorders The HTC concept was so successful that the scope of care to be provided by the HTCs was expanded to include patients with clotting disorders. A study by CDC found that hemophilic patients involved with a hemophilia treatment center are less likely to be hospitalized for bleeding complications and have a 40 percent decrease in mortality compared with those not enrolled. The HTC at the University of Iowa Hospitals and Clinics is the federally recognized bleeding and clotting disorders center for the state of Iowa.

Patients with hemophilia can develop complications. Some complications related to hemophilia include joint disease, hepatitis, HIV infection and inhibitor

development. These complications can result in surgery, organ transplants and expensive treatment.

In addition to providing direct patient care, HTC of Iowa is involved in research projects. Studies are being conducted in the areas of genetics, drug efficacy, and program evaluation. HTC also participates in a number of drug comparison studies and is enrolled with the Hemophilia and Thrombosis Research Society's national registries for hemophilia and thromboembolism patients.

The advisory committee has identified several activities to educate communities about hemophilia and bleeding and clotting disorders and advocate for hemophilic individuals and their families. Committee members will begin planning and carrying out these activities over the coming year.

- The committee recommends that basic health insurance policies cover the cost of clotting factor concentrate administered outside the hospital setting and that hospitals providing out-patient care to people with hemophilia be sufficiently reimbursed for clotting factor concentrates. The goal is to ensure continued appropriate out-patient services without financial penalty to the provider.

- Hemophilia is a life-long disease with no cure. Treatment is very expensive, so the committee recommends that lifetime insurance caps be eliminated or raised to a more appropriate level for hemophilic individuals. Existing insurance caps have not kept pace with the rising cost of medical care and have not changed significantly in the last 30 years.

- Factor replacement is not readily available in local communities. Therefore, it is recommended that persons with a bleeding disorder in Iowa have a current supply of their treatment product available in the home. The person can either use the factor at home or take it to their local hospital to treat an injury or bleeding episode. It is necessary that these products be covered by insurance programs.

Definition of Hemophilia

Hemophilia is an inherited blood clotting disorder which results in a deficiency of one of the clotting proteins in blood, primarily factor VIII (hemophilia A, classic hemophilia) or factor IX (hemophilia B, Christmas disease). The incidence of hemophilia is rare with only 1 in 5000 boys born with factor VIII deficiency and 1 in 30,000 boys born with factor IX deficiency. Hemophilia is an X chromosome-linked recessive disorder. It is typically expressed in males and carried by females. Approximately 30 percent of cases occur in the absence of a family history, reflecting a spontaneous mutation rate. Hemophilia affects all races and ethnic groups equally, and mild to moderate deficiencies are often under-diagnosed. Carriers may have lower than normal factor levels and may experience bleeding the same as someone with mild or moderate hemophilia. Carriers are treated as potential bleeders.

Clinical Picture

Although bleeding episodes may be precipitated by injury or surgery, internal bleeding can occur spontaneously in more severely affected individuals. Most bleeding takes place in the large joints (ankles, knees, hips, elbows), but can also occur in the muscles and/or vital organs. Recurring bleeding episodes can cause severe joint damage, resulting in crippling arthritis and limited range of motion. Individuals with bleeding disorders do not bleed any more rapidly than persons with normal clotting factors, but they bleed longer. Head bleeds, oral cavity bleeds or bleeding in vital organs may be life-threatening.

Genetic Inheritance

The genes involved in factor VIII and factor IX production are both located on the X chromosome; therefore, hemophilia is referred to as a sex-linked trait. A mutation in one of these genes can cause a clotting factor to be defective. The gene associated with hemophilia may be passed on to the subsequent generation by either parent. Women who carry the gene that causes hemophilia are called carriers. All affected members of a given family feature the same defect in their factor VIII or factor IX gene; as a result, these members will have the same severity of the disease.

Females have two X chromosomes, while males have one X and one Y chromosome. Each parent contributes one of these sex chromosomes to each offspring. Figure 1a illustrates transmission of normal genes, resulting in children who are not affected. In the case of a female carrier, there is a 50-50 chance that any given daughter will be a carrier and that any given son will have hemophilia

(Figure 1b). Figure 1c depicts a hemophilic father who only has an altered X chromosome, which he will pass on to all of his daughters, making them carriers. His sons, however, will not be affected. Some carrier females have low factor VIII or factor IX activity and are symptomatic; they are called symptomatic carriers. Symptomatic carriers often require treatment following traumatic injury or prior to surgery, including dental surgery.

It is possible, but rare, that both parents may carry affected genes. Sons born to a hemophilic father and a carrier mother stand a 50-50 chance of hemophilia. Daughters also have a 50-50 chance, since both parents have an X chromosome with the hemophilia gene. In this case, daughters who do not have hemophilia are carriers.

Hemophilia's inheritance pattern and its clinical pattern of bleeding have been known for many centuries. The earliest description of hemophilia is attributed to the medieval physician and rabbi Maimonides. He understood the pattern of sex-linked inheritance, and recommended against ritual circumcision in males whose brothers or male cousins had hemorrhaged during the procedure. The best-known cases of hemophilia are those among male descendants of England's Queen Victoria in the nineteenth and twentieth centuries.

Normal Mother | Normal Father

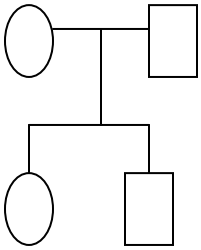

Figure 1a.
100% probability-normal child

Carrier Mother | Normal Father

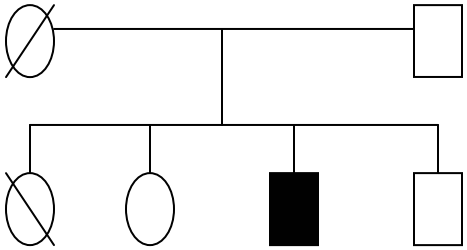

Figure 1b.
25% probability-carrier female
25% probability-hemophilic male
50% probability-normal male or female

Normal Mother | Hemophilic Father

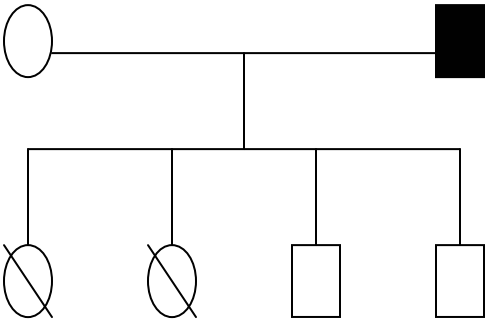

Figure 1c.
50% probability-carrier female
50% probability-normal male

Other Bleeding Disorders

The most common bleeding disorder is von Willebrand's disease, affecting 1 in 100 people. It is transmissible as a dominant or a recessive genetic disorder affecting both males and females. von Willebrand's disease is characterized by bleeding into the mucosal and soft tissues and is often seen following surgery. There are three types, ranging in severity from mild to severe. Women with von Willebrand's disease are particularly at risk for anemia, and if undiagnosed, are likely to suffer morbidity from unneeded gynecologic procedures, including hysterectomy.

Platelet disorders are not very common and involve defects in different areas of platelet functions. Bleeding is usually mild in nature with prolonged bleeding under the skin and in mucus membranes as well as bleeding with trauma, surgery or invasive procedures. Names of platelet disorders include qualitative platelet defect, platelet storage pool defect, gray platelet syndrome, Bernard-Soulier syndrome, and Glanzmann thrombasthenia.

Clotting Disorders (Thrombophilias)

Thrombophilia is a disorder in which the blood clots easily or excessively and increases the risk of blood clot formation in veins. Factor V Leiden mutation, prothrombin gene mutation, protein C deficiency, and protein S deficiency are inherited disorders that cause increases in fibrin production, an important protein involved in clot formation. Disorders such as disseminated intravascular coagulation (DIC) and lupus may be acquired after birth and increase the risk of clotting due to overactivation of blood clotting factors.

History of Hemostatic Therapy for Hemophilia

Whole blood and plasma transfusions were performed as part of hemophilia care prior to the 1960s but proved ineffective given the unpredictability of bleeding episodes, unavailability of blood products, and traveling distances to hospitals. Persons with hemophilia seldom lived beyond the age of 30. Those surviving were usually disabled with crippling musculoskeletal dysfunction. Surgery was extremely hazardous. The hemophilic individual was often prevented from pursuing educational and vocational objectives. A life of pain, unmet goals, and the continuing threat of hemorrhage took their toll on the psychological health of the affected individual and his family.

The 1960s saw the development of procedures to isolate cryoprecipitate, the first practical clotting factor concentrate, for use in treating bleeding episodes. Cryoprecipitate could be produced in blood banks during routine blood component preparation and was soon readily available nationwide. Still, its major

disadvantage was that it needed to be stored frozen and was not easily adaptable to ambulatory self-treatment.

Advances in plasma protein processing in the 1960s and the 1970s triggered emergence of the commercial plasma derivative industry. These companies engaged in bulk fractionation of human plasma from thousands of blood donors into albumin, immune globulins, and clotting factor concentrates. The advantage of commercially derived concentrates was that they could be freeze-dried in convenient dosage bottles for storage at room temperature and be self-administered following reconstitution, drastically reducing the number of hospital visits. A significant disadvantage of these products, also shared by cryoprecipitate, had been their potential for exposing individuals to hepatitis and other viral contaminants.

In the 1980s, hemophilia patients were struck a devastating blow when it was learned that clotting factor concentrates could become contaminated with the human immunodeficiency virus (HIV). Approximately half of persons with severe hemophilia in the United States at that time were thought to have become infected with HIV. Tighter screening methods were implemented and advanced modes of viral inactivation were developed for treating clotting factor concentrate to inactivate HIV and other viruses.

During the 1990s, technology for manufacturing purer clotting factor concentrates continued to advance. Using specific monoclonal antibodies and techniques, factors XIII and IX were separated from other plasma proteins. However, these production methods are more expensive, and treatment costs escalated. Factor VIII and factor IX concentrates may also be prepared through recombinant DNA technology. These products hold promise of eliminating the risk of transfusion-associated diseases. Synthetic drugs such as desmopressin acetate (DDAVP) were introduced to treat mild to moderate hemophilia A and von Willebrand’s disease.

Preventive treatment became more common during the 1990s. Implementation of prophylactic therapy prevents chronic bleeding episodes typically found in hemophilia, resulting in less pain and orthopedic damage and longer, healthier, more active lives.

The Comprehensive Hemophilia Treatment Center Model

During the 1970s, it became apparent to hematologists treating hemophilia that merely offering effective hemostatic therapy during a bleeding crisis was insufficient to improve patient prognosis. Several major hospitals and organizations in the United States developed what were to become models for a national network of comprehensive hemophilia treatment centers. These institutions documented a substantial improvement in quality of life for persons

with hemophilia when the venue of care moved from the hospital emergency room to a designated hemophilia treatment center emphasizing preventive care.

These successes attracted the attention of federal health planners, who recognized that comprehensive care for a complex and chronic illness such as hemophilia could serve as a useful model for dealing with rare, potentially high-cost, multi-faceted illnesses. In 1976, federal funds became available to establish a national network of comprehensive hemophilia treatment centers. Today the Iowa Hemophilia Treatment Center (HTC) is partially funded with federal money. The Bureau of Maternal and Child Health (MCHB) and the Centers for Disease Control and Prevention (CDC) provide partial funding for the HTC. The funds are used to pay for personnel, educational materials and travel costs that are related to HTC operation. State funds, hospital funds, money generated from studies and income from the hemophilia homecare program also support the HTC.

At the Iowa Hemophilia Treatment Center, a team of medical, nursing and psychosocial specialists addresses the full range of long-term needs of persons with hemophilia and other congenital bleeding and clotting disorders. The center provides and coordinates comprehensive, multi-disciplinary services, including hematology care, dental care, orthopedic care, physical therapy, psychosocial support, and infectious disease care. The hemophilia nurse specialist plays a pivotal role in patient care management. Typically, the hemophilia nurse has been the professional responsible for training patients and the family members in home administration of clotting factor concentrates.

A study by CDC found that hemophilic patients involved with a hemophilia treatment center are less likely to be hospitalized for bleeding complications and have 40 percent decrease in mortality compared with those not enrolled.

Blood Derivatives

Plasma-derived factor concentrates are produced for hemophilic persons worldwide. These concentrates can be prepared easily from a by-product of plasma procured for manufacturing more widely used derivatives such as albumin and immune globulins. Plasma derivative manufacturers obtain plasma primarily by plasmapheresis from paid donors. Plasma collected from 5000 to 40,000 donors is pooled and processed together. In fractionation plants, large containers of plasma are processed sequentially into clotting factor concentrate, albumin, and immune globulins. Prior to development of an HIV test in 1985, albumin and immune globulins had been sufficiently treated by heating during manufacturing to render them virus-free. Clotting factor concentrates could not be subjected to the same amount of heat without destroying their potency. Eventually, methods were developed to inactivate HIV and hepatitis during the manufacturing process, but not before many hemophilic individuals who had received clotting factor concentrates between 1979 and 1985 became infected

with hepatitis B virus (HBV), hepatitis C virus (HCV), and/or HIV. Now, viral inactivation techniques and donor screening render factor concentrates significantly safer from the risk of HIV and hepatitis virus infection. No cases of HIV transmission due to infusion of clotting factor concentrates have been reported in the United States since March 1985.

Several effective but expensive methods of purifying clotting factor concentrates are in use. Clotting factor may be concentrated by isolation from plasma using monoclonal antibodies. Another method involves physical/chemical separation by a process know as chromatography, and then virus-inactivation by heating, using certain solvents and detergents, filtration, or combinations of these methods. High-purity clotting factor concentrates are sold at two to four times the price of concentrates with a higher plasma protein content – the higher the protein content, the less pure the product.

Other Treatments

Genetically engineered factor VIII concentrate, commonly called recombinant factor VIII, and albumin-free recombinant factor IX are licensed for use by the Food and Drug Administration (FDA). In fact, 60 to 70 percent of all factor IX product dispensed is recombinant. Recombinant products hold the promise of eliminating most concerns about transfusion-associated disease, but costly production methods raise other considerations about costs, and, therefore, their availability to many hemophilic individuals may be limited.

In selected patients with mild factor VIII deficiency, symptomatic female carriers of hemophilia, and some forms of von Willebrand's disease, the drug DDAVP, which stimulates the body to release more of its own factor VIII, reduces or eliminates the need for blood products. DDAVP can be administered intravenously or as a nasal spray.

Complications of Hemophilia

Joint Disease

The most common and debilitating complication of hemophilia is joint arthropathy. It affects approximately 80 percent of the hemophilia population. Joint arthropathy results from recurrent hemorrhages within the joints. The synovial membrane that lines all joints secretes a clear fluid that functions as a natural lubricant. Repeated bleeding, whether spontaneous or due to trauma, causes inflammation of the synovial lining. Cells that mediate the body's inflammatory response digest not only unwanted blood in the joint, but also begin to digest the cartilage at the ends of bones. Without the protection of this cartilage, upon movement, friction between bones causes pain. Continued destruction results in scar tissue, pain, and stiffness, leading to arthritis.

Liver Disease

In the United States, hepatitis A is generally considered to be transmitted by the fecal/oral route via infected food handlers or drinking water. Although several outbreaks of hepatitis A from clotting factor concentrates have been reported in Europe, only a few cases have occurred in the U.S. The manufacturing process for factor concentrates has been enhanced by filtration or a heating process to help eliminate hepatitis A virus.

When clotting factor concentrate became widely available in the early 1970s, most persons with hemophilia were exposed to hepatitis B virus (HBV) and hepatitis C virus (HCV). Laboratory testing showed evidence of prior exposure, and some individuals presented clinical signs of chronic liver disease from hepatitis virus infection. About 15 percent of those exposed to hepatitis B exhibit persistent viral protein in the blood. These findings may be associated with increased likelihood of developing significant liver disease such as cirrhosis and liver cancer. Safe and effective HBV vaccines are available and should be strongly considered for hemophilic individuals. HBV vaccination is now routine for most children.

Hepatitis C occasionally arises in multi-transfused individuals. More than 90 percent of hemophilic persons have been exposed to the virus. In most cases this exposure leads to chronic infection. The single most common reason for patients to require a liver transplant in the U.S. is hepatitis C infection. At its onset, this infection does not cause any symptoms, but, as the decades pass, those infected are placed at increased risk of cirrhosis and liver cancer. Several medical therapies are in use or under development to eradicate chronic hepatitis C, but these efforts, to date, have not been very effective. As of 1997, there have been no reports of hepatitis C transmission through clotting factor when treated with newer process. Currently, a vaccine for hepatitis C is not available.

HIV Infection

Since AIDS reporting began in 1983, eight pediatric patients in Iowa have acquired HIV through hemophilia treatment. This accounts for 33 percent of all pediatric HIV exposures.

Persons with hemophilia, cared for at comprehensive hemophilia treatment centers, receive counseling about HIV exposure and its effects. HIV testing, as well as clinical and laboratory immunologic surveillance, are essential aspects of comprehensive hemophilia care. Past studies have indicated that from five to 20 percent of sexual partners of HIV-infected men with hemophilia may have become infected as well. Because of concerns about increased heterosexual and maternal-fetal transmission of HIV, specific risk reduction programs have been developed for sexually active individuals. The hemophilia treatment centers continue to facilitate access to specialized counseling services, support groups and other regional resources.

Results of recent clinical trials suggest that the onset of AIDS in HIV-positive individuals can be postponed by early intervention with complex and expensive combinations of anti-HIV medications. In some instances, these medical treatments have significantly improved the quality of life of infected individuals.

Inhibitors
In some patients with hemophilia, the immune system produces an antibody that inhibits the action of replacement blood products and prevents clot formation. This antibody is known as an inhibitor. The presence of an inhibitor makes the treatment of bleeding episodes more difficult. An inhibitor destroys the clotting factor before it has a chance to stop the bleeding. The reason inhibitors develop in unknown, but it is not related to the number of treatments an individual receives. Inhibitors usually occur in the first 5 to 10 years of life.

Cost of Care

Self-treatment at home has been tremendously successful in reducing the cost of care, limiting disability and decreasing unemployment. Analyses by the National Hemophilia Foundation have shown that hemophilia treatment centers have saved federal and state governments, as well as commercial insurers, hundreds of millions of dollars by reducing the need for hospitalization and decreasing clinic or emergency room visits. The savings are realized because the nurses at the treatment centers provide patients with education on self-treatment.

Most clotting factor concentrate (90 percent) is administered at home, with its final price dependent upon the nature of the distribution system and how much health insurers are willing to pay. Fully developed distribution systems provide medical treatment coordination, shipment of concentrates and collection of used injection materials for medical waste disposal.

Even with these measures in place, clotting factor replacement therapy represents the most costly aspect of hemophilia treatment. The following is an example of the expense involved:

For a factor VIII deficient patient with an elbow bleed, the patient, who weighs 165 pounds (75 kg), would need to treat themselves with 25 units of factor/kilogram (kg). The average cost of factor is approximately $1.00/unit.

75 (kg) X 25 (units/kg) = 1875 units X $1.00/unit = $1875.00.

After an individual has met insurance deductibles, most insurance plans pay on an 80%/20% basis (if the factor is paid from the major medical portion of their insurance). The standard policy would pay 80% of the cost ($1500.00), leaving the patient with a $375.00 liability for that bleed. Many hemophilic patients meet their annual maximum out-of-pocket expenses early in the year. Many patients

also reach their insurance's lifetime caps at a young age due to the expense of their treatments.

Concerns/Challenges

The medical needs of hemophilia patients are emergent, episodic and ongoing. However, some patients continue to receive nearly all medical treatment in the hospital emergency room despite the fact that comprehensive care is available at comprehensive treatment centers. While the primary care physician might be contacted by telephone, unless hospitalized, the patient might not be seen by a physician with hemophilia experience. Such fragmented, crisis-oriented care still persists for many individuals with hemophilia.

Health Insurance

In recent years, the driving force within the health insurance industry has been cost containment, posing a challenge for carriers, providers and patients. Most health insurance coverage provided by employers involves managed care arrangements that attempt to limit access to specialty care by using patients' primary care physicians as "gatekeepers" to these services.

Prompt access to essential emergency clinical services has been hindered by problems associated with required determination of medical necessity prior to authorization for care. Many hemophilic individuals report limitations on the frequency of visits and/or reimbursement problems for specialized emergency and consultative services received at their hemophilia center. Annual and/or lifetime caps are frequently imposed on routine and preventive office-based services, as well as specialty and hospital-based care and clotting factor concentrates. Moreover, even when these services are available, they may be subject to high deductible payments. Coverage for clotting factor concentrates can be subject to co-payments that are unaffordable for many families. Coordination of care between the primary care physician and the specialist is imperative in order to maintain the standard of care for this chronically ill population and, therefore, maximize treatment outcomes.

Because of inadequate health insurance coverage, many adult patients and parents of pediatric patients must choose between viable careers and working in lower-paying positions or not working al all, in order to qualify for government assistance.

Medicaid

Many hemophilia patients do not qualify for Medicaid benefits simply because of their present ability to work. Significant concerns have been raised that restrictions in future health insurance benefits may lead to impoverishment of more persons with hemophilia and the need for expansion of Medicaid benefits.

Medicare
Most people with hemophilia are under 65 years of age and, as a result of hemophilia treatment, are not permanently disabled. Those under 65 with permanent disabilities are eligible for Medicare benefits after a two-year waiting period. Still, as HIV infection progresses, more infected adults become disabled. Medicare reimburses up to 80 percent of approved blood product costs incurred on an outpatient basis. Recent increases in clotting factor price make the 20-percent Medicare co-payment impossible for most beneficiaries to meet.

Supplemental Security Income (SSI)
Eligibility requirements for Supplemental Security Income (SSI) as a means of accessing disability benefits have been tightened. Many people with hemophilia are likely to be adversely affected by such a change because their disabilities are made less evident through treatment. Yet, without this entitlement, they may not be able to continue to receive comprehensive treatment.

Hospital Inpatient Care
Hospitals providing in-patient services to people with hemophilia must be adequately reimbursed by all third parties for the cost of administered clotting factor concentrates. These costs must be "carved out" of contractual arrangements between the treating hospital, private health plans, and government payors.

Beginning in 1998, federal law has provided for a "pass-through" of clotting factor concentrate inpatient charges for Medicare patients. This provision allows the hospital to bill Medicare for actual charges for clotting factor concentrates administered to inpatients. The Hemophilia Advisory Committee strongly recommends that Iowa consider a similar inpatient pass-through for Medicaid patients' clotting factor charges.

Research

The Hemophilia Treatment Center of Iowa, at the University of Iowa Hospitals and Clinics, is involved in a number of research projects:

- **PEP Evaluation –** A study to evaluate, by use of a survey form, the content and effectiveness of the Parents Empowering Parents (PEP) Program (a program for parents of children with bleeding disorders).
- **Molecular Study of Familial Idiopathic Thromobocytopenic Purpura (ITP) –** A study to identify gene(s) involved in the pathogenesis of familial ITP. Blood samples will be obtained from consenting family members, and DNA will be extracted for genetic mapping studies.
- **Molecular and Clinical Biology of von Willebrand Disease (vWD) -** A study to determine the relationship between genetic defects of the von

Willebrand factor (vWF) or related genes and the clinical impact on the diagnosis and management of patients' vWD bleeding disorder.

- **Genetic Modifiers of von Willebrand Disease -** To identify genetic loci for bleeding modifiers, by performing a small genome scan. These loci will be the basis for further analysis using positional cloning strategies, including comparison of results between populations and replication in additional population specific panels of families.
- **International Immune Tolerance Induction Study, Genotyping Companion Study – A** study to evaluate the predictive value of determining subjects' genotypes. If preliminary clinical observations hold, this study will establish genotyping as an important clinical factor in determining the risk of developing an immune response.
- **Role of Genetic Modifiers in Bleeding Disorders - A** study to determine the genetic difference between individuals with severe and mild or moderate von Willebrand's Disease.
- **International, Randomized, Controlled, Trial of Immune Tolerance Induction -** A study to compare different treatment plans for the treatment of inhibitors, which make the infusion of factor concentrate ineffective to stop bleeding.
- **Data Collection on the Complications of Hemophilia and Serum Testing and Storage -** A study to: 1) identify persons diagnosed with hemophilia, von Willebrand Disease, acquired inhibitors and other bleeding disorders; 2) identify persons who have a bleeding disorder and who are also hepatitis B and C positive, and HIV positive; and 3) identify the joint status of the subjects. The information gathered from this study will be utilized by the Iowa Hemophilia Treatment Center to assist in caring for our patients. The Centers for Disease Control and Prevention will utilize the information to develop and evaluate programs to reduce or prevent the complications of hemophilia.

HTC also participates in a number of drug comparison studies and is enrolled with the Hemophilia and Thrombosis Research Society's national registries for hemophilia and thromboembolism patients. The registries were designed to collect data to improve the understanding of the epidemiology, pathophysiology, and outcome of patients suffering from these disorders.

Committee Activities

The advisory committee has identified several activities to educate communities about hemophilia and bleeding and clotting disorders and advocate for hemophilic individuals and their families.

- Make an easier, "no gap" transition between Medicaid and Medicare.

- Utilize out-patient treatment and home care for patients.
- Promote independence in patients.
- Increase awareness of bleeding and clotting disorders in the medical community to reduce misdiagnosis and mistreatment.
- Protect free choice of factor products as there is a difference in efficacy for some patients.
- Provide education about bleeding and clotting disorders to the general public.
- Present legislative issues to the committee for advice and information.
- Assure that every patient in Iowa with bleeding or clotting has access to proper medical care with no cap on insurance to assure that care.
- Educate patients and families about stop-gap measures.

Conclusions

- The comprehensive hemophilia treatment center is an integral and essential aspect of contemporary hemophilia care, and serves as a model health care system for other life-long conditions such as sickle cell anemia, cystic fibrosis and thalassemia. Government support must be adequate to ensure that persons with hemophilia receive the full range of medical and counseling services necessary to treat the disease.

- The principal obstacle to accessing comprehensive hemophilia care is unavailable or insufficient health insurance. Approximately 30 percent of people with hemophilia have nonexistent or inadequate health insurance coverage. In light of modern therapies available, a person with hemophilia need not be disabled or impoverished. Universal and unrestricted access to health insurance could prevent a life-long medical condition from becoming a personal or societal catastrophe.

- At the present time, no publicly sponsored medical insurance plan addresses the hemophilic individual's requirement for lifelong treatment without prior assessment of financial need or designation of a disabling condition. Moreover, ***hawk-i*** does not include clotting factor concentrate in its outpatient formulary.

- Variations in medical benefits offered by private and public health plans prevent smooth transition of families undergoing changes in their hemophilia care eligibility and entitlements.

- Development of genetically engineered clotting factor products and changes in production methodology offer the hope of diminishing the incidence of transfusion-associated diseases, but at increased costs. Adequate supplies of clotting factor concentrates must be produced at affordable prices.

- Nationwide, HIV infection and the threat of AIDS remain an alarming reality for many persons with hemophilia and their families. AIDS continues to reverse two decades of progress in hemophilia treatment, as people with hemophilia become disabled and die of this unexpected complication.

Recommendations for Action

Health Insurance
Legislative action is required to mandate that basic health insurance policies cover the cost of clotting factor concentrate administered outside the hospital setting. Whenever these costs are covered separately as a major medical benefit, lifetime ceilings provide only limited relief for a lifelong chronic hemophilia condition. Similar legislation already exists in several other states and is necessary to provide all citizens of Iowa, including those with hemophilia, with comprehensive and affordable health insurance. Clotting factor concentrate should be added to the ***hawk-i*** formulary to provide coverage for those children whose families do not qualify for Medicaid but cannot afford private health insurance. This would assure coverage for all of Iowa's children.

Hospital Reimbursement
Hospitals providing out-patient care to people with hemophilia must be sufficiently reimbursed for clotting factor concentrates to ensure continued appropriate out-patient services without financial penalty. Therefore, any proposed ambulatory case-payment method should be assessed as to its potential impact on the price and distribution of clotting factor concentrates for home use. The committee recommends that the cost of clotting factor concentrates for inpatients be separately reimbursed for Medicaid patients, as it is for Medicare patients.

Lifetime Insurance Caps
Most insurance companies have $1 million cap on claims per person, the standard since the 1970s. Many hemophilic individuals exceed these lifetime caps by the time they are in their early 20s. This creates an untenable situation because the patient is then unable to purchase factor replacement products unless they are eligible for Medicaid or the IowaCares program. There has been very little upward movement on lifetime caps in the last twenty years. Allowing for inflation, caps today should be $18 million.

Access to Care
Factor replacement is not readily available in local communities. In the state of Iowa, all factor products are available at University of Iowa Hospitals and Clinics (UIHC); a selected few plasma-derived and recombinant concentrates are known to be available at Iowa Methodist Medical Center and Mercy Medical Center in Des Moines. Therefore, it is recommended that persons with a bleeding disorder

in Iowa have a current supply of their treatment product available in the home to either use at home or take to their local hospital to treat an injury or bleeding episode. It is necessary that these products be covered by insurance programs.

Individuals covered by the IowaCares program must go to UIHC or Broadlawns Medical Center for outpatient or inpatient treatment. Factor replacement is not available at Broadlawns. Factor cannot be dispensed for outpatient use since it is not generic and, therefore, not covered by IowaCares. Due to the distance a patient may have to travel to UIHC to obtain care, the patient is at risk for complications of the bleeding episode. These complications increase the likelihood that numerous treatments and hospitalization may be required to resolve the bleed which increases the cost of hemophilia management. This treatment regimen does not support the goal of independence related to the health care needs of the individual and preferred treatment of hemophilia care standards.

Some patients who need low-molecular weight heparin (LMWH) (e.g., Lovenox) have trouble with insurance coverage. Some patients may need LMWH only for a short period, but others may need it chronically. Lovenox is expensive, and most insurance carriers will cover it only for treatment of deep vein thrombosis and pulmonary embolism. Medicare requires these injections be given at a clinic or emergency room to be reimbursed.

APPENDIX A

For more information regarding emergency management of hemophilia and other congenital bleeding disorders, contact the Hemophilia Treatment Center of Iowa.

Hemophilia Treatment Center of Iowa
University of Iowa Hospital and Clinics
200 Hawkins Dr. 2507 JCP
Iowa City, IA
800-272-3547 (Toll-free from Iowa)
319-356-4277

APPENDIX B
Hemophilia Data
Hemophilia Treatment Center of Iowa Patients
Through October 2007

Table 1. Patients by Factor Deficiency

Deficiency	Mild	Moderate	Severe	Total
Factor VIII	76	21	76	173
Factor IX	29	48	19	96
von Willebrand factor				139
Platelet/Other				83

Table 2. Patients by Age and Race

Age (years)	Race/Ethnicity			
	White	Black	Hispanic	Asian
0 to 4	30	4	1	0
4 to 15	102	8	11	1
16 to 21	66	5	2	0
22 to 40	136	3	2	1
41 to 60	76	4	0	0
>60	38	1	0	0
Total	**448**	**25**	**16**	**2**

Primary Source of Insurance Coverage

Age (years)	Private Insurance	Medicaid	Medicare	Other	No Coverage	Unknown
0 to 4	17	12	0	0	3	3
5 to 15	59	51	0	1	11	0
16 to 21	45	22	0	2	4	0
22 to 40	88	22	8	12	10	2
41 to 60	54	7	12	2	5	0
>60	11	23	3	0	2	0
Total	**274**	**137**	**23**	**17**	**35**	**5**

APPENDIX C
Voluntary Hemophilia Organizations

Hemophilia of Iowa
1-866-464-8061
http://hemophiliaofiowa.com

Hemophilia of Iowa (HOI) is devoted to improving the health and welfare of Iowa residents with hemophilia, von Willebrand's disease, and other bleeding disorders. Their mission is to provide education and support for people with bleeding disorders and their families and friends.

National Hemophilia Foundation
116 West 32nd St, 11th Floor
New York, NY 10001
212-328-3700
www.hemophilia.org

The National Hemophilia Foundation is dedicated to finding better treatments and cures for bleeding and clotting disorders and to preventing the complications of these disorders through education, advocacy and research.

World Federation of Hemophilia
1425 Rene Levesque Boulevard West, Suite 1010
Montreal, Quebec H3G 1T7
Canada
514-875-7944
www.wfh.org

The World Federation of Hemophilia improves and sustains care for people with inherited bleeding disorders around the world.

APPENDIX D

Members of Iowa Hemophilia Advisory Committee

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Health Insurance Representative
Vacant

Member of Voluntary Health Organization Serving Hemophilia, Bleeding and Clotting Disorder Community
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