Topics in Hemophilia

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National Hemophilia Foundation Walk ’08

On Sunday, June 1, the National Hemophilia Foundation held their New York City Hemophilia Walk ’08 at Riverside Park. It was a beautiful day for the walk with a turnout of approximately 700 people.

The Coalition for Hemophilia B attended with some of our members from New York, Texas and Illinois. A special thank you to Steven (age 5) and Alecia (age 9) Scalfani for designing our team t-shirts. Steven and Alecia, you both did a wonderful job!

Monies raised for this event will go towards advocacy, education, and research.
New Coalition Member!

Eli Roland is one of our newest members for 2008.

As of June, the Coalition for Hemophilia B has 50 new Factor Nine family members.

NHF Appoints New Director

Val Bias has been appointed the new Executive Director of the National Hemophilia Foundation. We wish him much success!

COTT Co-Founder Dies at Age 62

Jonathan Wadleigh, a co-founder of the Committee of Ten Thousand, died on Wednesday, June 4, 2008 at Beth Israel Deaconess Medical Center in Boston, of Liver Cancer.

Wadleigh and Tom Fahey founded COTT in 1989. Both men had severe hemophilia and contracted HIV and Hepatitis C. COTT was established to be the voice of a growing number of people with Hemophilia who contracted HIV/AIDS through contaminated blood.

A memorial service was held for Jonathan on Saturday, June 14 at First Parish in Brookline. He is survived by his wife Joanne Womboldt. Our prayers go out to his family.

The Legend of the Ducks

How did the tradition of the ducks in the Peabody Hotel fountain begin?

Back in the 1930s, Frank Schutt, General Manager of the Peabody Hotel, and a friend, Chip Barwick, returned from a weekend hunting trip in Arkansas. The men had a little too much Tennessee sippin’ whiskey and thought it would be funny to place some of their live decoy ducks (it was legal then for hunters to use live decoys) in the beautiful Peabody fountain located in the Grand Lobby.

Three small English call ducks were selected as “guinea pigs” and the reaction was nothing short of enthusiastic. Thus began a Peabody tradition, which was to become internationally famous.

The Hemophilia Federation of American held their annual conference at the Peabody Hotel this year in Arkansas. Each morning the ducks are brought down in the elevator and walk the red carpet to their fountain where they stay all day. At 5 p.m., they depart with another red carpet ceremony. It was a fun event for all to see and some had the pleasure of participating in the activities. We thought you would get a kick out of seeing some photos.
Conventional wisdom usually holds that female carriers of hemophilia B should not have bleeding problems. The only exception is the rare case in which a woman has defective factor IX genes on both of her X chromosomes, which usually only happens when the woman is the child of a father with hemophilia and a mother who is a carrier. Chromosomes are the structures in the nucleus of all of the body’s cells that hold the genes. Normal humans have 46 chromosomes, two of which are the X and Y chromosomes that determine a person’s sex. Males have an X and a Y chromosome, while females have two X chromosomes. People inherit an X chromosome from their mother and either an X or a Y chromosome from their father.

The factor IX gene is located on the X chromosome, so males who have a defective factor IX gene will generally have some level of hemophilia B because they only have one X chromosome. A woman who has a defective factor IX gene on one of her X chromosomes will usually have a normal factor IX gene on the other X chromosome. It has been thought that having the one normal factor IX gene should be enough to prevent a woman from having bleeding problems. After all, males without hemophilia only have one factor IX gene. However, it is becoming more apparent that carriers often do have bleeding problems, as was seen in a 2006 study from the Netherlands. We have also seen this among the families in the Coalition for Hemophilia B, where many of the female members have told stories of unexpected bleeding problems. In the Dutch study, which covered both hemophilia A and B, the 225 carriers for whom factor levels were available had levels ranging from 5 % to 220 % of normal, compared with a control group of non-carriers who had levels ranging from 45 % to 330 % of normal. Note that even among “normal” individuals there is a wide range of factor levels.

The Dutch group found that carriers had, on average, about twice the risk of having joint bleeds or excessive bleeding from small wounds than did the non-carriers. The carriers also had two or more times the risk of excess bleeding during tooth extractions or surgical procedures, and many had excessive menstrual bleeding. Of course, not all carriers have bleeding problems, but enough do that a woman who knows she is (or might be) a carrier should be aware of the possibility. The Dutch group recommends that all carriers have their factor levels checked.

One reason for the low factor IX levels in some carriers may be because of a poorly-understood phenomenon known as X chromosome inactivation. It appears that in women, one of the X chromosomes in each cell becomes inactivated early in the embryo stage of development in the womb. The actual reason for this is unknown, but it probably happens so the body does not produce an excessive amount of the proteins encoded by the genes on the X chromosome. That could happen if both X chromosomes were active. The inactivation is usually random, so about half of the cells in a woman’s body will have the X chromosome inherited from her father as the inactive one, and the other half of her cells will have the X chromosome inherited from her mother.

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as the inactive one. Therefore, if she is a carrier, about half of her cells will have the X chromosome with the defective factor IX gene as the active one. Those cells will either produce defective factor IX or no factor IX, and she will thus have less normal factor IX in her bloodstream.

However, the wide variation in factor IX levels in carriers, as well as in the normal population does not seem to be totally explained by X chromosome inactivation. Researchers have looked at carriers with skewed X chromosome inactivation, in which one of the X chromosomes is preferentially inactivated. For instance, some carriers have the X chromosome with the defective factor IX gene as the active gene in most of their cells. That would be expected to lead to very low factor IX levels, and it does in some cases, but not all. In general, it is not known why there is such a large variation in clotting factor levels, either in carriers, or in the general population.

This all just goes to show how little we really know about how the human body works. Back in the second half of the 20th century when the genetic code was finally worked out, many people thought it was the beginning of a new era in which many diseases, especially genetic diseases, would be easily cured. It was the beginning of a new era for medical science, but it is one in which the true complexity of the human body is only starting to be realized.

Gene therapy is the general process of treating genetic diseases by introducing normal genes into the body to replace defective genes. Hemophilia B is a good subject for gene therapy research because the genetic defect is fairly well understood, and the factor IX gene is a convenient size to work with. If a “good” factor IX gene could be introduced into a hemophilia patient’s body, he could potentially start producing his own factor IX and not have to rely on factor infusions.

However, gene therapy has turned out to be much more difficult than scientists once thought. All clinical trials of gene therapy in humans were stopped a few years ago after three boys developed leukemia during a trial of gene therapy for severe combined immunodeficiency (SCID). SCID is the “bubble boy” disease in which the body does not make antibodies and therefore cannot fight off any infections. SCID is a completely different disease than hemophilia B, but the gene therapy methods used were very similar to those being tried for hemophilia B.

There are many potential ways to get a new gene into the correct cells in the body. The most popular is to use a modified virus in which some of the viral genes have been removed and replaced with the new gene, for instance a factor IX gene. When a normal virus infects cells, it injects its genes into the cell causing the cell to make more viruses. Similarly, a virus modified to contain a factor IX gene would cause a cell to make factor IX. That has worked both in animals and in humans, but there have been problems in getting enough factor production. Factor IX levels have been low and have only lasted a few weeks in many cases.

One of the main problems is controlling where the new gene inserts itself among all of the other genes in a cell. Originally, scientists thought that they could just let it insert itself randomly, that the chance of it ending up where it could cause trouble was remote. However, the SCID trial showed that the chances were not low enough. Apparently, some of the new genes inserted themselves next to genes that control the production of white blood cells, interfering with the control of those genes. That led to over-production of white blood cells, which is leukemia, a cancer in which too many white blood cells are produced. Scientists are now working on ways to control where a new gene is inserted, or to use genes that remain active in cells but do not insert themselves in with the other cellular genes. One approach being investigated is to actually introduce two new genes, for instance, a normal factor IX gene and a gene that produces an enzyme that can control where the factor IX gene is inserted.

The limited production of factor IX in the few human trials is now thought to be due to the body’s immune response. Researchers have always been concerned that gene therapy could result in development of inhibitors to the protein made by the new gene. However, they have also found that the modified viruses and the cells containing the new gene are often attacked by the immune system. One of the immune system’s jobs is to eliminate cells that are “different.” That is a good thing when the different cells are cancer cells or cells infected by a disease-causing virus, but not when the different cells are ones that contain a good factor IX gene. Therefore, scientists are also looking at ways to control the immune response. Some of what they find could also possibly help to prevent or treat inhibitors in hemophilia patients receiving normal factor IX infusions.

In the 1990s, it seemed that gene therapy, as a “cure” for hemophilia was right around the corner. However, since then scientists have learned that there is much that they still do not understand about how genes and the immune system work. They now know more than ever and are probably following the right paths. Success does not look as close as it once did, but most scientists are still very optimistic that it will happen.

Although gene therapy will be a benefit for hemophilia patients who currently are treated with infusions of factor IX, the real benefit may be for the estimated 300,000 individuals around the world who receive little or no treatment.
The Coalition for Hemophilia B would like to extend our sincere appreciation to our Corporate Sponsors of our 2008 Educational Programs!

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On August 23, 2008, the 7th Annual Adirondack Spintacular will be held at 10 am in Mayfield, New York. Rain or shine you can run, cycle, or walk for hemophilia and to raise organ donor awareness.

The Spintacular is a community based volunteer driven 5K, 1, 6, or 12 mile cycle, run, or walk that is family oriented, promotes physical fitness, recreation, and a healthy way to spend time. After the ride there is a BBQ, silent auction, children’s activities and a bounce house. Awards are presented to the top overall finishers in Running, Cycling and Walking (not the 1 mile) events, and to the top two male and female winners in each event by age divisions.

Historically, over 400 people, ranging in age from 1-88 years young, have participated in the Spintacular. Many people from the surrounding areas attend as well as persons from outside New York state. Proceeds from this event benefit the Lawrence Madeiros Scholarship founded in 2001, in memory of Larry Madeiros, who had severe Hemophilia B, HIV, and Hepatitis C. In 2001, at the age of 38, Larry passed away awaiting a liver transplant.

He was a passionate, positive, caring, loving husband, father, and friend. He touched and inspired many people’s lives and always asked “What is your passion?” Larry firmly believed that every child should have the opportunity to further his or her education, and overcome any illness, disorder, or adversity and realize their passions, goals, and dreams. Scholarships are awarded to the inspiring young people who live daily with tremendous chronic disorders and still excel scholastically and contribute to their communities. For more information on how to attend or contribute, please contact Lisa or Carol at (518) 661-6005, website: www.adirondackspintacular.com.
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Columbus, Ohio  August 1-3, 2008
In conjunction with
16th Annual FAMOHIO Event
Columbus Crowne Plaza North  (614) 885-1885
6500 Doubletree Avenue; Columbus, Ohio 43229

Lincoln, Nebraska  August 8-10, 2008
In conjunction with
Nebraska Chapter of NHF Educational Conference
Cornhusker Hotel  (402) 474-7474
333 S. 13th Street; Lincoln, NE 68508

Indianapolis, Indiana  August 22-24, 2008
In conjunction with
Hemophilia of Indiana Annual Meeting
Holiday Inn North West (near the Pyramids)
(317) 872-9790
3850 Depauw Blvd; Indianapolis, IN 46268

Saturday, August 2, 2008
10:30 AM Breakout session
Hemophilia B Information and Sharing

Saturday, August 9, 2008
Factor Nine Family Meeting
Evening Breakout Session

Sunday, August 24th 9:00 am
Factor Nine Family
Breakfast Meeting

For more details regarding any of the scheduled Factor Nine meetings, please see program agenda upon arrival at the conference or email Kim Phelan at hemob@ix.netcom.com.

We look forward to seeing you!

Special thanks to FAMOHIO, Nebraska Chapter of NHF, and Hemophilia of Indiana!

The Coalition for Hemophilia B would like to wish everyone a wonderful summer!

For back issues of Factor Nine Newsletter or for more information on research, please call or write to:
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