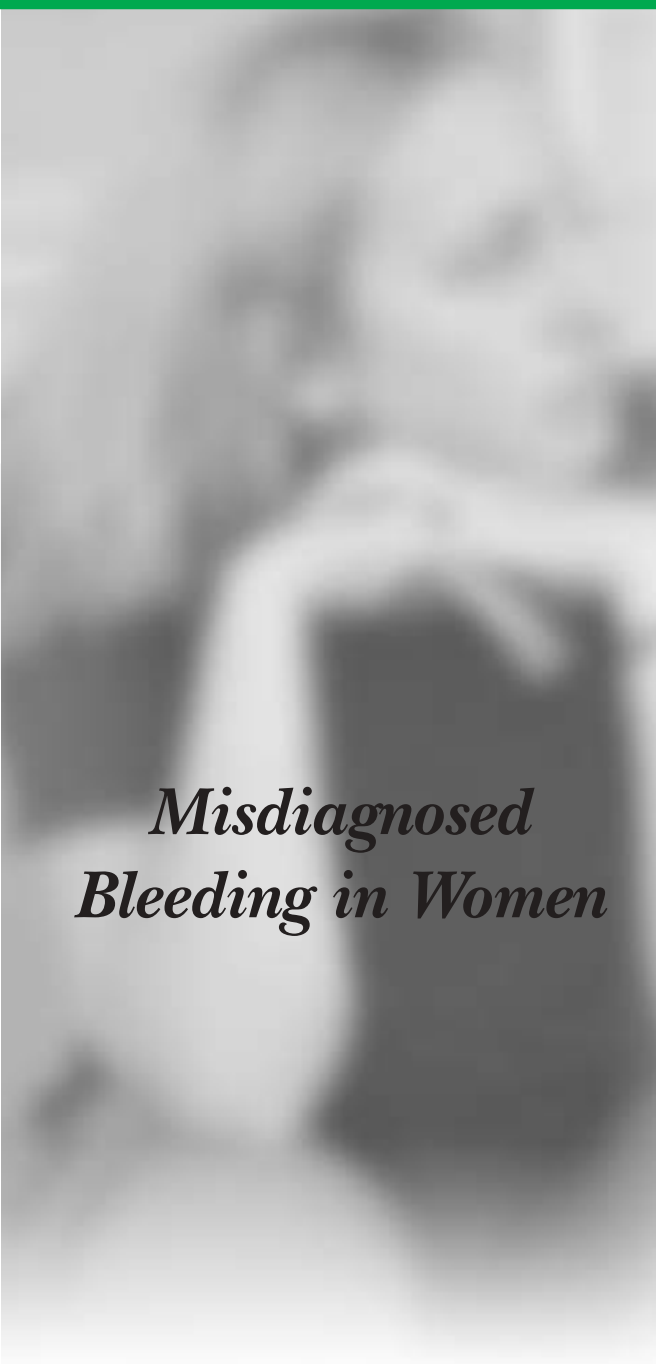
May 2004 • Volume 14 • Issue 2

Parent Empowerment Newsletter



Misdiagnosed Bleeding in Women

What Your Doctor Doesn't Know Might Hurt You

by Paul Clement

Crack! The sound of the bat hitting the ball was Sherri's cue. The ball sailed overhead into the outfield. Sherri, mother of a child with hemophilia, left second base and raced toward third base. Suddenly the third baseman, a young boy less than half Sherri's size, stepped between Sherri and the base. Sherri had to make a quick decision: plow into the boy and risk injuring him and herself, or try to sidestep him. Sherri chose the latter. As she maneuvered to dodge the boy, she felt an intense pain in her lower right leg and fell. For Sherri, a city recreation department baseball game with parents and kids ended with a trip to the local emergency room.

Sherri knew she had broken her leg. In the ER, X-rays of her lower leg confirmed her suspicion. Sherri had broken both the tibia and fibula, the bones of her lower right leg just above her ankle. Doctors would later determine that the broken bone ends had also severed a nerve and ruptured blood vessels. An orthopedic surgeon was called, and later that evening Sherri was finally able to go home–with two metal plates and ten screws holding her bones together, and a cast on her lower leg.

For the ER physicians and orthopedic surgeon, Sherri's case appeared uneventful–after all, they see broken bones every day. As they would soon learn however, Sherri's was not a typical case.

Carriers, VWD Patients and Bleeding: A Hidden Problem?

Although Sherri's case appeared run-of-the-mill to ER staff, an important fact noted in her chart was ignored: Sherri is a hemophilia A carrier with low factor VIII levels. These doctors didn't realize that Sherri has a bleeding disorder. Sherri is among millions of American women who are estimated to

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inside PEN

LA Kelley Communications, Inc.

welcome

AS MOTHERS OF CHILDREN with hemophilia, our focus is usually on our children. We sometimes forget that we also may carry the gene, and that we might need medical attention. I'm as guilty as any other mother. During the last 15 years I've been asked countless times during speaking engagements, at hemophilia meetings and via the internet, "Are you a carrier?" Most people assume that I am. The truth is… I don't know. I've never been tested. Oh, I was asked–especially by my husband Kevin after Tommy was born! But I chose instead to focus on my son and his needs. I also decided to get pregnant again (and again) without carrier testing. In one sense, it didn't matter to me: We have excellent medical care, we can infuse at home, and I wanted children no matter what. But I admit that I often had a cavalier attitude about carrier testing: *Hey, lighten up!* Maybe we worry too much about medical probabilities, I thought. Maybe we should just let nature decide. Maybe our desire to have a child should be our first priority, and we can worry about carrier stuff later.

After reading Paul Clement's excellent article, I am now an advocate for testing mothers and daughters, especially if there is *any* suspicion that they might have a bleeding problem. I'm lucky. I've had three children–two girls after my boy with hemophilia–two major surgeries and several dental extractions. I lead a pretty active life that includes rock climbing and skydiving. I've even been told that I'm a "fast healer." Like many parents, Kevin and I decided to wait until our daughters were of marriageable age to get them carrier tested. But we had suspicions when our one-year-old daughter Mary developed some unbelievable nosebleeds. At times, all she had to do was bend over and the "faucet" was turned on. So we had her promptly tested for VWD and hemophilia only, not thinking that carrier status might also mean excessive bleeding. Luckily, she has only a predisposition to torrential nosebleeds.

Mary is ten now and we still don't know whether she is a carrier, although her factor VIII levels are normal. And we don't know about 13-year-old Tara. When I read Paul's article, a light bulb finally went on in my head. I saw my girls' potential for risk. So I'm going to get my girls tested for their own medical safety.

Might you be a carrier? Might your daughters? Does your health insurance cover testing? Like me, when you read Paul's article you may discover that you want the peace of mind that comes from knowing that you and your daughters are–or are not–carriers. Learning that you or your daughters are carriers through a carrier test means that now you can arm yourself with knowledge, just as you did when you learned of your son's hemophilia. And you'll be prepared for whatever hemophilia or VWD may bring.

PARENT EMPOWERMENT NEWSLETTER MAY 2004

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Funding provided through generous grants from our corporate sponsors (page 16)

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letters

Your programs, educational resources and speaking engagements have certainly brought information to my family and to others in my area. I am truly grateful that LA Kelley Communications brings such knowledge to the table. Thank you for your caring attitude toward me and others with bleeding disorders.

CHRIS QUESENBERRY
Missouri

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by Peter A. Kouides, M.D.

Hemophilia Carriers: *Fact and Fiction*

Women and girls who are hemophilia carriers have special needs. Unfortunately, in both recognizing and treating bleeding problems, these needs may be ignored or mismanaged by physicians, or even by the patient herself. Sometimes, needs are ignored because of misunderstandings or misperceptions about what being a carrier really means.

Recently Eric*, an 11-year-old boy with severe hemophilia A, was "horsing around" in the kitchen with his sister Maria, a hemophilia A carrier with a known factor VIII level of 30%. While wrestling, the siblings fell backwards through a glass window separating the kitchen from the sun porch. The sister fell first through the window, taking the brunt of the fall. Both children were bleeding considerably, and were rushed to the emergency room. The family has taken their son to this ER in the past; the staff understand Eric's need to receive infusions for his severe hemophilia. Although both children were injured, their parents noticed that the ER team was working intently on Eric, while Maria was still waiting to be examined. The mother pointed out that Maria had taken the worst of the fall and, above all, that she has hemophilia, too. Unfortunately, these experienced caregivers falsely assumed that hemophilia affects only boys, and that girls who are hemophilia carriers do not have bleeds.

Now consider the case of Anne, a patient of mine whose father has moderate hemophilia A. Anne is automatically a carrier of that gene, since she had to have inherited her father's affected X chromosome. Not surprisingly, since Anne still carries one normal X chromosome, it's improbable that she would have a factor VIII level below normal, or that she could bleed from having factor VIII deficiency. Yet from childhood, Anne was "labeled" by her pediatrician as having hemophilia–because of frequent nose bleeding, gum bleeding and menorrhagia (heavy menstrual bleeding). When Anne was referred to me for her menorrhagia, we checked her factor levels and found her factor VIII level normal, in the 60% range. I explained to Anne that bleeding from the mucous surfaces typically cannot be attributed simply to a low factor VIII level, and reassured her that this would not be the cause of her bleeding symptoms. Instead, I explained, just like any adolescent with heavy menstrual bleeding, Anne had statistically a 10% to 20% chance of having von Willebrand Disease (VWD). Anne's von Willebrand factor (VWF) levels were indeed in the 20% to 25% range, again with a normal factor VIII level. I made the diagnosis of mild Type 1 von Willebrand factor deficiency. Her father's VWF levels are normal. Interestingly, it was somewhat difficult to change Anne's perception that her bleeding was *not* from inherited hemophilia, but from a separate bleeding disorder, von Willebrand Disease.

In hopes of educating the hemophilia community about the potential for hemophilia carriers to bleed, I stress that a patient must first arm herself with information. Here's how:

1) Order genetic testing for hemophilia in female family members if there is a known detectable genetic abnormality. Up to 40% of boys with hemophilia should have a detectable genetic abnormality; the sisters and mothers of these boys should have the same genetic test performed.

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** Names have been changed to protect patients' anonymity.*

by Paul Clement

Mad Cows and CJD IN THE USA

As yet, no case of CJD transmission by human blood products has been documented and, according to the CDC, the risk of getting CJD from contaminated blood products is probably extremely small.

In December, a case of Mad Cow Disease was discovered in Washington state. In an attempt to restore "consumer confidence" in the safety of American beef, a massive media public relations campaign was launched by the US beef industry, supported by the US Department of Agriculture (USDA) and Food and Drug Administration (FDA). The campaign's primary goal was to avert any negative impact on beef sales. For many outside the beef industry, the overwhelmingly positive "spin" of the USDA and FDA press releases mirrored that of beef industry releases, harming the credibility of the USDA and FDA. This episode brought to light the often conflicting double mission of the USDA: to protect the health of consumers by ensuring that our food is safe and, at the same time, to promote sales of American agricultural products, including beef.

Fifty-five nations have now banned US beef imports, in response to the Washington case of Mad Cow Disease. Of particular concern to the beef industry and USDA is Japan. Japan is the largest importer of US beef in the world, and also the country with the strictest testing requirements for Mad Cow Disease. Japan tests *every* domestic cow for Mad Cow Disease, whereas the US has performed only token testing: of the approximately 490 million American cattle slaughtered over the past 14 years, to date the US has tested only 57,362 for Mad Cow Disease–a rate of 0.01%. Although the USDA currently refuses to test every cow, it has proposed significant changes in the US beef and rendering industry to prevent the spread of Mad Cow Disease–some changes that critics say should have been implemented a decade ago.

Beyond the implications of Mad Cow Disease for the beef industry, many health professionals are concerned about the potential for transmission to humans of Mad Cow Disease and related diseases. Users of blood products are also worried. Can diseases like Mad Cow be transmitted via blood products? To shed some light on some of these concerns, let's examine the characteristics and modes of transmission of these disturbing and worrisome diseases.

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Bedridden and frustrated: Confined to bed frequently and living in poverty, Alexandru often felt angry and defeated.

Alexandru Caruseru: The Boy Who Loves Books and Bikes

by Adriana Henderson

Romania is a small country, but its problems are immense. Fifty years of communist dictatorship have left Romania in disastrous social and economic condition. Here, hemophilia is a matter of survival. Of the 1,800 registered people with hemophilia, most are infected with hepatitis B and C. This is a direct result of reusing needles, a widespread practice of the former communist regime.

As president of the S.T.A.R. Children Relief Organization, I have been involved with hemophilia in Romania for the past four years. Twice a year I crisscross the country, visiting large hospitals in major cities and small hospitals in towns and villages. I visit patients in their homes, no matter how remote.

Alexandru Caruseru is one of these patients. Alexandru is twelve, lives in a remote mountain village and doesn't attend school. There are no hemophilia treatment centers within 100 miles of his village. I met Alexandru for the first time last year. He and his brother and three sisters live in a one-room house containing two beds, a small table and a wood-burning stove. The bathroom is an outdoor wooden shack. When I arrived, I noticed that some porridge had been left on the stove from the day before–this was the children's everyday meal. Alexandru was bedridden, bored, sad and in pain. His father had abandoned the family and his mother was an alcoholic. When I asked Alexandru if he would like a toy, he surprised me by asking instead for books. I was confused. How could he read a book without knowing *how* to read? He recognized the letters, he told me. When I left him, I was in emotional pain myself. I worried about what Alexandru would eat the next day, and how he would spend the rest of his life. He was defeated, alone and hopeless.

When I returned to the US, I contacted Project SHARE to request factor for Alexandru. Project SHARE shipped the factor to Aurora, a local nurse who regularly arranges Alexandru's 100-mile trips to the nearest hospital qualified to administer factor. I kept in touch with Aurora for news of Alexandru's progress, and soon learned that he was pain-free and beginning to walk again. I eagerly looked forward to seeing Alexandru after his treatment. I wanted to see his miraculous improvement with my own eyes.

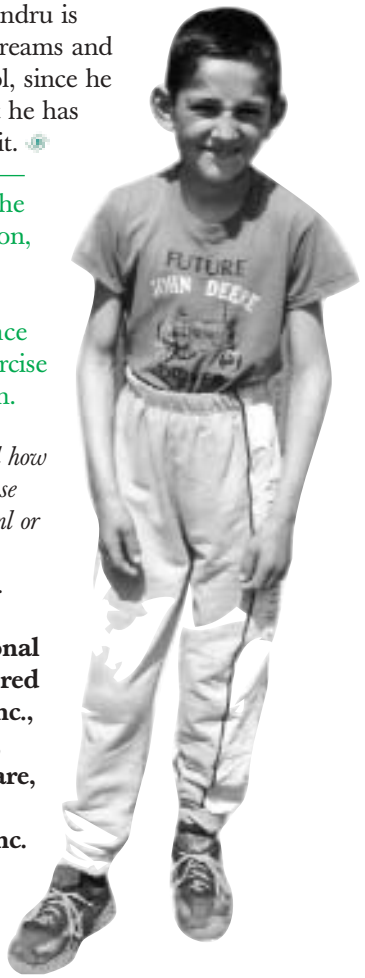
Six months after Alexandru's treatment began, I again made the trip to Romania and found a completely different child. As I drove into the village, I saw Alexandru playing in the street. He had a happy face and a big smile. I asked, could he run? He began running in circles, on and on without stopping. No, it didn't hurt, and no, he wasn't tired. He asked if he could have a bicycle. While shedding tears of happiness, I began to laugh. Alexandru had wished for books to read when he was bedridden; but now that he could run, he wanted to ride a bike. He didn't think about falling and getting hurt. He just wanted to be like the other kids–playing, running and riding.

Thanks to Project SHARE, Alexandru is happy and confident. He now has dreams and wishes. He still doesn't attend school, since he is far behind the other students. But he has taught himself to read and he loves it.

Adriana Henderson is president of the S.T.A.R. Children Relief Organization, a California nonprofit that provides humanitarian relief to children in Romania. Project SHARE, in alliance with S.T.A.R., has purchased an exercise bicycle for Alexandru's rehabilitation.

To learn more about Project SHARE and how you can help patients like Alexandru, please visit www.kelleycom.com/iha/projshare.html or contact Director Annie Schwechheimer at 978) 352-7657 or annie@kelleycom.com.

Project SHARE[SM] is an international humanitarian program administered by LA Kelley Communications, Inc., in partnership with ZLB Behring, Baxter BioScience, Bayer HealthCare, Hemophilia Health Services and Novo Nordisk Pharmaceuticals, Inc. Factor donations are primarily from private sources.



Hope regained: Thanks to Project SHARE, Alexandru is now playing, running and reading like other boys.

photos: Adriana Henderson

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Women's Experiences with Undiagnosed Bleeding Disorders

Many women with bleeding disorders, both hemophilia carriers with low factor levels and women with von Willebrand Disease (VWD), experience numerous bleeding problems because their bleeding disorder was undiagnosed, sometimes for decades. Below are the experiences of five women with bleeding disorders.

As a child, I bruised colorfully, occasionally with little knots or lumps in the bruises. I was famous for my nosebleeds. One night, I swallowed so much blood that I vomited on a rug, and when I looked at the puddle I thought, *this seems odd.* Cautery was suggested, but I resisted. Later in life, I had extremely heavy periods that left me tired and listless for days, but birth control pills improved this situation.

After my son Elisha was born, I had no hemorrhaging and the C-section seemed to be healing well. About two weeks after the birth, and not long after Elisha was diagnosed with hemophilia, I picked him up and felt an internal tearing on the right side of my incision. My obstetrician believed that any tearing was unlikely. Even though I had a child with hemophilia, she saw no "excessive bleeding" while performing the surgery. Of course not! There wouldn't be *more* bleeding, just a tendency for bleeding to continue. Yet several months ago, after a routine internal exam, my doctor noted "unusual scarring" on the right side of my incision.

We completed genetic testing when Elisha was about one year old. I had repeated stress nosebleeds the week prior to the test, so I expected to hear that I was a carrier, and indeed I was. But getting the news was still like being punched in the stomach. My factor level was about 40% while on birth control, which means that 1) my factor level would be lower if I weren't on the pill, and 2) my symptoms are surprisingly severe for someone with that much factor. Tests for VWD were negative.

Now I go to a hematologist for factor level tests. I've been told by the HTC staff that Stimate® may help with my frequent nosebleeds.

I hope that now I can get my nosebleeds under control, and help is ready if I need it. My nosebleeds give me the chance to talk to Elisha about holding pressure, and to model calm responses to bleeds. Hemophilia is largely a mother-son experience, partly because moms do most of the ER trips, HTC visits and support group chatting. Genetics play a part, too: a dad with hemophilia won't share the gene with his son, and a child with hemophilia won't share the gene with his dad. Sharing this gene seems to be shaping a real bond between my "little bruiser" and me, while I escape the worst of the effects. Being a female has some benefits!

Ziva Mann, ***Massachusetts***

Once when I was a little girl, I was sitting at our table as my parents watched a news story about hemophilia. I asked my mother what hemophilia is, and she said, "It's when people can't stop bleeding." The memory sticks with me. I didn't know what was in store for me, but I remember thinking, *that must be horrible.*

I was a "little bruiser" myself, and didn't know it. I was an average 'tomboy' who played sports, climbed trees–anything imaginable. My mother once brought me to the doctor because a lump and bruise had appeared in the middle of my back next to my spine. I was examined and told that it was just a bad bruise. Once I fell on the edge of an in-ground pool, and had a lump the size of an egg on my shin. Again, it was "just a bad bruise." Huge deep purple bruises appeared all over my body for what seemed like no reason. Once I was playing with my cousin, and when we both bent to pick up something, I hit my eye and cheekbone on his head–not hard, but I had a huge black eye and cheekbone. Everyone said, "She's just being a kid."

My son was born in 1999. He was three days old when we learned that he has severe hemophilia A. A year later, I had two wisdom teeth removed. I bled periodically for four days. I took Advil® to relieve the pain, which made the bleeding worse. I thought all of this was normal. In 2002 I learned that I'm a symptomatic carrier for hemophilia A. I'm 30 now and, to this day, my factor level has been tested only once: the result was 37%.

At times I had extremely heavy menstrual periods. Again, I thought this was normal. My doctor said, "It happens sometimes. That's the way your cycle goes." To relieve menstrual cramps, I always took ibuprofen for the duration of my period. This made the bleeding worse. Since I learned my carrier status, I now treat heavy bleeding with Stimate spray, and within 30 minutes everything is under control.

In the fall of 2003, I was diagnosed with Epstein-Barr virus. In March, I returned to my doctor because my throat had started to swell up again. He began writing a prescription for ibuprofen to relieve the pain. I had to remind him that I can't take that.

I've worn a MedicAlert® bracelet since I learned my carrier status. The first time I put it on, I felt almost embarrassed. Now I'm used to it–it's a part of my life.

Melissa Wright, ***New Jersey***

My daughter has mild factor IX deficiency. She was diagnosed at age ten, but by then she already had problems with her wrists from doing cartwheels. Her orthopedist prescribed wrist braces. Although she has a younger brother with severe factor IX deficiency, no one suspected that she was having bleeding episodes. Her first period lasted 34 days. Only birth control pills control the bleeding.

Several years ago, we went to the ER for an ankle bleed. Despite the fact that she wore a MedicAlert bracelet, the ER doctor insisted that she can't have hemophilia because she's female. My daughter turned over her MedicAlert bracelet and said, "Read this!" I gave the doctor the name and number of our hematologist, and he left the room. A few minutes later, a nurse appeared to infuse my daughter with the factor we had brought. The doctor didn't show his face again, perhaps due to embarrassment. Following this experience, I began infusing at home. It's easier than dealing with uninformed ER doctors.

Recently, my daughter had a spontaneous bleed in her ankle area. The local hospital in her college town did a CAT scan. When the technician informed her that there was fluid behind her Achilles tendon, she explained that it wasn't fluid–it was blood, because she has hemophilia. The hematologist arrived and infused her, followed by another infusion the next day.

Because my daughter was not diagnosed until age ten, she now has joint damage and experiences arthritic pain in her knees and hips. She has called home from college, crying because of joint pain. Since she started taking glucosamine with chondrotin, things have improved. She was on her high school swim team, and very athletic. But at college, it's more difficult for her to find time for the exercise that is so important for people with bleeding disorders. Early diagnosis in females is an excellent way to avoid potential joint damage and prolonged menstrual periods.

Nina Duggan, ***Virginia***

I'm glad that I was *not* diagnosed with VWD earlier–when all the symptoms where there. I experienced problematic menstrual cycles, enough for doctors to suspect miscarriage or ovarian cysts. Never were my factor levels mentioned, considered or tested. I had a major postpartum hemorrhage a few hours after the birth of my first son by C-section. I lost consciousness several times, was transfused with five units of blood, and taken back to the OR to find and correct the source of bleeding. All to no avail. There was so much blood that its pressure on my diaphragm caused me to lose sensation and use of my arms. No tests were done for bleeding disorders, although I doubt that they would have been accurate. Post trauma I was loaded with donated blood, which fortunately helped stop the bleeding. Doctors drew blood when I was hemorrhaging and concluded that iron deficiency was the cause.

Three years later, when I was pregnant with my second son, I didn't return to the same hospital because the medical care was substandard. My new doctor at our city's top government hospital tested my clotting factor levels, and told me that everything was normal. However, I don't know whether von Willebrand factor (VWF) was tested, or what other tests were done, nor do I know the actual results. A contingency plan was made for the caesarian birth, including blood matching and having blood available for immediate infusion, but there was no birthing problem. I was relieved to have minimal postpartum bleeding, and just shrugged off my first C-section experience.

We chose to have Justin circumcised at age five weeks, and learned that he has VWD, Type 3 severe. Then, after several weeks of continually changing information and repeated blood tests, we learned that I have VWD, Type 1 mild. My partner was also diagnosed with it, although he's often asymptomatic, with symptoms occurring when he's physically exhausted or ill.

If I had understood the risk of having a child with a bleeding disorder, we may not have chosen to have another child due to my ignorance of the reality of living with VWD. Although Justin is severe, we still feel very lucky. We infuse him prophylatically every three days. Justin has had his own trials and tribulations, and we are on first-name basis with our medical team. But he is a blessing to our whole family, and I shudder to think that I might have made the decision to have no more children, without understanding that the disorder is so treatable.

Of course I don't advocate withholding testing from anyone. I know how crucially important it is to have access to proper treatment in an emergency. I have repeatedly asked the women in my family to be tested. All family members of a person with a bleeding disorder should be repeatedly tested to ensure appropriate emergency care.

Susie Couper, ***Perth, Western Australia***

At age 18 months, I was diagnosed with VWD, Type 3. My menstrual cycle started when I was 12. The blood loss was intense and I wasn't prepared! I bled heavily for 21 out of 28 days and lost clots the size of a fist. Inevitably, I missed some school. When I was in school, each class lasted 35 minutes; between every class I had to change sanitary protection. How embarrassing! I was afraid to sit down properly on my chair in case I flooded, so I perched uncomfortably on the edge. At night I also wore plastic pants so I wouldn't bleed on the bed. I felt tired, drained, breathless, dizzy, listless and uninterested in everything. I was weepy every day, and had painful cramps in my calf muscles. Strangely, I didn't say anything to anyone–I thought that *all* girls must feel like this. I didn't know that what I experienced wasn't normal. When I was diagnosed, no doctors told us that I might experience menorrhagia.

After the second month of bleeding, I was referred to a hematologist who confirmed that my hemoglobin count was six. When she asked how I was feeling, I burst into tears

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have von Willebrand Disease (VWD), or are hemophilia carriers. Yet many women with bleeding disorders are undiagnosed. Some physicians erroneously believe that bleeding disorders affect only males, and only over the last few years has the medical community become more aware of bleeding disorders in women. For these women, lack of physician awareness is a serious problem. Not knowing your carrier status or VWD diagnosis–or not knowing that your condition can cause excessive bleeding–leaves you vulnerable to the kind of inappropriate treatment that Sherri received.

When Sherri returned home from the ER, her pain continued to increase despite pain medication. Her ankle, foot and toes began to swell and throb. Instead of subsiding over several days, like the pain from most broken bones, the pain in Sherri's foot remained intense. Sherri was getting little sleep, and kept her foot elevated above her head just to tolerate the throbbing pain. On the second day after surgery, Sherri's husband Henry drove her back to the hospital to see the orthopedic surgeon. The surgeon examined Sherri and determined that all was well. Sherri returned home but her pain continued. Nearly two weeks after surgery, Sherri accompanied her son Loren, who has severe hemophilia A, to his hemophilia treatment center to see his hematologist. Still in pain, Sherri hobbled into the examination room with Loren. The hematologist took one look at Sherri's swollen purple toes and told her that she was bleeding, then ordered DDAVP®[1] to control the bleeding. After receiving the DDAVP, Sherri's swelling and pain finally subsided.

Sherri is a carrier of the hemophilia A gene, but she also has low factor VIII levels (27%). Although this information was noted in her ER chart, her regular doctors overlooked it or failed to appreciate its importance. Unfortunately, Sherri's experience is not uncommon for women with bleeding disorders–it's more often the norm. Outside of hemophilia treatment centers (HTCs) and hematology/oncology wards, many physicians are not familiar with rare bleeding disorders, even though some bleeding disorders are not as rare as many people think. Bleeding disorders in general affect more than two percent of the population. Von Willebrand Disease alone affects one to two percent of the population, or approximately 1.4 to 2.8 million Americans–women and men equally. Yet the possibility of medical complications due to a bleeding disorder may not be on the radar screen of some physicians. Even when women visit their doctors for excessive menstrual bleeding–a sign of a possible bleeding disorder–many doctors don't order advanced tests for bleeding disorders. As a result, most women with bleeding disorders go undiagnosed, and many with excessive menstrual bleeding undergo unnecessary surgical procedures in a misguided attempt to control their bleeding.

Primary Cause of Misdiagnosis: Lack of Physician Awareness

Menorrhagia, or excessive menstrual bleeding, is by far the most common symptom of VWD in women and hemophilia carriers.[2] Various studies have determined that from 73% to 86% of women with VWD, and approximately 57% of hemophilia A or B carriers, experience menorrhagia. In the general population, fewer than 10% of women have menorrhagia. One study reports that 20% of women who consult their doctors because of menorrhagia actually have a bleeding disorder.[3,4] That's one woman out of five.

According to a nationwide online survey of 1,083 women aged 18 to 45, just over half (54%) of the women surveyed reported that they, or someone they knew, had sought medical treatment for a menorrhagia.[5] Statistically, at least 100 of these women should have been diagnosed with a bleeding disorder. However, not one of them received a diagnosis of VWD or any other bleeding disorder. According to the survey, the most common diagnoses were fibroids (25%), endometriosis (21%), hormonal imbalance (17%), polyps (8%) and cancer (3%). And 17% of these women reported that no diagnosis was made. Other studies report that physicians cannot find a cause for menorrhagia in 50% of women seeking treatment. Instead of determining the cause of bleeding, many physicians treat the symptom by performing surgery to remove the uterus (hysterectomy). Alternatively, to control bleeding, physicians may perform a less invasive procedure, called endometrial ablation, that destroys the inside of the uterus. Approximately 600,000 hysterectomies are performed annually in the US. Hysterectomy is second only to Caesarean delivery as the most frequently performed major abdominal surgery in women. Of these surgeries, 50% are performed for the treatment of abnormal uterine bleeding.[6]

Why are bleeding disorders in women so underdiagnosed? The primary reason is that physicians who are not in hematology/oncology are unfamiliar with rare bleeding disorders. This is a serious problem that is finally receiving attention.

The extent and impact of inherited bleeding disorders in women is an area of ongoing study at the Centers for Disease Control and Prevention (CDC). In collaboration

[1] Desmopressin, a synthetic hormone that releases stores of von Willebrand factor and factor VIII in the bloodstream. [2] Paper, Renée and Laureen A. Kelley, *A Guide to Living With von Willebrand Disease*. LA Kelley Communications, 2002. Menorrhagia is subjective and often difficult to define. Some signs of excessive bleeding include regularly soaking through a pad or tampon more often than every two hours; problems with leakage or staining of clothes during the menstrual period; or bleeding that interferes with a woman's ability to function. Periods that last longer than eight days are considered prolonged. [3] Kadir et al, *Haemophilia*. May 1998. [4] Kadir, et al, *The Lancet*. February 14, 1998. [5] Harris Interactive® Online Survey, conducted between August 1 and 8, 2003: www.harrisinteractive.com/news/allnewsbydate.asp?NewsID=713

with the Rollins School of Public Health of Emory University, the CDC is trying to learn why some physicians aren't diagnosing bleeding disorders, and to determine whether they are even aware of bleeding disorders as a possible cause of menorrhagia. Together, the Rollins School and CDC surveyed members of the Georgia Chapter of the American College of Obstetricians and Gynecologists to understand methods of diagnosing and treating menorrhagia; and to determine physicians' experiences and perceptions concerning bleeding disorders, particularly VWD. The survey targeted gynecologists, since approximately 10% of their patients complain of menorrhagia. According to this survey, about three million American women annually have menorrhagia.

The results of this survey are enlightening–and shocking. For example, physicians were given a list of medical conditions, including VWD, and asked to rank each condition as a *likely, uncertain*, or *unlikely* cause of menorrhagia. Only 3% of responding physicians considered VWD a likely cause of menorrhagia in women age 15 to 44. When asked how many women with menorrhagia might have an inherited bleeding disorder, the average response was less than 1%. And, most shocking of all: After practicing an average of 20 years, 42% of responding physicians reported never having seen a woman with menorrhagia who had a bleeding disorder! Not surprisingly, the survey showed that gynecologists rarely refer a woman with unexplained menorrhagia to another specialist.[7]

Get the Proper Blood Tests

Women's bleeding disorders often go undiagnosed because the proper blood tests were not ordered, not done at the correct time, or not repeated. According to a CDC survey of 75 women who were receiving care in American HTCs, mainly for VWD, an average of 16 years elapsed between the onset of symptoms and the time that a woman received her VWD diagnosis. More than half of the women surveyed were tested multiple times before receiving a diagnosis.

Surprisingly, typical blood screening tests for bleeding disorders don't supply enough information to accurately diagnose the most common bleeding disorder, VWD. These tests include bleeding time (how long it takes for a small cut to stop bleeding), PT (prothrombin time) and APTT (partial thromboplastin time). Yet in women with VWD, the PT is always normal, the APTT is almost always normal, and the bleeding time is often normal.[8,9]

Even when more advanced tests are done for bleeding disorders, such as tests for factor VIII and von Willebrand factor (VWF) levels, the results may be inconclusive. This is because factor VIII and VWF levels can vary, depending on when in a woman's cycle testing occurs. Levels may also vary depending on the mental state of the patient at the time of the test. Several stimuli, including hormones, can cause a transient or sustained increase in factor VIII and VWF levels in women who are hemophilia A carriers or who have VWD Type 1. Due to elevated estrogen levels, sustained rises in factor VIII and VWF occur during pregnancy. Surgery, chronic inflammation and several diseases such as cancer can also cause sustained rises in factor VIII and VWF. And, due to the effects of adrenalin, even exercise, fear and stress can cause transient increases in factor VIII or VWF levels. The "boost" in factor levels during these conditions or situations is usually about twice the woman's normal factor level. So a woman with

[6] Bachman GA, "Hysterectomy – a critical review." *J Reprod Med* 1990, 35:839-854. [7] www.cdc.gov/ncbddd/hbd/documents/hemaware0103.pdf [8] US National Hemophilia Foundation's Medical and Scientific Advisory Council [MASAC] advisory #303: www.hemophilia.org/research/masac/masac074.htm [9] Canadian Hemophilia Society's *Women with Inherited Bleeding Disorders* web page: www.hemophilia.ca/en/2.5.php

Q: What are the symptoms of bleeding disorders? How would I know if I had one of these disorders?

A: Symptoms of bleeding disorders include the following:

- Very heavy bleeding during menstrual periods (menorrhagia)
- Unusual bleeding after injury or surgery
- Bleeding from small cuts that starts and stops over several hours
- Frequent or prolonged nosebleeds
- Unusual bleeding from the mouth or gums after a tooth extraction

If you have any of these symptoms, you should inform your healthcare provider. Your doctor may order tests to rule out a bleeding disorder, including tests for VWD. Be aware that your test results could be influenced by your menstrual cycle. Because of this, tests may need to be done at different points in your menstrual cycle. Even though your mother or sister may also have had heavy periods, this may *not* be normal for you. If you are having heavy periods with no known cause, you should be tested for VWD. Remember that not all healthcare providers test for VWD when a woman is having heavy bleeding.

Source: US Department of Health and Human Services, Office on Women's Health

a factor VIII level of 30% may have a factor level of 60% during pregnancy and childbirth, and her bleeding disorder may go undetected.

The CDC currently recommends blood testing for factor levels during the first four days of a woman's menstrual period, when factor levels are lowest. Ideally, to avoid the influence of hormones, these blood tests should be performed when the woman is not in pain, not ill, and not pregnant. The CDC and NHF's MASAC also recommend that blood testing be done in consultation with a hematologist who is well-versed in diagnosing bleeding disorders. Many hematologists specialize in oncology–the study of tumors and cancers–and know relatively little about rare bleeding disorders. If possible, blood tests for bleeding disorders should be done at an HTC where the staff has more experience in performing and interpreting these tests.

Hemophilia Carriers and Low Factor Levels: An Under-Appreciated Risk

Being a hemophilia carrier is a red flag for a potential bleeding disorder. Unlike women with undiagnosed bleeding disorders–whose physicians often aren't sure what they're looking for–carriers of hemophilia are *known* to be at risk for a bleeding disorder. In these cases, trained physicians have a much easier time diagnosing the disorder because they know what to look for: low factor levels. The normal range of factor VIII and IX levels is between 50% and 200%. Most people have a factor level close to 100%.

How does genetics cause low factor levels in many hemophilia carriers? Every woman has two X chromosomes (XX), one X from her mother and one X from her father. Every man has one X chromosome from his mother, and one Y from his father (XY). A woman who is a hemophilia carrier typically has factor levels from 30% to 70% because only half of her X chromosomes (from her mother) have a functional gene for factor VIII or factor IX. The other half of her X chromosomes (from her father) carry the inherited mutated factor VIII or factor IX gene that does not produce functional factor. Why don't the "good" X chromosomes from the woman's mother produce enough factor to keep her in the normal range? No cell can have two X chromosomes "turned on" at the same time. To prevent two X chromosomes from being active in a cell simultaneously, the body randomly "turns off" one X chromosome. This random inactivation doesn't always result in an even split of X chromosomes from each parent. In other words, more than half of the "bad" X chromosomes from the father could be inactivated–causing the woman to have more "good" X chromosomes from her mother, resulting in normal factor levels. But sometimes, more than half of the "good" X chromosomes are inactivated, leaving her with more of the "bad" X chromosomes–resulting in lower factor levels. In extremely rare cases, a woman's body may inactivate *all* the X chromosomes from her mother, leaving her with severe hemophilia.

So it's not uncommon for a carrier to have factor levels below 30%, classifying her as having mild hemophilia.[10] Studies have shown that 50% of women who are carriers for hemophilia A or B have factor VIII or IX levels below 50%. This puts them at increased risk of bleeding, especially during menstruation, surgery or an accident. And it's possible, but rare, for a woman to have severe hemophilia. Needless to say, knowing your factor levels is essential. All women who are carriers should have their factor levels checked at least twice to rule out low factor levels.

Why Do Many Carriers Remain Untested?

As Sherri's experience illustrates, an untreated bleeding disorder can complicate an otherwise routine medical procedure, prolong recovery time and result in unnecessary pain. And, at the hands of a physician who isn't aware of the significance of a bleeding disorder, an untreated disorder may result in risky and unnecessary surgery. In the case of significant trauma, failure to correctly identify and treat a bleeding disorder may even mean death.

Considering these potentially grave implications, all hospitals routinely check the factor levels of all their hemophilia carriers, right? Wrong! Unfortunately, many hospitals don't routinely check the factor levels of women suspected of being carriers of hemophilia A or B; and many carriers don't even know their actual factor levels. Some women, by default, are "known" carriers, meaning that they are known to carry the gene for hemophilia. Known carriers are called *obligate* carriers–their fathers had hemophilia, so they certainly carry the gene. However, even these women may not have their factor levels checked until they're pregnant. And, for carriers of hemophilia A, factor level readings are likely to be misleadingly high due to the effects of elevated estrogen levels. Because of inadequate health insurance coverage, insurance restrictions and high costs, many obligate carriers don't return to the hospital for additional tests after their deliveries, and don't know their actual factor levels.

Women with no family history of hemophilia, and who give birth to a boy with hemophilia, are *assumed* to be carriers unless proven otherwise.[11] Women who

[10] Mild hemophilia is diagnosed when a person has factor levels between 6% and 30% of normal. [11] Some women are "genetic mosaics," meaning that some of their eggs have the hemophilia gene, but the rest of the cells in their bodies do not carry the hemophilia gene.

are assumed to be carriers very likely *are* carriers, so are at increased risk of bleeding due to low factor levels. Yet many of these women don't return to the hospital for factor level testing after their deliveries–at least not until they contemplate having another child, and want to know their carrier status. When they do return, it's routine for physicians to first check factor levels, since very low factor levels almost guarantee that a woman is a carrier and additional tests may be unnecessary.

Perhaps the largest group of women who may have low factor levels but haven't been tested are the daughters of carriers. Daughters of carriers have a 50% chance of inheriting the gene for hemophilia. Many families mistakenly believe that their daughter's carrier status is not significant until she reaches childbearing age–completely overlooking the fact that if she is a carrier, she may also have mild hemophilia and be at increased risk of bleeding.

Resources on Women's Bleeding Disorders

Online

www.4woman.gov
The National Women's Health Information Center, a project of the US Department of Health and Human Services, Office on Women's Health.

http://projectredflag.com
Project Red Flag, the National Hemophilia Foundation's public awareness campaign to help women recognize the symptoms of bleeding disorders. The website is a partnership between the CDC and NHF.

www.hemophilia.ca/en/2.5.php
The Canadian Hemophilia Society website contains excellent, easy-to-read and in-depth information on women's bleeding disorders.

www.shemophilia.org/index.html
The website "Empowering Women and Anyone Living with the Challenges of a Rare or Inherited Bleeding Disorder" is operated by Cindy Neveu, a woman with a bleeding disorder.

www.allaboutbleeding.com
VWD website sponsored by Aventis Behring.

www.hemophilia.org/bdi/bdi_women.htm
The NHF's *Bleeding Disorders Info Center*.

www.cdc.gov/od/spotlight/nwhw/pubs/bleeddis.htm
The CDC's Office on Women's Health website.

Articles

- **www.cdc.gov/ncbddd/hbd/women_facts.htm**
- **www.hemophilia.org/resources/women.htm NHF "Bleeding Disorders in Women: A Fact Sheet"**
- **www.cdc.gov/genomics/info/reports/research/Menorrhagia.html**

Practical Advice for Carriers

So what should you do if you're a carrier or possible carrier? Have your factor level and that of your daughters checked. To avoid a test result that's higher than your normal factor level, have your level checked during the first four days of your period, when you are healthy and relaxed. Remember that pregnancy will also increase your factor level, resulting in misleadingly high factor VIII readings. If possible, have your factor level checked at an HTC to ensure that the tests are correctly performed and the results accurately interpreted.

If you're being tested for VWD, you may require multiple tests at different times to ensure an accurate diagnosis. If the tests come back negative, ask to have them repeated at a different time. If your factor level is low, particularly below 30%, have this noted in your medical chart. But be careful–as Sherri discovered, having your factor level noted in your chart may not be enough. You must become your own advocate. Learn all you can about your bleeding disorder, and know the correct treatment if you suffer trauma. Wear a MedicAlert® bracelet or necklace.

If you consult a physician who is unfamiliar with your medical history, speak up! Explain that you have a bleeding disorder and how it might be treated. The preferred treatment for people with mild hemophilia A and some forms of VWD is DDAVP injection or Stimate® nasal spray. These treatments may be given only once a day for two to three days; each subsequent DDAVP or Stimate treatment becomes progressively less effective as the reserve supplies of factor VIII and VWF are depleted, and the risk of serious side effects increases. If you have very low factor levels, keep Stimate on hand in case of emergency. Should you suffer major trauma or experience bleeding for more than a few days, you may require factor replacement. Know the name of a hematologist who is familiar with bleeding disorders, understands your case, and can answer the questions of your regular physician. Arm yourself with knowledge about your bleeding disorder to ensure that you receive proper care and don't face the unnecessary pain and suffering that Sherri experienced.

Paul Clement is a high school science teacher and contributing editor to *PEN* who has written extensively for the hemophilia community for more than a decade. Mr. Clement has a BS in biology and MA in science education from California State Polytechnic University. He lives in Southern California with his wife Linda, and children Erika and Brett, who has severe hemophilia A.

Medicare Outpatient Reimbursement Rates Increased

Bleeding disorders patients using Medicare and receiving treatment in a hospital outpatient setting will now receive greater reimbursement for plasma-derived and recombinant therapies. The increase comes after the **Centers for Medicare and Medicaid Services** (CMS) issued a correction to its December 8, 2003 "generic" classification of many plasma therapies. The generic classification led to severely decreased reimbursement rates for these products in 2004. The rate increase is a victory for the **Aventis Behring** (now **ZLB Behring**) Health Policy team, patient advocacy groups and allied trade associations, who lobbied together for the change. The new payment rates replaced the interim rates on April 5, 2004. They are retroactive to January 1, 2004.

For more information visit the CMS website at http://168.143.181.41/bio2/govrel/3-1-04 Corrections for OPPS improper multi-source designation.pdf
Or visit ZLB Behring at www.aventisbehring.com/ab/n25121pr3223142/MedicareOutpatientRe.htm

Source: ZLB Behring and CMS

Advate Receives European Marketing Authorization

Advate recently received marketing authorization from the European Commission (EC), allowing manufacturer **Baxter Healthcare** to sell the product in all 15 European Union (EU) member states. Advate will also be sold in Norway and Iceland, which take part in the EC's centralized evaluation procedure for new drug applications. Advate will automatically receive marketing authorization in other countries that join the EU. Availability will vary by country based on timing of reimbursement approvals. Separately, the Swiss Healthcare Organization SWISSMEDIC issued marketing authorization for Advate in February. Advate is the first and only recombinant factor VIII medicine made with no added human or animal plasma proteins or albumin in the cell culture process.

For more information visit www.baxter.com
Source: Baxter Healthcare and IBPN*, March 2004*

Bayer First to Receive FDA Approval for In-House HIV Screening

Bayer Biological Products received US FDA approval to conduct in-house nucleic acid testing (NAT) for HIV in plasma donations. Bayer says it can now expect greater control in confirming the safety of its plasma donations and reinforcing the strict standards in place for the screening and donation process. Bayer is the first plasma fractionator to receive approval for in-house HIV screening using an FDA licensed test.

For more information visit www.bayerbiologicals.com
Source: Bayer HealthCare and IBPN*, March 2004*

NovoSeven® Approved for Factor VIIa Deficiency in Europe

The European Commission (EC) has approved Novo Nordisk's recombinant factor VIIa product NovoSeven for the control of bleeding in patients with Glanzmann's thrombasthenia and factor VIIa deficiency. NovoSeven is currently indicated for hemophilia patients with inhibitors.

Source: IBPN*, March 2004*

CSL Completes Acquisition of Aventis Behring

CSL Limited has completed its acquisition of Aventis Behring. CSL is combining Aventis Behring with its ZLB Bioplasma division to create a new business, **ZLB Behring**. The move will position CSL as a leader in plasma therapeutics. According to ZLB Behring, the existing portfolio of products, services and distribution methods for both Aventis Behring and ZLB Bioplasma will continue for the present. ZLB Behring will be headquartered in King of Prussia, PA, the longtime location of Aventis Behring.

For more information visit www.zlbbehring.com
Source: ZLB Behring

Insights... continued from page 4

What is Mad Cow Disease?

Mad Cow Disease is the informal name of the cow disease called *Bovine Spongiform Encephalopathy*, or BSE. It is transmissible to cows through the factory farming practice of *rendering*, or feeding the processed, ground-up remains of dead cows and other animals to other cows. BSE symptoms become noticeable in a cow long after infection–typically four to five years. Most US steer are slaughtered for beef at age 12 months, and most dairy cows are slaughtered, or "culled," at age four years. Because most American cows are slaughtered at a young age, they could be BSE positive and no one would know it, yet they would still be infective. A trained eye can sometimes detect changes in cow behavior indicative of BSE before the cow becomes incapacitated (a symptom of BSE); yet no simple blood test exists for BSE. Current tests for BSE require that the cow be slaughtered and a sample of the brain removed for testing.

Why Should I Be Concerned About a Cow Disease?

Concerns about BSE center on the fact that the disease can "jump species," infecting people who eat BSE-tainted meat with a human form of the disease. BSE is a type of disease known as a TSE, or *Transmissible Spongiform Encephalopathy*. The meaning of "transmissible" is obvious. "Spongiform" refers to the sponge-like holes that appear in the brain of affected individuals as brain cells die and the disease progresses. "Encephalopathy" refers simply to a disease of the brain. So a TSE is a transmissible brain disease with Alzheimer's-like symptoms such as dementia. (Alzheimer's is *not* a TSE, although some cases of human TSEs are misidentified as Alzheimer's disease.)

Human TSE diseases are very rare. The most common form is classical Creutzfeldt-Jakob disease, or CJD, which affects between 1 and 4 people out of one million. Almost all cases of human TSE diseases are either *inherited* or *sporadic* (with no known cause), and a very small number are *iatrogenic* (inadvertently transmitted through a medical procedure). In some cases, humans can also contract a TSE by eating an animal infected with a TSE. For example, humans who eat BSE-tainted meat may become infected and develop the human equivalent of BSE: a form of CJD known as *variant CJD*, or *vCJD*.

Once infected with a TSE such as vCJD, a person may not show signs of the disease for many years, possibly several decades. Because of the long latency period, it's very difficult for physicians to determine when, where and how someone contracted CJD. However, once symptoms (typically dementia) appear, death follows within a year. There is no cure for CJD or any TSE–they are always fatal.

What Causes CJD?

TSE diseases, including BSE and CJD, are caused by abnormally-shaped *prion* (pronounced "PREE-on") *proteins*. Normal prion proteins, or prions, occur naturally in the body and are found primarily on the surface of nerve cells. The exact function of prions is unknown; however, it is known that without prions, nerve cells die. The TSE disease process is believed to begin with an abnormally-shaped prion (called a "rogue prion" to distinguish it from a normal prion). The rogue prion, perhaps introduced into the body through contaminated beef, comes in contact with a normal prion and causes it to change shape. As the process continues, these abnormally-shaped rogue prions become templates for changing the shape of more prions. The process begins slowly, then moves at a faster and faster rate as more and more prions are converted to the abnormal shape. Rogue prions do not function normally, cannot be broken down by the body, and accumulate in the brain in sheets of starch-like plaques. Brain cells die, and eventually the infected individual dies. At least 20 known mutations in the prion protein gene sequence result in the spontaneous formation of rogue prions. Each mutation creates a slightly different protein shape, causing differing strains of TSEs with differing pathology. But regardless of the mutation, the spontaneous rogue prions can change non-mutated normal prions into the disease-causing rogue form.

As a disease agent, prions are unique. They are not alive. They have no DNA or RNA. They are highly resistant to sterilization procedures commonly used for medical equipment. They cannot be destroyed or inactivated by any means currently used to kill bacteria or viruses in human-derived tissues or products, such as blood products. Currently, there are only two ways to prevent transmission of CJD through human-derived products. First, products can be screened for the presence of rogue prions *before* the product is manufactured or harvested. This is difficult to do, since there is no simple test for the disease. Second, the prions can be removed from the product during the manufacturing process. Promising research is being conducted on methods to destroy rogue prions on medical instruments, but at present there is no foolproof method of cleaning or sterilizing many types of surgical instruments and tools that might come in contact with CJD-infected tissues.

How Can BSE or CJD Affect Me?

The risk of contracting vCJD from eating contaminated US beef is exceedingly small. In the United Kingdom, where the world's first and largest BSE outbreak occurred in the 1980s and 1990s, an estimated 1.9 million cows were infected with BSE. Approximately 1.6 million of these cows entered the food supply, yet only 145 people to date have contracted the disease.[1, 2] Of course, the exact number of people who have vCJD is unknown, since there is no blood test and the disease may take decades to surface. Your risk of dying of bacterial food poisoning from eating undercooked beef in America is

[1] http://news.bbc.co.uk/1/hi/sci/tech/2310663.stm

[2] www.dh.gov.uk/AboutUs/HeadsOfProfession/ChiefMedicalOfficer/ CMOArticle/fs/en?CONTENT_ID=4073785&chk=fLfkvL

actually *thousands of times greater* than the risk of contracting vCJD; yet most people find these risks acceptable, and continue to eat beef.

Of concern to many health professionals is the transmission of CJD through contaminated medical instruments and human tissues, especially blood. Worldwide, more than 250 people have contracted CJD from medical procedures or tissues. The infected individuals are primarily recipients of human growth hormone and *dura mater* grafts (brain-covering grafts) from cadavers. Yet the major concern is the potential for transmission through blood or blood products, simply because of the sheer number of people who could be at risk. Animal experiments have shown that blood carries a low level of CJD infectivity–meaning that blood carries few prions, and is relatively inefficient at transmitting the disease. Worldwide, only a half dozen people are reported to have developed CJD after receiving blood transfusions from people who later died of CJD. However, this data is inconclusive because it's unknown whether these victims developed CJD from a blood transfusion, or simply by coincidence.

Using pooled plasma (combining many units of plasma when producing plasma-derived clotting factor concentrates) greatly increases the potential for exposure to rogue prions. About a decade ago, plasma pools used to make clotting factor concentrates contained up to 400,000 units of plasma. Using the conservative estimate of one CJD infection per million people, it's believed that anyone exposed to more than one lot of factor concentrate from such a large pool would have been exposed to plasma from someone with CJD. Today, plasma lots are limited to 60,000 units. To help identify and track cases of CJD, the Centers for Disease Control and Prevention (CDC) established the Creutzfeldt-Jakob Disease Surveillance System in 1996. As yet, no case of CJD transmission by human blood products has been documented and, according to the CDC, the risk of getting CJD from contaminated blood products is probably extremely small.

To further ease the concerns of consumers of fractionated blood products like factor concentrates, in December 2002 Aventis Behring (now ZLB Behring) reported that the cleaning process it uses on the production equipment of fractionated blood products is capable of removing prions.[3] In November 2002, Bayer HealthCare reported that its plasma protein purification processes, such as those used for factor concentrates, are capable of removing prions from plasma.[4]

Regardless of the ability of the plasma purification process to remove potential pathogens, consumers of products containing plasma-derived proteins continue to worry about the potential for transmitting diseases like BSE and CJD. They also worry about the continual stream of new or emergent viruses in the blood supply. Their wish, and the goal of factor concentrate manufacturers, is a factor product containing no extraneous human or animal proteins–to avoid altogether the possibility of disease transmission through plasma-derived proteins. Such a factor IX product has been on the market for several years. Now, "second-generation" and "third-generation" recombinant factor VIII products are also available. Second-generation products have no extraneous human or animal proteins added to the final product. Third-generation products have no extraneous proteins in the final product or in the production process. With the advent of third-generation recombinant factor VIII products, the fear of contracting a disease like CJD through a factor product will finally be laid to rest.

[3] www.aventisbehring.ca/ABCMSPRDI/n95055pr146387/NewStudyinBloodRepor.htm [4] www.bayerbiologicals.com/News_Center/Press/2002/20021112.asp

Parent-to-Parent... continued from page 7

and told her exactly how bad I felt! I was given a term off from school and oral iron supplements. By December, my hemoglobin was eight, so I received an iron infusion. Several hours later, I had a fever and couldn't move my joints. I'd had an allergic reaction: I felt terrible, my stomach was distended, and I spent the next two weeks in bed.

I was put on Norethisterone (a synthetic hormone similar to progesterone) continuously for several months to give me a complete break from bleeding. Although it helped immensely, I still had intense mood swings and gained weight. I had the same results with birth control pills, which I have refused to take for the past several years since they make me depressed, even suicidal.

At age 27, childless, I was offered a hysterectomy. I declined. At age 31, I'm still declining! Hysterectomy is a feminist issue. I will fight to keep my womb and my potential fertility, despite the adverse effects on my health, and even my employment.

Recently I suffered six months of *metorrhagia* (constant menstrual period). I've had blood transfusions and daily Humate P® (a factor VIII concentrate with VWF) infusions but to little avail. I've been absent from work for 54 days. I sought second opinions on both my hematology and gynecology management, and am confident that this year we'll make a positive change by improving my poor vascular access. I'm considering having an arterio-venous fistula (AVF) created [see "Another Option for Venous Access in Children with Hemophilia: The Arterio-Venous Fistula," *PEN*, May 2003], allowing me to self-infuse. I now take a combination of tranexamic acid (an antifibrinolytic drug) and mefanamic acid (an analgesic), along with hormone therapy to control my bleeding.

HELEN CAMPBELL, *Leeds, United Kingdom*

Helen sponsors a women's bleeding disorders support group at http://groups.msn.com/WomenwhoBleed.

Letters... continued from page 2

Thank you for everything you have done to help my son Alejandro. The factor that was sent [through Project SHARE] helped a lot during his surgery, and he is doing very well now. He is receiving physical therapy and getting the rest of the factor periodically to make sure that he doesn't get a bleed.

Alejandro and I are very grateful and hope that some day you might also help my brother and nephew, both of whom have hemophilia. We cannot afford to buy the medicine since I am a teacher and my salary is very low.

IVONNE ARROYO
Ecuador

My heart breaks to hear of boys like Quang Nguyen ["A Project SHARE Story: Quang Nguyen's Brief Holiday From Pain," *PEN*, Feb. 2004]. I hope that the ancillary supplies I donated may help others like him. Thank you for *PEN*–you were there from the beginning!

MARNI KNOWLES
Washington

Editor's note: The supplies that Marni donated will be shipped at a future date to a patient, hemophilia camp or society in need. If you'd like to help patients through Project SHARE, please contact Annie Schwechheimer at annie@kelleycom.com.

As I See It... continued from page 3

2) What is the factor level? Many physicians don't realize that although a hemophilia carrier should have one normal X chromosome coding for factor VIII, because of a phenomenon where the X chromosome can undergo inactivation ("lyonization"), the factor VIII level may be below 50%. This is seen in up to one-third of hemophilia carriers. These patients are at risk for bleeding. However, it's important to remember that their levels shouldn't be as low as those of the male family member. Consequently, these patients should not experience joint bleeds. Furthermore, their bleeding should not occur "out of the blue," but only after injury or surgery. A patient like Anne, with a mild factor VIII deficiency–that is, a carrier who has a factor VIII level in the 20% to 30% range–should not have dominantly mucous bleeding, such as nose or gum bleeding or menorrhagia. If this type of bleeding does occur, it's important to do testing for the far more common bleeding disorder, VWD.

Why is it critical to learn whether a female who is a known hemophilia carrier also has a low factor VIII level? The most important reason is to determine whether she should receive Desmopressin (DDAVP) to prevent excessive bleeding in the event of surgery or dental work.[1]

It's also essential to recognize that hemophilia carriers who have low factor VIII levels should not have a factor VIII level so low that they develop large bruises. In general, bruising is a very frequent symptom in women. My colleagues and I published a study[2] revealing that 24% of 150 women with no documented bleeding disorder reported easy bruising. These women had no factor deficiency. Consequently, we must be very careful not to "blame" hemophilia for bleeding symptoms. Instead, a baseline factor level and genetic analysis are the best means for both patients and physicians to avoid well-meaning but misinformed diagnosis and treatment of bleeds.

Dr. Peter A. Kouides is an Associate Professor of Medicine at the University of Rochester School of Medicine and Research Director of the Mary M. Gooley Hemophilia Center. He and his family count the New England Hemophilia Association Summer Camp as one of their favorite all-time summer experiences.

[1] Since factor VIII levels can fluctuate, a patient with a "normal" level between 50% and 75% should probably have repeat testing on at least one occasion. [2] Kouides, P. A., Phatak, P. D., Burkart, P., Braggins, C., Cox, C., Bernstein, Z., Belling, L., Holmberg, P., MacLaughlin, W., Howard, F., "Gynaecological and obstetrical morbidity in women with type I von Willebrand disease: results of a patient survey." *Haemophilia* (2000), 6, 643-648.

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Do you want to join the PEN Research Team?
○ ***Yes!*** ○ **No**

PEN maintains a special network of patients and parents to provide us with information for upcoming articles and projects. We want to get your ideas, opinions and experiences periodically through telephone surveys, interviews, or written questionnaires. If you'd like to be on our elite team, check "Yes" in the box at left, and send or email this form to us.

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