PEN

inside

Prophy and the Young Adult: Can We Achieve Adherence?

Christine Bergeon Burns

Whether people with hemophilia follow prescribed prophylaxis treatments is an important and complex issue faced by our community. Prophylaxis—"prophy"—in hemophilia is often described as the preventative infusion of factor concentrates to keep levels above 1%. In other words, prophy aims to keep circulating factor levels in the mild-to-moderate range in people who would otherwise meet the diagnostic criteria for severe hemophilia. But prophy regimens are variable. For example, some people may be prescribed a treatment schedule based strictly on time intervals, such as infusions every two to three days. Others may have a treatment plan that involves infusing before rigorous physical activity instead of, or in addition to, interval dosing. Individual regimens vary as children grow and change, and as factor products evolve.

Over the past several years, multiple studies have indicated that continuing prophy beyond childhood results in decreased bleeding and pain, better joint health, and improved quality of life. Yet children may resist prophylaxis as adolescence approaches, and may struggle to accept responsibility for regularly scheduled infusions. Parents may be unsure if the way they are currently handling their young child's prophylaxis regimen will effectively set the stage for independent prophy down the road. Adolescents and young adults as a group are widely considered rebellious, irresponsible, and "non-adherent" in all sorts of ways. It's natural to wonder, then, how important is adherence to a regular treatment regimen after childhood? Can we as parents realistically hope that our children will stick with their prophy? How can we ensure them a healthy future?

Prophy: Costs versus Benefits

Whether parents infuse their child prophylactically is almost always decided by weighing costs and benefits. Initially, this breakdown is done in the doctor's office, at the time when a treatment plan is put in place. Benefits of prophylactic infusions include decreased bleeds and pain, increased opportunity to participate in activities, increased long-term joint health, and peace of mind.

On the other hand, costs involve financial hurdles, pain and difficulty with needlesticks, and the requirements of time, space, and planning for infusions. Both costs and benefits may include short- or long-term aspects, and patients often weigh various costs and benefits differently, depending on their own unique life situations. Still, many parents of children with severe hemophilia come to agree that the benefits of prophy outweigh the costs. Parents find a way to make it work from day to day—sometimes benefiting from interventions such as numbing cream and ports—on the promise of providing both short-term and longer-term benefits for their kids' health and quality of life. Indeed, it's now universally recognized that prophylaxis is the standard of care for children with severe hemophilia.

But lately, patients and even some parents have been uncertain about whether continuing prophy into adulthood is appropriate. When young people, aged 12 to 22, become responsible for their own prophylaxis, they may hastily reevaluate the relative benefits and costs of infusing. A college student may not leave enough time to infuse before his morning

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welcome

It's hard to recall a world without cell phones, internet, Kindle, or Facebook. Or prophylaxis! But parents in my age group all raised children without prophy as an option. We infused on demand, and we became adept at reading our child's body language, facial expressions, and even mood as we tried to detect a coming or current bleed.

To us, "prophylaxis" referred to birth control, and "ports" were where ships docked. But in 1999, the results of a long-term Swedish hemophilia study showed the undeniable benefits of prophy on joints as children grew. America was hooked, and prophy became the standard.

And then, over time, we had a new problem. Kids were growing up not really knowing what bleeds were. Some couldn't read their own bodies. They had never experienced a bleed, so they didn't know what symptoms felt like. Some felt invincible. Some were in denial. When they were old enough to leave home for college or travel, some young adults decided to give up prophy. Why bother infusing so much when they never bled?

And then the inevitable happened: they got bleeds. And they learned. After experiencing bleeds now as young adults, would they choose to go back to prophy? To find out, read our feature article by Christy Bergeon Burns. And read Hunter Montgomery's article about deciding whether to continue on prophy.

To learn more what young adults think about hemophilia after growing up on prophy, read *Teach Your Child About Hemophilia*, available soon at www.kelleycom.com. And open a dialogue with your teenager about prophy: its purpose, and the consequences when you don't follow it. Just like using toothbrushes, seatbelts, and birth control—an ounce of prevention is worth a pound of cure.

Laurie Kelley

inbox

"The Impossible," PEN August 2017

Great issue! It would be smart if Bioverativ became a Benefit Corp. Thanks for all you do!
Jill Sallade-Packard
Executive Director
Hemophilia Alliance of Maine
Maine

Fantastic article! This reads like that miracle we always pray for, but does not happen. Only now it does!
Lenox Mhlanga
Zimbabwe

An insightful article. A hooray for those who cared to fight for this big donation.
Marelle Hart
Belgium

Everything is possible, even the impossible.
Adriana Henderson
North Carolina

Wow! I'm always amazed at how ordinary people who make themselves available can change lives. That goes for you as well as those in the article.
Ladonaa Pettus
North Dakota

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Would I Ever Consider Quitting Prophylaxis?

Hunter Montgomery

Prophylaxis, which we affectionately nickname "prophy," is now considered optimum care for people with access to plenty of factor.[1] Although prophy can be expensive, it is shown to dramatically reduce the number of joint bleeds and increase the longevity and health of joints.[2] However, while NHF's Medical and Scientific Advisory Council (MASAC) recommends that prophy begin at a young age, "there are no clear cut guidelines as to when to stop prophylaxis."[1]

That means that young adults like me, now without the safety net of our watchful parents, must decide how often to "stick" ourselves. That decision isn't made only in the sensibility-inducing atmosphere of a doctor's office, but every frantic morning in a college dorm room where, at least for me, the choice is often between eating breakfast and infusing.

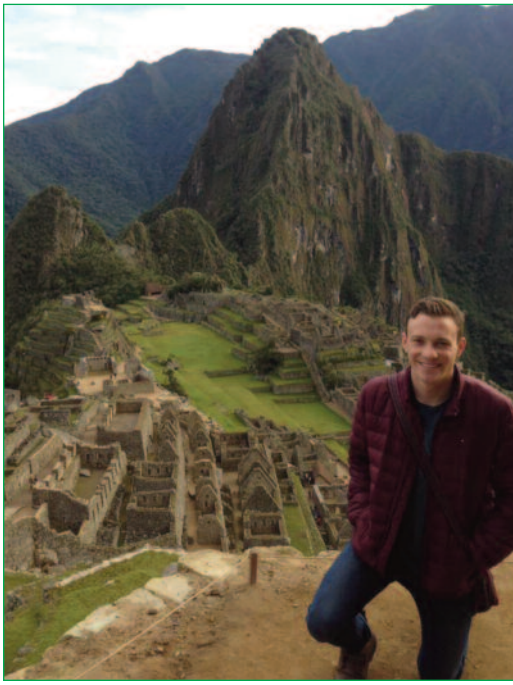
When I was a toddler in the late 1990s, factor products were being recalled because of possible contamination. This was disturbing for my parents, who, to reduce the risk of disease, only treated me when necessary.

As time went on, my parents became more confident about the factor, and "when necessary" turned into twice a week before my rec league soccer games. When I was eight, I made it onto a club soccer team, and as the practice schedule increased to three times a week, so did my treatment schedule. Around this time, I started to self-infuse. My mom taught me that just like my shin guards and cleats, my little syringe full of factor VIII would help keep me safe out on the field so I could keep playing the sport I loved.

At hemophilia events I met older guys with hemophilia who had severe joint damage, replaced knees, fused ankles. This scared me into diligence with my pre-soccer infusion regimen, but I got to a point where I was so sick of needles that I dreaded doing my infusions. Sometimes I would miss a dose here or there. Occasionally a week would go by without an infusion.

Then I had an ankle bleed of my own. I remember the exact moment it happened. A player on the other team and I both tried to kick the ball—in opposite directions at the same time. My ankle got twisted. I finished the game, but the next day my ankle was swollen to twice its size. I had to sit out practice for a few weeks; and for many months after that, I did strengthening exercises before each practice. In high school I switched to swim team, which I knew would be better for my joints in the long run.

As I got ready to move away to college, my mom reminded me that if I were to have a bleed while living on my own—one that prevented me from walking to class for even a few days—I could quickly fall behind and lose my scholarships. I had already experienced the debilitating consequences of a joint bleed and realized I didn't have time for bleeds.



Some young adults might stop prophy because of time restrictions or complacency. Some might be forced to stop because of the expense. I enjoy an active lifestyle and hate the idea of being slowed down by injuries that could be prevented by simply keeping my factor levels up. This, combined with a mostly healthy fear of permanent joint damage, is what drives me to wake up a few minutes earlier or skip breakfast if I have to, three days a week to infuse. Sure, I have some nice scars on my two favorite veins, but I have healthy joints and I look forward to a future free of bleeds and full of the activities I love.

Hunter Montgomery, age 22, has severe hemophilia A. He is a junior at Brigham Young University in Provo, Utah, majoring in viola performance and pre-medicine. Hunter recently returned from six weeks in Cusco, Peru, where he volunteered as a phlebotomist and lab technician. He plans to become a hematologist and run an HTC.

1. https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendation-Concerning-Prophylaxis.
2. https://www1.wfh.org/publication/files/pdf-1472.pdf, p. 12 #3; p. 13 #7.

Cazandra Campos-MacDonald

What Causes Inhibitors?
Part 1

In the summer of 1997, my one-year-old son Julian, who has hemophilia, was diagnosed with an inhibitor. In a whirlwind week, he received the diagnosis, had a port placed, and my husband and I began learning how to access it. I was weak at the knees and still in shock over this new diagnosis. Where did it come from? Did I do something to cause the inhibitor?

As a newcomer to the world of bleeding disorders, I thought an inhibitor was something that "other people" dealt with. But after our child's diagnosis, we became the "other people." I learned that inhibitors are antibodies that develop and attack the factor that is infused into the body. Our immune systems produce antibodies to protect us from disease-causing organisms such as bacteria or viruses. But when someone receives an infusion of clotting factor, sometimes the immune system identifies the factor as an invader, and then produces antibodies designed to attach to specific areas on the factor molecule. These antibodies—or inhibitors—inactivate the factor, stopping it from doing its job. A nurse once explained to me that an inhibitor is like Pac-Man, traveling through the body, eating up the factor as soon as he finds it. To this day, I see that image in my mind.

So what causes inhibitors? We don't know exactly. The immune system is incredibly complex, and in some respects each person's immune system is unique. But we're aware of certain risk factors that may increase the possibility of developing an inhibitor. Even so, risk factors don't tell the whole story: a person with few risk factors may develop an inhibitor, while a person with many risk factors may not. Even in a family like mine, with two boys with hemophilia sharing many of the same risk factors, one child may develop an inhibitor while the other will not.

Genetic risk factors, environmental effects, and exposure to clotting factor are causes for inhibitor development. In this article, we'll look at genetic risk factors.

Inhibitors and Type of Hemophilia

Did you know that people with hemophilia A are 10 times more likely to develop an inhibitor than people with hemophilia B? It's true: inhibitors happen in up to one-third of people with hemophilia A. This is called *incidence*, which means the number of new cases during a specific time period. With hemophilia A, the caregiver—who is already concerned about bumps and

bruises, mouth bleeds and playgrounds—now has another issue that feels overwhelming. But your loved one inherited a rare bleeding disorder, and the possibility of developing an inhibitor is real.

Although one-third of people with hemophilia A may develop inhibitors, only about 5% to 7% of them are living with an inhibitor at any point in time: that is, living with an active inhibitor in their bodies. This is called *prevalence*—the proportion of people who have a disease or disorder during a specific point in time. In other words, prevalence refers to people who are living with inhibitors over the long term. But "long term" can mean many things. Living with an inhibitor for months sounds like an eternity, yet long term can mean years or even a lifetime. An inhibitor is not often a diagnosis that resolves in a very short time.

So why is the prevalence of inhibitors in hemophilia A lower than the incidence? Because many inhibitors are *transient*—they go away on their own. And up to 80% of the remaining cases of hemophilia A inhibitors can be eliminated through immune tolerance therapy (ITT).

What about hemophilia B? It's estimated that the incidence of inhibitors in hemophilia B is 2% to 6%, and the prevalence

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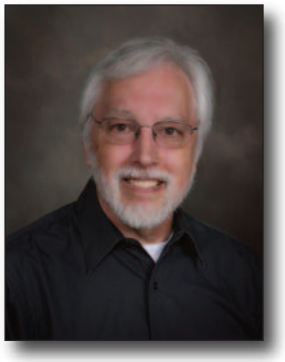
richard's review



Linda Weaver's Studio

Richard J. Atwood

Dancing with Hemophilia: Janet Baldwin

We repeatedly hear the message that regular exercise is beneficial for our health and well-being. Yet always heeding that advice over a lifetime can be a challenge. My suggestion? Include dancing as a fun component in your repertoire of exercises.

Exploring the world of dance, I became intrigued with Janet Baldwin, a hemophilia carrier. Janet made a lifelong career of dance in Canada, even performing at the 1936 Olympics. As part of her legacy, Janet inspired the award-winning Canadian author Timothy Findley to create a fictional character modeled on her life.

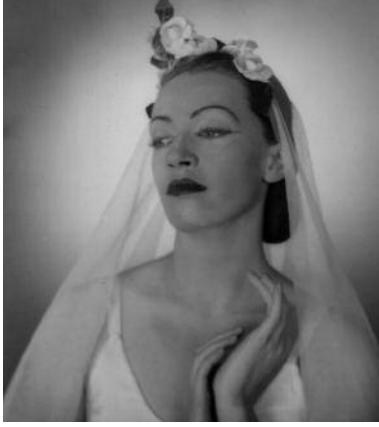
Catherine Janet Baldwin was born in 1912 in Toronto. Her family were descendants of the politician Robert Baldwin (1804–1858), who in 1841 brokered the coalition of Upper and Lower Canada—now known as Ontario and Quebec. This was an important step in the eventual formation of the provincial government of Canada. Something of a rebel in her wealthy family, Janet followed her passion for dancing to become a professional dancer, teacher, and choreographer. She studied ballet in Canada, America, and England. Janet went on to found her own ballet studio and to co-found the Canadian Dance Teachers Association. She was a member of the Royal Academy of Dancing.

A boost to Janet's early dancing career was her 1936 marriage to Boris Volkoff (1900–1974), a ballet master who is sometimes called the father of Canadian ballet. Janet progressed from being Volkoff's student to being his wife and then his business partner in the Boris Volkoff School of Dance. Janet's family did not approve of the marriage. The older, irascible Volkoff kept his Russian accent. He taught the more athletic style of ballet that he learned in Russia before defecting to Canada in 1929. The couple's personalities contrasted: Janet was known for her infectious energy, while Volkoff was considered flamboyant.

Helen Pritchett Electronic Archives, Dance Collection Danse

Boris Volkoff, Jack Lemen, Helen Pritchett, Margaret Clemens, Pauline Sullivan, Janet Baldwin, Mildren Wickson, Clara Ord, Joan Hutchison, Marsden Hall, Billy Cochrane, Mary Wilder, Jim Pape, Berlin Olympics, 1936

Just a month into their marriage, the Volkoffs led a delegation of about 14 amateur Canadian dancers to the International Dance Competitions at the 11th Olympic Games in Berlin, 1936. The Germans wanted "art competitions," including dance, added to the Olympics, but the International Olympic Committee denied the request. Instead, the choreographer Rudolf von Laban organized dance celebrations before and during the athletic events. For political reasons, countries including America, England, France, Sweden, and Russia boycotted the dance competitions held in Nazi Germany; still, 14 countries participated. Because Olympic medals could not be awarded in dance, each participating dancer, including Janet, received a diploma. Volkoff, always a promoter who loved to exaggerate, maintained that of the six honorable mentions awarded, the Canadians were the only amateurs, while the other countries had professional dancers.



Sara Sutcliffe Portfolio, Dance Collection Danse

Janet Baldwin

Boris Volkoff Portfolio, Dance Collection Danse

Janet Baldwin and Boris Volkoff in Volkoff's Death and the Maiden, c. 1937

Boris Volkoff Portfolio, Dance Collection Danse

Boris Volkoff, c. 1948

Returning to Toronto, in 1938 Volkoff formed the Boris Volkoff Canadian Ballet, a nonprofessional ballet company, with Janet as his business partner. The couple also helped to organize the annual Ballet Festival, beginning in 1948, which brought together the existing Canadian ballet companies. Volkoff envisioned a touring professional company, but failed in his effort to be artistic director of the newly founded National Ballet Company of Canada in 1951. Instead, the chosen director was Celia Franca, who promoted the British style of ballet, leaving Volkoff bitter and disillusioned.

The Volkoffs had a contentious marriage. A major issue was children. Volkoff wanted children, but Janet felt she shouldn't have any because she was a hemophilia carrier. She feared that any male child with hemophilia would bleed to death. Janet had multiple abortions in Buffalo and Chicago under appalling conditions. After Volkoff had affairs with younger women, the childless couple divorced in 1951. Volkoff remarried, but when he was

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Factor Dosing: How Do You Weigh In?

Paul Clement

Parents: When was the last time you thought about how your child's factor is dosed? Never? Many parents just leave the dosing to the physician. But let's look again. For many children with hemophilia, especially if they're not seen at a hemophilia treatment center (HTC), weight may be the primary—or only—consideration when calculating dosage. But dosing based only on weight may become more and more inaccurate as a child grows, and can result in underdosing or overdosing. How do you know if your child is receiving the correct dose of factor?

The answer may lie in pharmacokinetics (PK) testing, which determines how factor behaves in the body.[1] Several things affect factor behavior, including half-life, inhibitors, and body weight. To accurately dose factor, you really need a PK study. Without PK results, dosing is based mainly on body weight, after accounting for the type of hemophilia (A and B are dosed differently), the severity, and sometimes the person's activity level.

So how is a dose of factor measured? Factor concentrates are measured in international units (IU), or "units."[2] Dosage is the number of units of factor needed to raise a person's clotting factor to a desired level (the "correction level"). The desired level is a percentage of a normal factor activity level of 100%. There is no standardized treatment protocol for hemophilia, so the "desired" increase in factor activity level after factor VIII treatment varies widely—from HTC to HTC, and sometimes from person to person—but it's usually between 40% and 100%.

What Does the Formula Say?

The package insert of all factor VIII products includes a formula to determine the number of units of factor required to reach a certain desired activity level. Here's a typical factor VIII formula:

Number of factor VIII units required = body weight x desired factor VIII increase x 0.5 unit/kg

In this formula, body weight is measured in kilograms (kg), and desired factor increase is measured as a percent. One kg equals about 2.2 pounds.

So to calculate the number of units required to raise the factor level to 80% in a 100-pound (45-kg) person:

45 kg x 80 x 0.5 IU/kg = 1,800 IU

This formula is based on an expected factor VIII recovery of 2%. In other words, it assumes that each unit of factor VIII infused per kg of body weight will increase the circulating factor VIII level by 2%. This formula holds true in general, but some factor brands have a lower recovery than others, so the dose must be adjusted upward. And the recovery may vary from person to person, especially in response to inhibitors.

Recovery also varies by body weight. Several studies have shown that in obese people, factor VIII recovery is higher than in people of ideal body weight, often 20% to 30% higher than expected. But recovery is *lower* in underweight people, compared to people of ideal body weight. What does this mean? If you're obese, your increase in factor level will be greater than the formula indicates. And if you're underweight, you are receiving a lower level of factor than the formula indicates.

Here's why: After a factor infusion, the difference in the expected rise in factor level in obese and underweight people is related to (1) how factor VIII is distributed within the body, and (2) how the volume of blood plasma varies with weight. Many drugs are dosed by weight, because once absorbed, they're distributed more or less equally throughout the body. But this isn't the case with factor VIII; instead of being distributed equally throughout the body, most of it—about 86%—stays in the blood.

Here's where the effect of blood volume comes in. When calculating a factor dose, the more a person's body weight varies from the ideal, the less accurate the formula becomes. That's because there is no direct relationship between body weight and blood volume. And the difference is greatest in obese people: as they become increasingly obese, their blood volume does not increase proportionally. In other words, obese people have less blood volume than their weight would suggest. That's because fat has far fewer blood vessels than muscle, so it holds a lower blood volume. If blood volume is measured against weight, an obese person may have as much as 40% less blood per pound, compared to someone of ideal weight. And someone who is significantly underweight may have as much as 30% *more* blood per pound, compared to someone of ideal weight.

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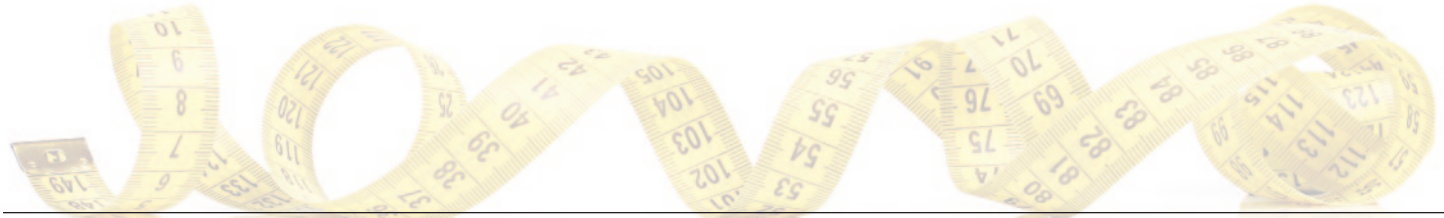


1. See "And Now, a Few Words about PK!," *PEN*, August 2016. 2. One unit is equivalent to the amount of factor activity found in 1 milliliter (mL) of fresh plasma (the liquid portion of your blood).

class. Or a young adult who switched pharmacies after moving out of the house may procrastinate on ordering factor. Someone else may want to forget about hemophilia or hide it. We're now at the point where some young people on prophy have never experienced a bleeding episode. So they may justify stopping prophy, thinking that hemophilia causes no complications or symptoms. Often, young people simply forget. Healthcare personnel and parents hope that growing boys and young men will adhere to prophy—but many studies indicate that some won't.

Sticking To It: What Is Adherence?

Following through with a doctor's recommendations is called *adherence*. Historically, doctors have used the term *compliance*, but adherence is now preferred for several reasons, including the term's connotation that the patient has an active role in his or her own healthcare plan. In fact, in recent years experts have been discussing whether the standard of hemophilia treatment—prophylaxis—is actually better described as being based on *concordance*, or mutual agreement between patient and physician about the care plan. Adherence, then, would refer to the success of the patient in following through.

Natalie Duncan, program manager and adherence researcher with the Indiana Hemophilia and Thrombosis Center, reports that prophylaxis in the US is increasingly being prescribed beyond childhood, and as a result, more and more adolescents and adults with hemophilia are benefiting from prophy. Yet despite this uptick in the number of people being prescribed prophy, Natalie notes that the percentage of patients who *adhere* to their treatment is inadequate, with reports ranging from 42% to 80%.

A small proportion of the non-adherence measured in research studies can be attributed to the process of individualizing broad prophylaxis guidelines for unique patients. For example, an adult who was never on prophy as a child, but is prescribed prophy in adulthood due to recurrent bleeding issues, may have trouble initially sticking to the plan—because it differs from the care plan he has followed for years. This is a case of non-adherence that would ideally be addressed by working with the patient to identify the barriers he encounters when incorporating prophy into his lifestyle, and finding solutions: for example, email reminders of upcoming infusions if scheduling is challenging.

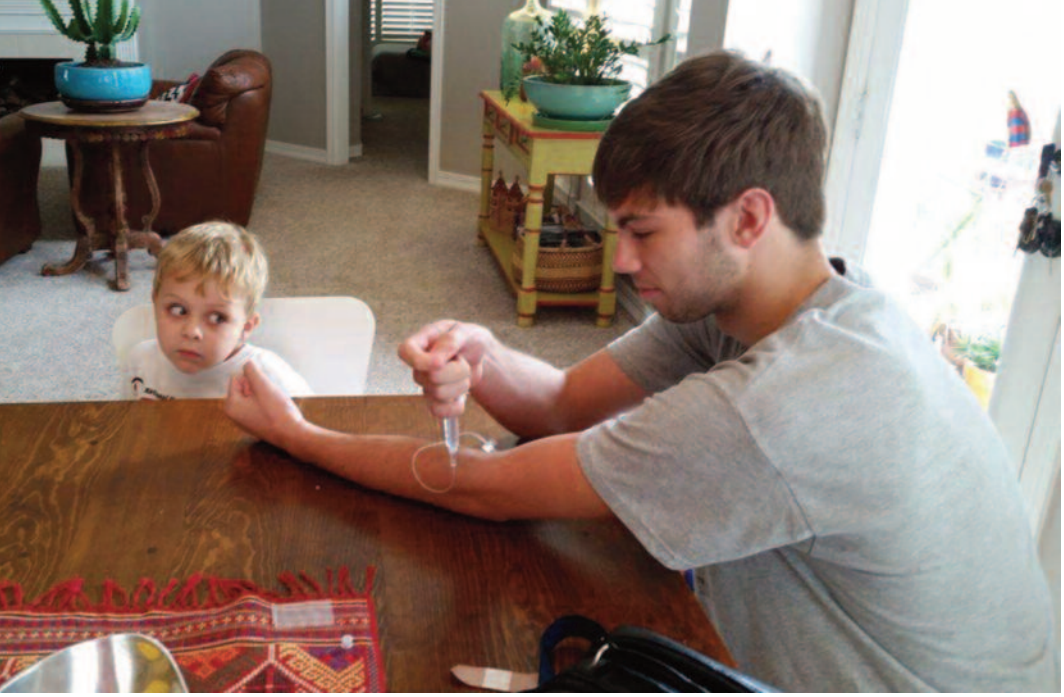
But many more cases of non-adherence are not so straightforward, and, while they need our attention, they are not as easily resolved. Natalie reports that although parents tend to follow treatment recommendations, there is a significant drop-off in prophy adherence when pediatric patients reach age 12 or 13 and start managing their own infusions. Another age-related drop in adherence is observed around the time that most teens move out of their family home and are without parental oversight.

The Tween Years, and Earlier

The tween years—during middle school, ages 9 to 13—mark the time when many children with hemophilia are expected to begin taking responsibility for their disorder. Yet non-adherence to prophy in middle school isn't entirely surprising. Tweens are undergoing physical, social, and academic changes, only some of which are hemophilia related. Natalie suggests that the best way for parents to encourage adherence at this age is to begin the transition earlier. She notes that sometimes, parents take so much control of managing the disorder that their children may not have a firm enough foundation to confidently and successfully transition to managing their own prophy when the time comes.

Natalie recommends that parents start involving their children in managing their prophy schedule and infusions before the tween years. For example, children can keep their own calendar to help them remember which days are infusion days, or they can log the infusions. As children move into the teen years, Natalie suggests that parents gradually let them assume increasing ownership of their hemophilia management, until they're successfully doing it all on their own.

Yet Natalie warns that parents still need to stay plugged in, so they're aware when barriers to prophy arise, and they can help their children. Patrick James Lynch, an adult with hemophilia A, and co-founder and CEO of Believe Limited, agrees. He points out that while many parents are educated on the importance of transitioning their children to self-infusion, they can also offer monthly planning and organizational tasks to make sure young people adhere to prophy. Patrick recommends that parents also gradually expose their kids to tasks such as organizing and storing infusion supplies or placing a call to the pharmacy when it's time to order more factor.



At a hemophilia event, Hank watches while Jack infuses himself

Limited Prior Experience with Bleeds

Regardless of age, knowledge about hemophilia and factor infusions is a predictor of adherence. In other words, education is a motivating force. When people with hemophilia understand *why* they're on prophy, they're more likely to do it. Although education about hemophilia and infusions ought to fall to healthcare providers, parents are not off the hook. Young adults with severe hemophilia in the US today have largely grown up on prophylaxis, and can live healthy, active lives. They don't know what life was like before prophy became the standard of care. In contrast, their parents have probably experienced sleepless nights worrying about bleeds or injuries, or remembering traumatic bleeds from their child's infancy before prophy. In some cases, parents with a family history of hemophilia may also remember the challenges faced by affected relatives of previous generations; these memories offer a built-in recognition of the value of prophy and modern factor products. Both Natalie and Patrick stress that it's important for parents to recognize how naïve their children may be about what life looks like *without* factor. Some young adults may leave the house to start out on their own, thinking, "I don't need prophy because I don't have many bleeds."

This idea is very personal for Patrick. Both he and his brother Adam were born with severe hemophilia A, but their disorder took vastly different paths during childhood. Patrick was physically active, which led to some injuries and bleeds. He also developed an inhibitor, resulting in bleeds and some limits on his activities. Yet he feels that these experiences taught him boundaries, and helped him learn to read his body. He notes, "The bleed is the greatest educational tool." Patrick was empowered from a young age to make good choices about infusions, sometimes sacrificing short-term convenience for longer-term health. In contrast, Adam was fortunate to be relatively bleed-free. Patrick explains that there was a mindset surrounding Adam: "If we didn't tell him he has hemophilia, he would never know." As the brothers became teenagers, Patrick took ownership of prophy as a means to stay well. Adam was adherent while under his parents' supervision, but he stopped infusing regularly when he headed to college. An intracranial hemorrhage took Adam's life at age 18.

Parents of young children with hemophilia often strive to keep their children as bleed-free as possible. For those lucky enough to succeed at keeping painful or traumatic bleeds at bay, how can we teach children the value of prophylaxis?

Patrick, now a well-known and widely respected advocate in the hemophilia community, points out that while his brother's death was a worst-case scenario of non-adherence, stopping prophy will more likely cause joint damage, which is permanent and can be avoided. Patrick stresses how crucial it is for young people with hemophilia to stay aware of what's happening internally, and to remember that they have a life-threatening chronic disorder. Similarly, Natalie points out how important it is for parents to reinforce that negative symptoms are being prevented by prophy. Hearing stories or seeing photos of relatives who have experienced bleeds may be effective for some young people to appreciate the value of prophy.

Normalcy versus Acceptance

Many parents of children with hemophilia are told that they should treat their child like any other child, with only a few restrictions. Although it may take a while for parents of a newly diagnosed child to begin feeling confident that they have protections in place in case of bleeding, striving for normalcy often follows soon after. "Don't wrap him in bubble wrap," they might tell daycare providers, because despite worrying about bleeds, these parents recognize the value of learning to walk and play with peers. "Keep an eye out for bleeding symptoms," parents may say, "but try not to mention hemophilia too much around him or his playmates. We don't want him to feel different."

However well intentioned, the quest for normalcy can backfire if it comes at the expense of identifying as a person with hemophilia. It's so much easier for prophy to slip through the cracks when a young person resents or rejects his diagnosis. Many leaders in our community suggest that parents should foster in their growing child the identification as a person with hemophilia, however fortunate he may have been with his bleeding history to date. Although ownership of hemophilia may seem to conflict with parents' early efforts to not let hemophilia define their child, striking a good balance will probably be worth the effort. Growing children need to learn that while hemophilia does not define them, they *do* have hemophilia. Further, they must understand that effectively managing their disorder is something positive they can do to enhance their quality of life—that is, being active, traveling, and being free from pain. Learning about the subtle differences in the language surrounding prophylaxis may help.

Not ideal:	Try instead:
√ Focus on adherence or compliance *(I need to infuse three times a week.)*	√ Focus on wellness *(This will help me stay well for the swim meet next week!)*
√ Health as a state of BEING *(I'm feeling great, so I don't need prophy.)*	√ Health as a state of DOING *(Doing prophy keeps me healthy.)*
√ Infusions are a task *(I do them TO myself.)*	√ Infusions are a tool *(I do them FOR myself.)*

In Patrick's view, identifying as a person with hemophilia is facilitated when kids are engaged in the hemophilia community. Patrick's business, Believe Limited, works to create programs and multimedia entertainment targeting teens, young adults, and new families with bleeding disorders. Patrick describes his approach as engagement first, with education as a secondary goal. He believes that you can't force a teen to be eager to participate in hemophilia activities, prophy or otherwise: teens must arrive at that decision on their own. Similarly, hemophilia camp can draw kids in with entertainment. First, says Patrick, "they are just excited to take part in summer camp activities. But as an important secondary outcome, they become more engaged with their community and begin to identify as someone with hemophilia."

It's probable that people who remain plugged into the community may be the most likely to stay adherent to prophylaxis, perhaps recognizing that they're not alone. They share experiences, and support good choices made by others. Parents can lead by example, too, getting involved with their local hemophilia chapter or hemophilia groups online, with a goal of finding a balance between normalcy and the positive acceptance of the reality of hemophilia in their own lives.

Risky Behaviors in Adolescent Boys

Adolescents sometimes engage in risky behavior during their transition to adulthood: experimenting with drugs and alcohol, driving recklessly, or even committing crimes. Some research contends that these behaviors can be explained by the development of brain systems that control both *sensation seeking* and *impulse control*. Risk taking is thought to happen during a period of development in which sensation seeking is higher than impulse control. It's unfortunate that this same period of development tends to be when most parents of children with hemophilia lose oversight of their child's adherence to prophylaxis. The fact that most people with severe hemophilia are males only compounds the problem. Males tend to score higher than females in sensation seeking, and lower than females in impulse control; and when compared to developing adolescent females, males experience a longer window of vulnerability, the period of time in which these two systems are unmatched.

Stated more simply: Males have an invincibility complex. As Patrick describes it, some young guys with hemophilia move out of the nest and begin to think, "My lifestyle has changed, I'm an adult now, I don't have to do this, I'm hanging out with people who don't have hemophilia." It's essential that parents not simply shrug off this well-documented aspect of human male development as "boys being boys." Rather, parents must recognize that it's likely to pose an additional barrier to prophy adherence, and then work hard to overcome that barrier! Fortunately, research also indicates that differences in impulse control are strongly influenced by childhood experiences. Providing early training on self-discipline can reduce tendencies to be impulsive. This insight is useful for parenting in general, but especially useful for prophy adherence.

Relationship between Patients and Healthcare Provider

When people with hemophilia have good relationships with their healthcare providers, adherence is increased. Natalie stresses that patients should actively discuss their treatment regimen with the medical team. "If a patient has been prescribed three prophylactic infusions weekly, and knows in that very moment that they won't be likely to adhere to that plan, they should say so! Doctors want to formulate a plan that will meet the needs of their patients, and this requires an honest dialogue." Often, patients may simply need more information about the reasoning behind their physician's recommendation before they are willing to adhere to the treatment plan. For young adults who have recently taken charge of their own care, engaging in such discussions may be key because they may have deferred to their parents during past discussions with caregivers.

Sometimes, discussions between patient and physician about a treatment plan will lead to a more individualized prophy regimen, which may deviate from the more frequently prescribed plan. For example, Natalie notes that some pediatric patients reach adulthood, become non-adherent, and find that they still don't

have bleeds. They may decide prophy isn't something that they will adhere to, and the doctor may agree. But this situation is rare. Most often, doctors will want to help patients better understand the benefits of continuing prophylaxis, while working with them to overcome barriers to adherence.

In recent years, many providers have participated with their patients in research studies that measure adherence using standardized scales. The Validated Hemophilia Regimen Treatment Adherence Scale–Prophylaxis (VERITAS-Pro), developed by Natalie and colleagues, enables researchers to measure adherence consistently across years and treatment locations. These types of scales aim to identify common barriers to adherence across large groups of patients so they can be addressed, for example, through the development of new patient resources or programming. In addition, these tools can give physicians insight into particular barriers to adherence on an individual level—that is, issues facing specific families and patients. For instance, if being organized is identified as a barrier to adherence for a particular young adult, the hemophilia treatment center (HTC) may be able to suggest ideas for a new system of storing or transporting infusion supplies and factor. If losing parents' insurance is a barrier, extra efforts can be made by the HTC social workers to help young adults secure coverage for their factor. Natalie notes that it's new for HTCs to have tools available to better identify these barriers. As more providers adopt measures to help decrease perceived costs of staying with prophy for individual patients, we may begin to see average adherence improving.

Psychological Barriers and Social Support

Key psychological and social issues can contribute to prophy adherence. One is needles. Despite treatment advances that have extended the half-life (persistence in circulation) of factor, prophy still requires intravenous infusions. Needle phobia can still plague some people with hemophilia, despite years of work to overcome this anxiety. Some patients face needle fatigue, which might be described as a feeling of emotional exhaustion at the idea of having to access a vein. These barriers are not often addressed in adherence literature. Patrick reports that having a good social system in place, including encouragement and empathy from friends and family, can often help young adults keep these needle-related challenges in perspective and work past the fear to get the infusion done. A visiting home nurse may also relieve the pressure of having to accomplish a needlestick.

Another social concern for some young people who are newly independent from their family may be whether or how to disclose their hemophilia to new roommates, friends, or partners. While parents of young children may choose to disclose their child's hemophilia for safety reasons (for example, in the event of a bleed), disclosure by young adults has important implications for identity and social support as well. Non-disclosure can lead to non-adherence, especially if a young person is embarrassed or hiding hemophilia. Natalie notes that it's essential for healthcare providers and parents to help children with hemophilia navigate decisions about when, why, and to whom to disclose information about their hemophilia. Education about peer disclosure should begin early. Although some young adults may fear negative attention when sharing this information, confidently disclosing to good friends is usually well received and is more likely to result in the young person adhering to prophy.

***

It's clear that for most patients with hemophilia, adherence to a regular prophy regimen beyond childhood will provide long-lasting benefits that should outweigh temporary costs. Yet parents and healthcare providers must set the stage for this transition. Our task is not just to educate our children on the importance of prophy, but also to prepare them from a young age to take ownership and responsibility for their own well-being as people with hemophilia. We must start early to teach them the planning, organizational, and practical skills they'll need to adhere to prophylaxis. Perhaps just as challenging, we must model acceptance, confidence, and positive thinking when it comes to hemophilia management.

Whether our efforts result in an adherent young person is hard to predict—especially given the unique physiological and social challenges facing young people as they mature. But with any luck, we may look back one day and find that not only have our kids remained adherent to prophy, but they have also grown and excelled beyond our highest hopes in all sorts of wonderful ways.

Christy Bergeon Burns lives in Bloomington, Indiana, with her husband Steve and their two sons, Charlie (6) and Kenny (3), who both have severe hemophilia B. Christy holds a BS in biopsychology from the University of Michigan and a PhD in biology from Indiana University. She is currently working toward her MS in genetic counseling at Indiana University School of Medicine.

headlines

manufacturer

Personalize Your Prophy

Personalized prophylaxis, using pharmacokinetics-guided dosing, may be effective in reducing frequency of infusions and the amount of factor used. This was demonstrated in a study with Octapharma's Nuwiq®, a recombinant factor VIII (rFVIII), in previously treated patients with severe hemophilia A. Why this matters: Nuwiq is a naturally long-acting rFVIII protein, produced in a human cell line without chemical modification or fusion with any other protein.

For info: www.octapharmausa.com

Helixate® FS Update

Helixate FS, a rFVIII product distributed by CSL Behring, will no longer be manufactured after December 31. Helixate FS is the same product as Kogenate® FS. CSL Behring acquired the rights to sell certain quantities of Kogenate FS every year as part of a lawsuit settlement from Bayer many years ago. The contract expires December 31. Why this matters: Patients using Helixate FS will need to choose a different therapy, although quantities of Helixate FS will still be available in the marketplace until late 2020.

For info: Talk to your HTC team; or CSL Behring My Source℠ Care Coordinator 800-676-4266

Bayer Research Awards

Bayer Hemophilia Awards Program (BHAP) distributed research grants of over $2 million to 16 winners from 8 countries. Grants will support research on a range of projects, including anxiety among female carriers of hemophilia, tailored hemophilia A therapies, and assessing therapeutic relationships in hemophilia care. Why this matters: BHAP has awarded more than 280 grants, totaling more than $33 million, to researchers and caregivers from 32 countries worldwide.

For info: www.bayer-hemophilia-awards.com

new from LA Kelley Communications, Inc.

Empower Yourself!

A hemophilia diagnosis can upset your beliefs, feelings, and life. This 38-page book offers concrete ways to regain feelings of control through empowered thinking and goal setting. Before-and-after illustrations highlight many situations you may face, and show you how to handle them effectively. Why this matters: Parents can absorb only so much information when dealing with emotional upset, and this brief book is the perfect tool to teach coping techniques. Free to families.

For info: www.kelleycom.com

global

Hemophilia in the Land of Braveheart

World Federation of Hemophilia World Congress
Glasgow, Scotland
May 20–24, 2018

Organized by WFH and hosted by Haemophilia Society (UK), the congress unites patients, patient advocacy groups, and healthcare providers from over 120 countries to participate in symposia, social events, and meetings. Why this matters: WFH congresses are the largest international meetings for the global bleeding disorder community.

For info: www.wfh.org

insurance

Taking a Stand

National Hemophilia Foundation, HFA, and Hemophilia of Iowa are seeking federal action against Wellmark Blue Cross and Blue Shield, Iowa's largest health insurer, for violating HIPAA and the Affordable Care Act. Wellmark publicly revealed the condition of one of its members with hemophilia, who is costing the insurer $1 million a month, and used this as one reason to exit Iowa's Health Insurance Marketplace. Wellmark claimed the patient's high costs contributed to premium hikes of around 40% for new ACA plans in 2017. Why this matters: This case could set a precedent for other conflicts in the insurance Marketplace, in which hemophilia patients are excluded from coverage when insurers withdraw.

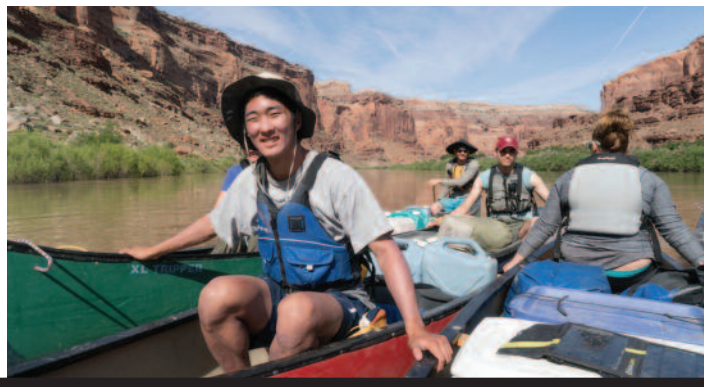
For info: www.hemophilia.org

patient programs

Leading X

This weeklong backcountry adventure teaches leadership skills and personal responsibility, and strengthens community bonds. Participants navigate river and sea to camp at new destinations every night. Funded by Pfizer; travel scholarships available. Why this matters: Developed and directed by GutMonkey, outdoor programs allow bleeding disorder patients to experience nature, learn about teamwork and leadership, and form new friendships in the community.

For info: www.gutmonkey.com



nonprofit

Memorial for Hemophilia AIDS Victims

The new Hemophilia Memorial, dedicated on September 16, is located in the National AIDS Memorial Grove in Golden Gate Park, San Francisco. A circle of stone honors people with hemophilia who died of AIDS; 100 names will be engraved, with more to be added. The space will have a seated bench of Minnesota limestone. Why this matters: The hemophilia community suffered one of the greatest medical disasters in history, and has long petitioned for a memorial to honor those who suffered and died.

For info: vimeo.com/227961238?ref=fb-sharew

soundbites

Including recombinant products, the 2016 US plasma proteins drug market totaled just over **$13.8 billion**, up 11.9% from 2015.

Catalyst Biosciences, based in San Francisco, announced a phase 1/2 study in South Korea to evaluate CB 2679d/ISU304, an investigational **subcutaneous factor IX** in development for hemophilia B prophy.

The **WFH Humanitarian Aid Program** treated 2,119 bleeding disorder patients in 2014, and more than 12,300 patients in 2016.

The newly launched **WFH World Bleeding Disorders Registry** (WBDR) is the only global registry collecting standardized clinical data on people with hemophilia worldwide.

Four specialty pharmacies and one drug wholesaler are **suing Tennessee** for breaking federal law and endangering people with bleeding disorders by reimbursing less for prescription blood-clotting drugs through the state's Medicaid program.

Octapharma's Nuwiq is now available in **2,500**, **3,000** and **4,000 IU** vial sizes, in addition to the strengths of 250, 500, 1,000 and 2,000 IU already available. Nuwiq is the only rFVIII in a wide array of vials with the lowest diluent volume of 2.5 ml.

New Hemophilia Nonprofit

United Hemophilia Foundation (UHF), headquartered in Georgia, was created to offer a variety of educational programs and events. In partnership with Hemophilia Federation of America (HFA), these programs will equip the Georgia bleeding disorder community with empowering information to enhance health, wellness, and quality of life. Why this matters: UHF may help reach and educate families and patients who are unable to attend national events.

For info: www.unitedhemophilia.org

science

Gene Therapy Keeps On

Shire's investigational drug SHP654 (BAX888), a factor VIII gene therapy for treating hemophilia A, was granted orphan drug status by the US FDA. Clinical trials will start soon. SHP654 is intended to provide a long-term, constant level of factor by delivering a B-domain-deleted factor VIII gene specifically to the patient's liver. Why this matters: Each new gene therapy trial brings us a step closer to making hemophilia gene therapy a reality.

For info: www.shire.com

More Good News for ACE910

Emicizumab (ACE910) is a once-weekly subcutaneous investigational treatment for hemophilia A. It was associated with a significantly lower rate of bleeding episodes when used prophylactically (as compared to no prophylaxis and prophylactic use of bypassing agents) in a phase 3 clinical trial (HAVEN 1) in adults and adolescents with hemophilia A with inhibitors. ACE910 bridges activated factor IX and X to mimic the function of activated factor VIII. In the group receiving ACE910 prophylactically, 63% of patients had zero bleeding episodes, as compared with 6% in the group treating on-demand with bypassing agents. Why this matters: ACE910 is being called a potential revolutionary treatment for hemophilia A, especially for inhibitor patients.

For info: www.roche.com

Death During a Clinical Study

A patient with hemophilia A without inhibitors enrolled in a phase 2 clinical study using Alnylam Pharmaceuticals' fitsurian (ALN-AT3SC) has died due to swelling in the brain. Fitsurian is an investigational RNA interference (RNAi) drug that reduces the level of the protein antithrombin, a natural inhibitor of thrombin, an important part of the clotting system. Low levels of antithrombin mean clotting proceeds more easily. The patient's CT scans confirmed that the initiating event was a blood clot in the brain. Why this matters: Alnylam has temporarily suspended dosing in its fitsurian studies to investigate and develop a plan to reduce risk.

For info: www.alnylam.com

EMA Rules on SIPPETT: No Go

European Medicines Agency (EMA), the European equivalent of the US FDA, concluded that there is no evidence of a difference in the incidence of inhibitor development between factor VIII concentrates derived from human plasma and those produced by recombinant DNA technology. Why this matters: EMA started its review after the 2016 publication of the SIPPET study (Survey of Inhibitors in Plasma-Products Exposed Toddlers), which concluded that recombinant factor VIII products had a higher incidence of inhibitor development than older plasma-derived versions.

For info: www.raps.org

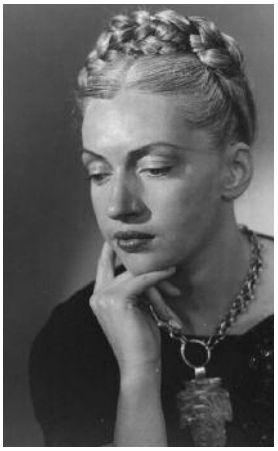
Richard's Review... from page 5

alone and dying in 1974, Janet remarried him without a license in a religious ceremony.

Janet founded the Janet Baldwin School of Dance, and directed it for over 25 years. Late in life, she developed emphysema and, at the end, dementia. Janet died in 1990 in Toronto. Very little information is available about her family history of hemophilia, almost as if the family wanted to keep it secret. No other family member is identified as having the hemophilia gene, and Janet's medical issues involving hemophilia are unknown.

Timothy Findley (1930–2002), author of *The Butterfly Plague* (1969), grew up in the prestigious Rosedale section of Toronto. He first met Janet Baldwin—notable for her white hair, blue eyes, and poise—when he was about seven years old. He remembered Janet dancing on the beach sand, or elegantly dressed at the Atlantic House Hotel in Maine where both their families vacationed every summer. Findley studied ballet, first from Volkoff and then from Janet, before a back injury ended his dancing career. He remembered the bruises caused by Volkoff's black walking stick, known as "Volkoff tattoos," during his ballet lessons. Findley then turned to speech and drama classes so he could express himself as an actor before becoming a writer.

The Butterfly Plague is set in Hollywood, 1938. Findley based his fictional character, Ruth Damarorsch, on Janet Baldwin—his friend, teacher, and dance collaborator—even dedicating the novel to Janet. There are several similarities between the real Janet and the fictional character: both are hemophilia carriers with white hair and blue eyes. But there are also some differences, for example, in physical appearance and talents. Ruth wins three gold medals in swimming at the 1936 Berlin Olympics. She eventually has children in the 1969 edition of the novel, but not in the 1986 rewritten edition. Yet as hemophilia carriers, both Janet and the fictional Ruth felt they had "tainted blood."



Sara Sutcliffe Portfolio, Dance Collection Danse

Janet Baldwin

Being a hemophilia carrier didn't prevent Janet Baldwin from dancing her entire life. Sadly, based on the medical care available in the 1930s and 1940s, Janet feared that any of her children would die from hemophilia, so she did not carry any pregnancies to term. Fortunately, today those medical concerns are allayed with appropriate treatment. I hope Janet's story will inspire you to consider dancing as a form of exercise throughout your life. If you're wondering whether I follow my own advice, let's just say that I tend to dance in private.

Inhibitor Insights... from page 4

is 2% to 3%. Why are these numbers almost the same for hemophilia B, but so different for hemophilia A? Mainly because ITT for hemophilia B inhibitors is often not successful, and in many cases can't even be started because hemophilia B inhibitors are frequently accompanied by severe allergic reactions (anaphylaxis) to infused factor IX.[1]

Inhibitors and Severity Level

People with severe hemophilia A or B have a higher chance of developing an inhibitor than do people with moderate or mild hemophilia. When you think about it, the immune system of babies is not fully developed at birth. As the immune system develops, it learns to identify which proteins belong, and which do not—in other words, proteins from bacteria, fungi, and viruses, which can cause disease and should be targeted and destroyed. Even if you have only a little factor in your bloodstream, your body will identify it as a good protein and leave it alone. So why do people with moderate or mild hemophilia develop inhibitors if they produce some factor? The exact reason isn't known, but we do know that inhibitors usually form after intensive factor therapy due to injury or surgery. And it's thought that inhibitors happen because the infused factor is slightly different from the person's naturally occurring factor.

Genetic Mutation

By far, the biggest risk factor for developing inhibitors is the type of gene mutation that causes a person's hemophilia. Mutations to the factor VIII or factor IX gene resulting in little or no factor being produced have the highest incidence of inhibitors.[2] Honestly, I never understood why I needed to know about my son's mutation. I initially thought my firstborn's disorder resulted from a spontaneous mutation, since I had no idea of a family history. Then when my second son was born and diagnosed with hemophilia, it never seemed to matter whether I knew anything about mutations. My older son previously had an active inhibitor, so I already knew my younger son's chance for an inhibitor was high. Knowing the mutation was not a critical piece of information that I needed, but understanding genetic mutations is important for some people. Knowing the mutation can help doctors understand why someone bleeds the way he does (someone with mild hemophilia who bleeds like a severe); can help verify a diagnosis; and can relieve the anxiety a family faces when a true spontaneous mutation has occurred and siblings will not be affected.

When you have a bleeding disorder, you want as much information as possible. My Life, Our Future is a nationwide campaign that offers free genotyping for families to capture more information about their bleeding disorders. Not only will genotyping help you know more about your diagnosis, but it will give researchers valuable information to create treatments in our future. To learn more about My Life, Our Future, talk to your hemophilia treatment center.

We can't control whether our child develops an inhibitor; that's out of our hands. What we *can* control is the amount of information we absorb to become better educated. We've talked about genetic risk factors that cause inhibitor development, and in a future issue of PEN, we'll cover environmental and treatment-related risk factors. Stay informed, keep learning, and never forget that there is no such thing as too much information. Living with an inhibitor was not your choice, but being informed is.

1. In a few cases, people with hemophilia A and inhibitors have developed allergic reactions to factor VIII, but anaphylaxis is extremely rare. 2. J. Oldenburg, J. Schroder, H. Brackmann, C. Muller-Reible, R. Schwaab, and E. Tuddenham, "Environmental and Genetic Factors Influencing Inhibitor Development," *Seminars in Hematology* 41, no. 1, suppl. 1 (2004): 82–88.

YOU... from page 6

Are You Getting Too Much or Too Little Factor?

What does all this mean for dosing factor VIII? Because factor is dosed by body weight, heavier people get a higher dose; but this is distributed over a proportionally *smaller* blood volume, resulting in a higher-than-expected factor level. The opposite is true for very underweight people: they're given a lower dose because of their lower body weight; but the dose is distributed over a proportionally *larger* blood volume, resulting in a lower-than-expected dose.

If obese people are receiving high doses of factor, can their factor doses be reduced without causing additional bleeds? Probably. Some small studies have found that obese patients could cut their factor usage almost in half—with no increase in bleeds—when dosed according to the ideal weight for their sex, age, and height. But these studies aren't the last word: they've been conducted for a short time, with few patients. To get better data—and possibly develop a new protocol for dosing factor VIII in underweight or obese patients—the University of Pittsburgh, in cooperation with Hemophilia Center of Western Pennsylvania, initiated a phase 2 clinical trial in September 2015.[3] The trial, to be completed in August 2018, is a randomized, controlled, crossover study. This means that some people will be dosed on their actual body weight and then switched to ideal body weight dosing; others will be dosed on their ideal body weight and then switched to actual body weight dosing. Researchers will record any differences in bleed rate or adverse events.

> If factor dosage is based only on weight, then obese people are likely being overdosed, and underweight people are being underdosed.

Parents, make sure you learn the desired factor correction recommended by your HTC.[4] And because children grow so fast, have their weight checked often at the HTC, and their factor dose adjusted.

Work with Your HTC

If your child is overweight, work with your HTC to develop better eating habits and raise activity levels. Obesity puts tremendous stress on weight-bearing joints, increasing the risk of bleeds in those joints.

Is your obese child receiving too much factor? Maybe. Maybe not. Young children clear (remove) factor from their bodies much faster than adults do, and factor in some children may have a half-life that's only 50% of what an adult may have. So your child may need a higher dose of factor to avoid prematurely falling below his targeted "trough level"—the lowest level of factor before his next infusion.

Remember, many considerations besides body weight determine how factor should be dosed. The only way to accurately dose factor VIII is to have PK testing to determine how factor behaves in your body. Without PK testing, factor dosing based mainly on weight is pretty much a shot in the dark.

3. https://clinicaltrials.gov/ct2/show/study/NCT02586012#contacts 4. To determine the percent correction your child is presently receiving, take half of your child's weight in kg and divide it into the number of factor VIII units he receives.

Inbox... from page 2

It's a matter of immense pleasure for me to provide feedback on the donation of factor by WFH. The humanitarian aid has made a great difference in the lives of people with hemophilia in Pakistan. This has enabled us to start the Low Dose Prophylaxis Project for children aged 2–10. We are observing a great difference, as bruises are disappearing and bleeding episodes have significantly reduced with this initiative. This has ultimately enabled us to form a community free of joint deformities and disability. Moreover, happy parents and healthy children.

One important point I would like to highlight: these are long-acting products with an extended shelf life, enabling us to manage bleeding episodes more effectively. Because the factor remains in the bloodstream for an extended period, we can manage repetitive bleeds more effectively, with top-notch results. Moreover, we've been able to perform elective surgeries, like total knee replacement and emergency surgical procedures. These have changed the lifestyle of those who had joint deformities, used crutches to walk, and led a restricted life. The humanitarian aid has caused a significant improvement in their well-being.

Dr. Shahla T. Sohail
Pediatric Hematologist/President
Pakistan Hemophilia Patients Welfare Society-Lahore
Pakistan

I've finally received my first infusion of factor in my life—1,000 IU! It took a long time for two interns to mix the formula and infuse it right, but with the help of videos on YouTube that I found, we finally did it! Thank you so much! It was a great experience for the interns as well as for me. I've learned how to mix it, but putting the needle in is still tricky. And I know I've thanked you at least a dozen times before, but I'll do it again because it means a lot to us to receive factor. Thank you and your team. You rock!

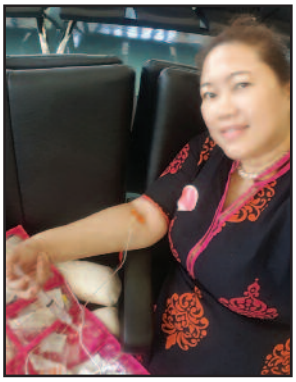
Kunaal Prasad
Fiji

Project SHARE

The wonderful gift for our boys with hemophilia has arrived. It's so impressive to see that, despite distance, without knowing them personally, you are thinking about them and always finding the right way to support their needs. Thank you with all my heart. I will give the factor to those in difficult condition, with frequent joint bleeds or a postoperative situation. Thank you also for supporting the summer camp, which took place this year in Buzias and was a great success. Wishing you good health and energy to continue your precious activity for the benefit of those in need.

Dr. Margit Serban
Romania

Infusing while waiting for my flight. I'm thankful to Project SHARE. It's been life-changing for me since I started having regular access to treatment. I used to get hospitalized to transfuse 30–35 packs of cryoprecipitate per day to control my heavy periods. Such an inconvenience for someone like me, who travels a lot for work. Unfortunately, VWF [von Willebrand factor] is not available in my country, and the only treatment options are blood products and tranexamic acid.



We are currently lobbying for a law on hemophilia care that includes access to treatment for everyone with hemophilia and bleeding disorders. I'm looking forward to that day when Filipinos will no longer be dependent on humanitarian aid.

Andrea Trinidad Echavez
President, Hemophilia Advocates
The Philippines

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Georgetown, MA 01833 USA
www.kelleycom.com

Hey! Did you visit your HTC this year?

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- **Loyalty Program†:** Redeem points to receive KOVALTRY® or KOGENATE® FS at no cost if you experience gaps or challenges with insurance coverage
- **$0 Co-pay Program‡:** You may be able to receive up to $12,000 in assistance per year
- **Live Helpline Support:** Our experts are waiting to help you with any insurance coverage questions you may have

*The KOVALTRY® or KOGENATE® FS Free Trial Program is available to newly diagnosed patients and patients who are currently using other therapy. Patients currently using KOVALTRY® and KOGENATE® FS are not eligible for the Free Trial Program. Participation in the KOVALTRY® or KOGENATE® FS Free Trial Program is limited to 1 time only. The medication provided through this program is at no cost to patients and is not an obligation to purchase or use KOVALTRY® or KOGENATE® FS in the future. Reselling or billing any third party for the free product is prohibited by law.

†Patients who have government insurance (Medicaid, Medicare, Tricare, VA/DOD) are not eligible for the Loyalty Program. The program does not guarantee that patients will be successful in obtaining coverage for products. Support medication provided through Bayer's assistance programs is at no cost to patients and is not contingent on future KOVALTRY® or KOGENATE® FS prescriptions. Reselling or billing any third party for free product provided by Bayer's patient assistance programs is prohibited by law. Bayer reserves the right to determine eligibility, monitor participation, determine equitable distribution of product, and modify or discontinue the program at any time.

‡People with private, commercial health insurance may receive KOVALTRY® or KOGENATE® FS co-pay or co-insurance assistance based on eligibility requirements. The program is on a first-come, first-served basis. Financial support is available for up to 12 months. Eligible patients can re-enroll for additional 12-month courses. The program is not for patients receiving prescription coverage for product under any federal-, state-, or government-funded insurance programs, or where prohibited by law. All people who meet these criteria are encouraged to apply. Bayer reserves the right to discontinue the program at any time.

Call **1-800-288-8374** 8:00 AM–8:00 PM (ET) Monday–Friday.
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