PEN

inside

Living with Hemophilia and Depression

Maria Iannone

Climbing the Seven Summits has been the dream of many adventurers. To date only 231 people in history have completed the Seven Summit list. As of March 2015, I have summited five … with only Mt. Vinson (Antarctica) and Mt. Everest remaining. Completing the Seven Summits is already an overwhelming endeavor; now imagine accomplishing this with a bleed[ing] disorder. I am excited to take on this task and educate others on hemophilia and overcome my own personal obstacles in the process!

Chris Bombardier
Adventures of a Hemophiliac Blog

Chris Bombardier is a 29-year-old with severe factor IX deficiency. He tells me he was not always so self-assured and inspired as his Seven Summits blog suggests. He has a phobia of needles and infusing, which he was only able to overcome because of his desire to play baseball in high school. He recalls feeling frustration and anger and, when he was younger, never really knowing why. After college, when his baseball career ended, Chris felt lost. He stopped infusing, started drinking, and was not active in the community. Chris was severely depressed. He did not know how to reach out to his hemophilia treatment center (HTC). When the HTC social worker asked, "How's it going?" in clinic, Chris would give the socially acceptable answer, "Fine."

Chris says he has always felt different, missing extra time from baseball because of his hemophilia. This spring he had a bleed that stalled his training for climbing Mt. Rainier. Chris knows how lucky he is to have access to factor, good medical care, and loving family and friends. But he continues to cope with feeling angry about having to overcome the pain and setbacks associated with living with hemophilia. He's not alone.

Lows and Highs: Chris experienced depression before he set out to summit the tallest mountains.

Depression Is Normal

Depression is a normal part of the range of human experience. We are drawn together as a species by our need to be engaged and connected with each other, and in the activities that make up our daily living. We would not have cohesive communities,

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welcome

Laurie Kelley

I'll never forget hearing in 1971 that my celebrity idol, actor Pete Duel of the hit TV show *Alias Smith and Jones*, had committed suicide in his Hollywood home. Why would someone with his looks, talent, fan base, and future do such a thing? As a young teen, it was the first time I'd considered depression as a serious condition. Since then, I've known classmates, friends, and family members whose depression overtook them, sometimes fatally. In the past two years, members of the hemophilia community have begged me to address this as an unspoken but desperate concern. At first I wasn't sure, but the more I speak to our young people with hemophilia, the more I learn that many are suffering, mostly in silence, masking their hopelessness and despair with anger, and sometimes even with success.

Depression is insidious. It carries such a social stigma that it silences the people who need to speak openly about it. And we as a community–and I am one of the biggest offenders–tend to praise the overachievers with hemophilia: they are our heroes, our role models in overcoming adversity. Yet, even some of our heroes suffer the long-term emotional effects of living with an intrusive, painful, and sometimes debilitating chronic disease.

We dedicate this issue to the problem of depression, and hope that you'll learn much from Maria Iannone's feature article. Some with hemophilia, like L.A. Aguayo (As I See It), have learned to overcome their depression. But so many others are waiting, silently and desperately, for permission to speak, for a community that cares, for help to arrive. Let's start helping them by understanding the symptoms of depression, by knowing that many more are depressed than we realize, and by reaching out to find them.

inbox

I HAD TO BAIL ON MY HTC (been going there since I was 4, and I'm 50 now) because no amount of cajoling and suggesting could get the team there to agree to let me try a prolonged half-life product. Not enough increase in half-life, too expensive, only for prophy, etc. I now have a new hematologist, and he is so much easier to deal with. And my specialty pharmacy now has a prescription for the product I want.

Anonymous

THE RECENT ARTICLE IN PEN by Glenn Pierce was fantastic! It is the best overview of where we are in terms of hemophilia research I have ever seen. Thanks so much for publishing this article–what a treasure.

Jasmin Eaglin
TEXAS

I THINK THAT PEN IS one of the best. Clear, easy to read, and filled with important information. Thanks also for the hard copy. I like seeing it arrive in the mail.

Mary Fitzpatrick
NEW HAMPSHIRE

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My Story—Rewritten

L.A. Aguayo

Severe hemophilia is a badge of honor that I display loud and proud. At every opportunity, I spread awareness about bleeding disorders and try to paint a realistic picture that will give others a glimpse into our lives. We face so many obstacles, but until we spread awareness and educate others, we will always be living in our own shadows and continue to be misunderstood. Having hemophilia is like a roller-coaster ride, with lots of ups and downs. Managing these almost made me throw in the towel, but I got some news that would change my life forever.

When I grew up in the late 1980s, information on hemophilia was scarce, and the only time my family learned anything new was when I went in for a yearly HTC checkup. To my parents, hemophilia was scary: it meant that I couldn't get hurt, or else I would bleed internally. If I did get a bleed, then I needed medication and I would eventually get better. When I was 15, my parents put the responsibility into my hands to either tell them when I had a bleed or just infuse myself. But while I was trying to accept this responsibility, my parents separated. My dad started a new family and my mom was busy working, trying to support her two boys. This left little time to focus on my hemophilia and my ever-changing needs.

Over the years I went from job to job and relationship to relationship, because nobody understood me. My employers wanted to know why I was always calling in sick, and my girlfriends never understood my anger and pain. I was an emotionally unstable person to be around. The only consistent thing about me was my desire to be a professional athlete. Though I dreamed of being a football player, basketball player, or professional wrestler, golf seemed most feasible. Year after year, I invested all my money to compete in US Amateur, Gateway PGA, and Metropolitan Golf Association events, where I played against the best. I always told myself that I would never give up on my dreams.

L.A. with Amanda, baby Harlo, and Dakota

Eventually, I was competing at a high level in professional golf events like the US Open Qualifier. Although outwardly, my golf career seemed to be looking up, internally I knew that I was getting worse. Having some pretty severe symptoms, like memory loss, lack of energy, sleepiness, and feeling very edgy, prompted me to make an emergency visit to my HTC.

This visit would change my life forever. Only 26, I was told that my liver was in the final stage of cirrhosis and that I needed treatment [for HCV] immediately. Treatment would consist of getting weekly injections of interferon for three months, along with taking two other pills (Sovaldi® and

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Inhibitors: More Prone to Depression?

Laurie Kelley

Many situations in life can cause us to feel overwhelmed, sad, or hopeless: loss, trauma, grief, financial trouble, unemployment, and even the weather. We may experience a depressive episode for a period of time, feeling sad, tearful, or irritable, losing our appetite, or having trouble sleeping. When the source of the stress is gone, usually our feelings of depression go away. When a depressive episode persists for weeks, months, or longer, it might be clinical depression.

Depression is a medical condition that interferes with your daily life and relationships, and can leave you feeling isolated, exhausted, and hopeless. Depression is one of the most common complications of any chronic illness, and having an inhibitor on top of hemophilia can magnify depression. Given all the physical, medical, and emotional challenges of having an inhibitor, are young people with hemophilia and inhibitors more at risk for depression than hemophilia patients without inhibitors?

"Since I was young I've tasted sorrow on my tongue"*

George and his wife were concerned about depression in their son Tim, now 17, because of how much Tim has suffered having an inhibitor. Tim's bleeding frequency and infusion schedule have been overwhelming. "He's been a tough case," George admits. "He bleeds a lot, usually every two weeks. We have to infuse him every two hours during those bleeds. He's had life-threatening situations, including head bleeds, a kidney bleed, spinal cord area bleed, another kidney bleed, and septic shock. He now gets two infusions a day. One is at 4:00 am. We've been infusing twice a day for three years." George sighs. "We use half a million dollars' worth of drugs a month. Insurance is tough for us." Because of Tim's "overwhelming infusion schedule," George worries about his son "leaving for college, being on his own. It's too much for me, and this might be too much for a young adult."

Sam, a 22-year-old college student who was diagnosed as clinically depressed, agrees that stress is a huge trigger for him, and believes that patients with inhibitors face great challenges. "Stress can trigger depression, there's no doubt. It's an 'overwhelmed' feeling. And when you get bleeds on top of that…this semester I missed an important exam due to a bleed, and there are only two chances in the year to take it."

Karen's son Nick became depressed after a particularly bad bleed. "One summer," she recalls, "just before Nick was going into fifth grade, we couldn't get his knee to stop bleeding. He couldn't use that leg for a year. Throughout that time, he struggled with depression."

Inhibitors complicate hemophilia treatment by causing relentless infusions, recurring bleeds, pain, and limitations to daily life. But why do some inhibitor patients endure depression while others don't?

Genetic Component

Inhibitors may or may not cause depression, but inhibitors can worsen depression that is already present. "I don't know if inhibitors are a source of depression," says Sam, "because my mom has depression, too."

"Our whole family has had bouts of depression," adds Karen, "even our child who doesn't have hemophilia. I can see it in all of our boys. And it never had anything to do with the inhibitors. Sometimes it's difficult to decide what comes from what."

Depression doesn't run in George's family. He hopes that his son won't develop it, despite the twice-daily infusions and bleeds. "Tim has not been diagnosed with depression. He's very active. And I think he is just the shy quiet type…until he's with his friends!"

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Linda Weaver's Studio

Richard J. Atwood

Remembering Fathers in Hemophilia: Samuel Appleton

I search for intriguing stories about people with bleeding disorders. By discovering those stories, including historical ones, I always learn something valuable. Often, I find inspiration in the stories of other family members, as in the case of the Appletons, who were connected with the powerful origins of our country.

One father of a child with hemophilia was Major Samuel Appleton (1625–1696). His son, Oliver Appleton, was the first person identified with hemophilia to be born in the American colonies.[1] Samuel spent a lifetime in public service fulfilling legislative, judicial, and military roles. He stuck to his principles about the illegality of improper taxation, and he remained calm in times of distress–during battle, and during the infamous Salem witch trials.

Samuel was only 11 when his family left England to settle in the Massachusetts Bay Colony in 1636. His father, also named Samuel, was one of the original settlers of historic Ipswich. The family owned a house and eight acres in town, and a 400-acre farm on the Ipswich River.[2]

One of five children, Samuel grew up to help run the family farm and businesses. He married Hannah Paine in 1651, and they had three children. After his wife's death, in 1656 he married Mary Oliver (1640–1698), a hemophilia carrier, and had eight more children, including Oliver in 1677. Oliver's bleeding disorder was noted by family members, but probably not as a genetic condition. Only later, in retrospect, did family members realize the distinctness of the bleeding.

Due to periodic threats of Indian attacks, Samuel Appleton led the local militia. From lieutenant in 1668, he rose to the rank of captain during King Philip's War, and commanded an infantry of 100 men. At the decisive battle near Hatfield along the Connecticut River in 1675, Samuel was commander-in-chief of more than 500 men. A turning point for the colonists, this battle proved that the Indian warriors could be defeated. During the fighting, a bullet passed through Samuel's hair. If he had died then, his son Oliver with hemophilia would never have been born.

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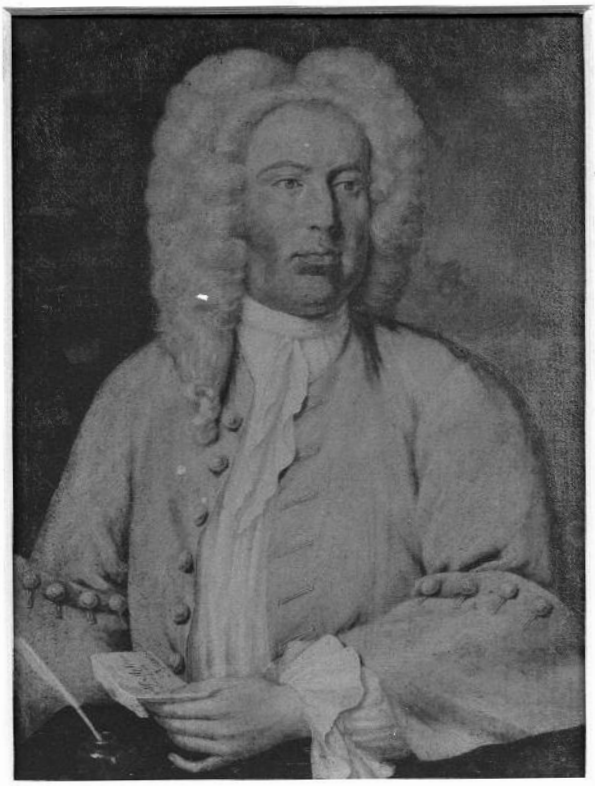

Samuel Appleton
Born Ipswich 16--, died London 1728
Merchant of New England
Son of Col. Samuel Appleton who died 1725
Grandson of Major Samuel Appleton
of Appleton Farms, who died 1696

Samuel held several elected offices. As a legislator, he was a commissioner of Essex County in 1668. He was a representative of the General Court from 1669 to 1680. And he served on the Governor's Council from 1681 to 1692. Appleton opposed the government of the colonial governor, Sir Edmond Andros. When in 1687 Andros levied a tax of one penny on a pound, the town of Ipswich refused to collect the tax, stating that it was against the rights of Englishmen for any taxes to be levied without consent of an assembly chosen by landowners, or "freeholders." An arbitrary and illegal warrant was issued for the arrest of Samuel and other leaders in the opposition to the tax. Samuel took refuge in Saugus, where he stood on a rock and denounced the government.

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1. "The Appletons: America's 'First Family' with Hemophilia." *PEN*, Nov. 2002. 2. That farm still exists today. Called Appleton Farms, it is the second oldest continuously run farm in America, now administered by the Trustees of Reservations, a nonprofit conservation organization in Massachusetts.

And now, a few words about PK!

Paul Clement

Thinking of switching factor brands or switching to a new prolonged half-life clotting factor? Having breakthrough bleeds on your current prophylaxis schedule? Planning on having surgery? Noticing your factor doesn't protect as long as it should? Dealing with inhibitors?

If you answered yes to any of these questions, then you should probably know a little something about PK–and probably have PK testing done.

What is PK?

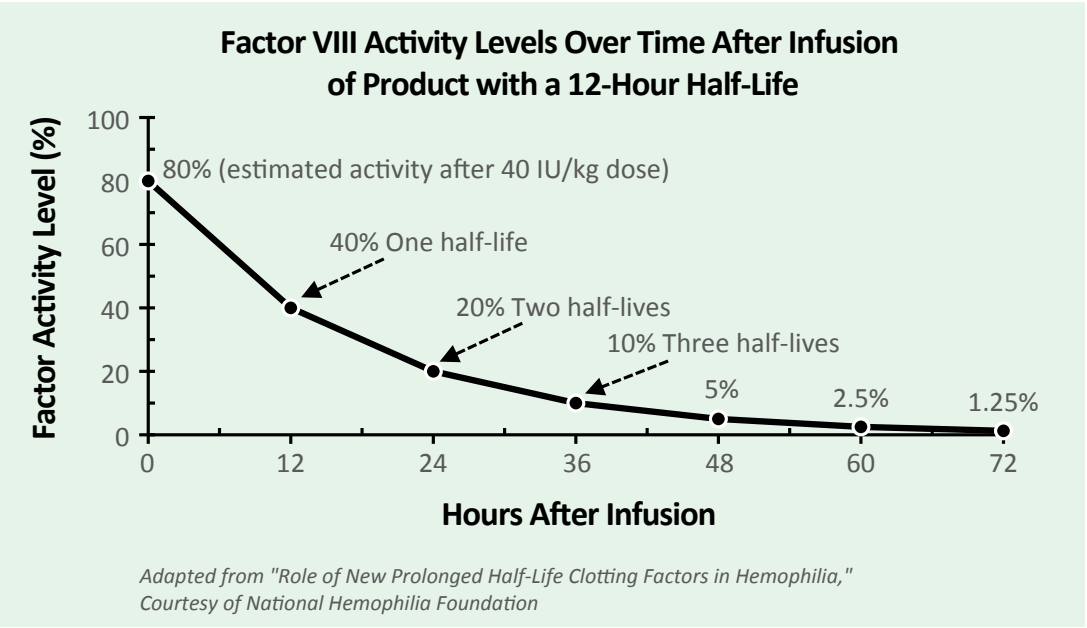
PK is the abbreviation for the word *pharmacokinetics*. Derived from the Greek, it means "movement of drugs." PK is a series of different kinds of measurements designed to show us what happens to a drug in the body over a period of time after it's ingested or infused. The measurements–or parameters–used to determine PK include half-life, peak factor concentration, and clearance (how quickly your body removes factor from your blood).

All of us who deal with a bleeding disorder have seen PK measurements. Every box of clotting factor has a product insert (PI) that includes a PK table showing the average PK measurements for that drug. If you've seen ads for the new prolonged half-life clotting factors now on the market, then you've also probably seen PK measurements and a graph of those measurements.

You may not have spent much time looking at PK measurements because they are often listed in PK tables using abbreviations, and they appear in unfamiliar units (like IU*hr/dL), making the whole thing look kind of scary.[1] But with a little effort, you can understand a few of the most common PK parameters, and this will help you ask your hematologist more informed questions about product choice or your prophylaxis schedule.

How is PK testing done?

PK testing requires multiple blood draws over a period of time: sometimes one before a factor infusion and then several after factor is infused. Depending on your HTC and the type of factor product (factor VIII, IX, or VII; standard or prolonged half-life), you may be asked to provide anywhere from 3 to 11 blood samples. For example, in a clinical trial of a prolonged half-life factor VIII product, 8 blood draws were recommended: within 30 minutes before infusion; 5–30 minutes post-infusion; then 3, 8, 24, 48, 72, and 96 hours post-infusion. Obviously, requiring a patient to stay near the HTC for days to complete this testing is inconvenient, especially for children, and for people who must travel long distances. This is the major reason that PK studies haven't been done more often in the past.



Adapted from "Role of New Prolonged Half-Life Clotting Factors in Hemophilia," Courtesy of National Hemophilia Foundation

A newer way to determine PK uses a statistical analysis method called Bayesian analysis, which involves using "population PK" data (results of PK

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1. Some pharmaceutical companies have become more consumer-friendly, and are now using words instead of symbols in PK tables.

families, and work environments if we did not feel deeply about each other and what we are doing. Because of this, when we feel a loss, we appropriately experience difficult emotional reactions like depression.

According to the *Diagnostic and Statistical Manual of Mental Disorders* (DSMV), sad feelings become a problem when they last longer than two months after a major loss, continue for at least two weeks, and cause problems in important areas of your life. For some, everything may look good from the outside, but it takes a monumental effort to keep up appearances and stay functional. Fortunately, depression almost always gets better with proper focused attention.

Unfortunately, depression is an illness that still carries with it a negative stigma for many people. Our cultural norms and societal values often leave little room for depression. Success means "living happily ever after." Depression is associated with immature coping skills, exemplified in common phrases like "Big boys don't cry" and "Put your big-girl pants on and get over it."

Depression strikes people of all ages, races, creeds, educational levels, and socioeconomic levels. The symptoms that depressed people experience are affected by the traits they inherit, and what they have learned about how to cope with stress. Stressful, long-term, difficult life challenges such as financial problems, physical limitations, pain, health issues, access to adequate healthcare, and the high cost of medications can all contribute to the emotional burden of stress. Depression is one of our most common problems. It is also a complex issue.

Depression and Chronic Illness

The Hemophilia Experiences, Results and Opportunities (HERO) study, conducted by the HERO Advisory Board,[1] found that 57% of parents of children with hemophilia feel the need for psychosocial support in coping with their child's hemophilia. In 2007 the Arizona Hemophilia and Thrombosis Center (AzHTC), where I work, found that a little more than 1 in 3 men with hemophilia experienced depression. We discovered that people with hemophilia who also reported a lack of social support or problems with unemployment were more likely to be depressed. Sadly, we also found that almost a quarter of all the people surveyed said they were without social support and almost half were unemployed.

The HERO study found that poor mental health puts a burden on relationships and employment. Imagine the downward spiral generated by being depressed and feeling isolated. Of the 57% of parents who reported feeling the need for psychosocial support in the HERO study, 33% did not actually seek the help they needed. This is what makes depression so debilitating. As early as 2004, the Cleveland Clinic Health System reported that as many as 1 in 4 men with chronic illness are suffering from symptoms of depression. In the general population the same year, 1 in 25 men in the US suffered from symptoms of depression. That means that living with a chronic illness increases the rate of depression by 6 to 8 times that of the general population.

Unfortunately, experiencing depression affects the way a person feels and thinks about his or her health. Depression can increase perception of pain. Chronic depression can also cause gastrointestinal problems, change immune function, raise cholesterol, and contribute to heart disease. The ENIGMA study, authored at the Brain and Mind Research Institute in Australia, shows that depression promotes changes in the brain that can affect memory. Depression can contribute to changes in ability to focus and concentrate. It's not surprising that people suffering from depression often feel in desperate need of immediate relief.

Depression is associated with an increase in risky behaviors like drug and alcohol abuse, poor adherence to medical treatments, and decreases in quality of life. The HERO study found that mental health can be an underlying force in choosing treatment regimes. At the AzHTC, we found that 2 in 3 of the men surveyed reported difficulties in their normal activities due to their depressive symptoms. Choices in hemophilia care treatment plans, as well as the ability to follow through with those plans, can be influenced by depression.

It is universally accepted within the bleeding disorder community that patients with hemophilia enjoy better health and quality of life when they engage in prophylactic treatment with factor. Straying from prescribed treatments is damaging and, at worst, life threatening. Unfortunately, factor replacement therapy often requires a demanding regimen of frequent intravenous administrations, usually 1 to 3 times per week. Taking factor as prescribed can be difficult because of the physical burden of venipuncture or central venous access, inconvenience, complications, fear of the risks of infections or inhibitors, and cost. Sometimes the emotional and practical toll of hemophilia care on patients or their parents can promote misunderstanding about when to treat or call a provider. For some, the experience can be so overwhelming that they stop paying attention and deny the negative consequences of failing to treat as prescribed. Adolescents are especially prone to feeling a lack of commitment to treat. Many are afraid of exposing their hemophilia diagnosis to family or friends, or in a public situation. It's not uncommon for people to limit their activities because they will take their medication only at home. Symptoms of depression and anxiety can further reduce one's ability to take proper care.

Fortunately, it is becoming widely accepted that mental health and the impact of living with a chronic illness are inseparably linked. Mental health screening and care are

1. http://www.herostudy.org.

increasingly available in HTCs. If we pay attention to depression, we can reduce the severity of the symptoms and improve quality of life.

Signs and Symptoms of Depression

Eight basic categories of symptoms are part of a clinical assessment for depression: sleep, interest, guilt, energy, concentration, appetite, lethargy or restlessness, and thoughts of suicide. All eight categories are broad in scope, and are evaluated based on whether a person experiences significant changes from normal behavior patterns.

1. Problems with sleep, such as having a hard time staying awake in the evening, waking up in the morning, or extra daytime napping; or, conversely, having trouble falling asleep, staying asleep at night, or waking too early in the morning.
2. A recent loss of interest in doing things that would normally be pleasurable, such as hobbies, friends, sex, exercise, or work.
3. A tendency to focus on unrealistic negative thoughts, feel guilty or preoccupied with past failings, or misinterpret trivial day-to-day events.
4. A disabling experience of tiredness or fatigue without physical exertion, such as being exhausted for no clear reason.
5. A lack of ability to concentrate or make decisions; a tendency to become easily distracted or have problems with memory.
6. Significant changes in appetite, resulting in weight changes that require forced eating or constantly craving food.
7. Problems with slowed speech, thinking, or body movements; or, conversely, rapid speech, rapid changes in the content of a conversation, an inability to sit still, pacing, hand-wringing, pulling or rubbing of skin or clothing.
8. Thoughts of death or suicide, thinking about giving up, "ending the pain," or a belief that "others would be better off without me."

According to the *Suicide Intervention Handbook*,[2] most suicidal people are unsure about dying and are desperately looking for a way out. Talking about suicide does not create or increase the risk; it *reduces* the risk. Often, nonfatal harmful behaviors such as unsuccessful suicide attempts, taking pills, cutting, and other high-risk activities are an invitation for others to help. Most people communicate how they are feeling by direct statement, physical signs (cutting themselves, losing weight, isolating), or emotional reactions (irritability, moodiness, sadness). Everyone thinking about suicide should be taken seriously. Feelings or events over a prolonged period of time are what typically contribute to a suicide attempt.

Depression and Families

The burden of raising a child with hemophilia can take a toll. According to the HERO study, parents may be coping with their own feelings of guilt, shock, disappointment, fear, or anxiety. Raising a child with hemophilia can place stress on parents' sense of self-esteem and personal relationships. This can lead to anger, resentment, guilt, and sometimes overcompensation in parenting style.

Children with hemophilia have the burden of coping with normal developmental milestones as well as frequent medical procedures and complications. Medical issues range from serious, requiring hospitalization, to routine, requiring frequent venipuncture. Medical treatment may be traumatizing, impact children's social lives, or limit their ability to fully participate in family, school, and community activities. Adolescence is complicated by the stress associated with developmental milestones in conjunction with changing hormones and great pressures to conform. Teens who are different at this stage can be bullied, feel ostracized, or have a sense of not being fully in control. Teens are trying to individuate from their parents. Some adolescents may have a "woe is me" attitude because of their bleeding disorder, feeling hopeless or overly cautious. Others may overcompensate for the restrictions imposed by living with a bleeding disorder, and may take unnecessary risks. The stress associated with growing up with hemophilia and raising a child with hemophilia increases the likelihood of symptoms of depression.

2. Richard F. Ramsay, Brian A. Tanney, William A. Lang, and Tarie Kinzel, *Suicide Intervention Handbook* (Livingworks, 1999).

Recognizing depression in children presents unique challenges. Zero to Three, a national organization dedicated to the mental well-being of children, emphasizes that children often do not have the verbal or cognitive skills to describe their experience. This leaves the burden of awareness on their primary caretakers. Changes in established patterns of behavior–especially persistent depressed mood or irritability–are clues to inspire questioning about whether depression is at play. As any parent knows, this is easier said than done. In infants and toddlers, we look for marked changes in sleeping or eating habits, and feelings of anger, irritability, or restlessness. In older children, we look for changes in eating or sleeping habits; depressed or irritable mood; restlessness, lethargy, or fatigue; feeling sad, hopeless, worthless, or guilty; having little interest in doing things that are normally fun; trouble concentrating or problem solving; trouble responding to teachers or caregivers; increased irresponsible or defiant behavior; or thoughts of death or suicide. Usually, attentive parents know when something is up, and it doesn't hurt to err on the side of caution and check with your doctor, HTC, or mental healthcare provider.

Learn About Treatment Options

Assessing depression is a complex diagnostic process that requires professional attention to medical issues, a full review of symptoms, collecting information from all possible sources, and getting a detailed medical and social history. Visit your HTC team if you suspect depression in yourself or a loved one.

When assessing medical issues, it is vital to consider risk factors such as medications that can cause depressive symptoms and medical conditions known to cause depression. In the current healthcare climate, it can be difficult for a provider to devote time to a full review of symptoms. In 2002 Dr. Ronald Remick, at St. Paul's Hospital in Vancouver, BC,[3] identified four common errors in recognizing depression. The first results from underdiagnosing depression because of incomplete assessments. The second results from a failure to collect information from family, friends, and caretakers, relying solely on the patient, even though the patient's view may be skewed because of depressive symptoms. Third, a provider may minimize a patient's depression because of the existence of other major health problems. This sounds something like, "Of course you're depressed; anyone with your disability would be depressed." Fourth, depression can be overdiagnosed when a provider bases the diagnosis on a "depressed mood" without a complete screening. It's important to learn how to be a smart consumer when it comes to depression care, increasing your chance for more effective care.

The Patient Protection and Affordable Care Act (ACA), enacted in 2013, has helped people with chronic illness by barring insurance coverage exclusions due to preexisting conditions. The ACA also expanded care to those in poverty. In 2014 many plans were required to cover 10 essential health benefits (EHB). Mental healthcare is among the EHB. Specifically, many plans require screening and assessing for depression, alcohol misuse, tobacco use, and domestic violence. Further, healthcare systems are being tasked with treating mental health similarly to physical health. Mental health assessment may be covered in your plan. Please don't let the fear of not having coverage keep you from asking your HTC for help.

Talk About It

If you suspect that you or a loved one may be depressed, first of all, talk about it. Talk to your doctor, family, friends, therapist, or clergy. Engage in support groups at your HTC, spiritual community, or neighborhood center. Get screened by a mental healthcare professional. Educate yourself: read books about depression, or search the Internet for professional articles from reliable sources. The National Institute of Mental Health (NIMH)[4] has many resources. Learn to advocate for yourself and your loved ones.

Overcome the stigma of depression. You have many choices when coping with depression, including making changes to your lifestyle, engaging in psychotherapy, or trying medication; even doing nothing is a choice. Successful treatment usually includes a combination of psychotherapy, medication, and lifestyle changes. However, treating depression is a highly individual process.

Think About How You Are Thinking

Unfortunately, when you're depressed, you don't feel like doing anything or talking to anyone. We react to life events based on automatic, sometimes subconscious interpretations. At times these automatic thoughts can promote depression, heartache, even physical pain in the present. Automatic thoughts can lead to a passive interpersonal style, where we go along with anything, whether we like it or not, to avoid conflict at all costs. Maybe as children, we learned to be very passive because we got a treat for being "such a good kid," but as adults, we're struggling with our jobs because we are not assertive enough. Sometimes automatic thoughts lead to an extremely aggressive interpersonal style where we push people to do or think as we do in order to control outcomes. Habits like this can reduce our success at home, work, and–especially important for those with a bleeding disorder–at the HTC. Learned habits can contribute to poor listening styles such as "spacing out," "pretend" listening, "selective" listening, inattention, or being self-centered. All of these

3. R. A. Remick, "Diagnosis and Management of Depression in Primary Care: A Clinical Update and Review," *Canadian Medical Association Journal* 167 (2002): 1253–60.
4. https://www.nimh.nih.gov.

strategies, if left unchecked, can affect our ability to maintain healthy relationships or be productive within our family, community, and workplace.

Fake It 'Til You Make It

One of the most effective strategies to combat depression is to engage in a pleasurable activity. But when you're depressed, this strategy is often one of the first things to go. When you're trying to reclaim your life from depression, you may have to "fake it 'til you make it." The bottom line is to begin engaging in activities that, over time, will make you feel good. These activities can include spending time in nature, eating well, exercising, pursuing spiritual goals, increasing creativity, getting involved in your community, and improving your sleeping patterns. The goal of these activities is to have fun, feed your spirit, relax, breathe deeply, stay connected, lighten up, and help others. Remember that change usually takes time. Give yourself time, be patient, be compassionate. Treat yourself as you would your best friend.

If you need to improve your sleep, try an improved "sleep hygiene" routine. Cognitive behavioral therapists and physicians may be skilled in coaching you through modifying your sleep hygiene. Healthy sleep hygiene includes having a regular bedtime and waking time; "smart" napping and fighting after-dinner drowsiness; increasing your daytime exposure to natural light; boosting melatonin at night by making the room dark (no phone, TV, computer, e-reader); keeping your bedroom quiet, cool, and comfortable; refraining from big late-night meals; avoiding alcohol before bed; eliminating caffeine 4 to 6 hours before bedtime; and refraining from smoking.

Make relaxing your goal, not sleep, and try to postpone worrying or brainstorming. See your doctor if you experience persistent problems such as daytime sleepiness or fatigue, loud snoring, difficulty falling or staying asleep, frequent headaches, crawling sensations in your legs or arms at night, inability to move while falling asleep, physically acting out dreams during sleep, or falling asleep at inappropriate times.

Medication versus No Medication?

Whether to treat your symptoms with an antidepressant medication is a topic about which many people are passionate. There are many reasons some folks don't believe in taking medication. Other folks just want a pill so it can make them feel better. Healing is a process in which we need to stay engaged and open-minded. It's fine to try the path of least resistance, but if that doesn't work, be willing to reassess and make adjustments. Be an active, open-minded partner in your recovery from depression. There are myriad antidepressants from which your healthcare provider can choose to tailor a medication protocol that works for you. Proper follow-up after an antidepressant is started is to see your healthcare provider after two weeks, four weeks, and then monthly until symptoms are improved and side effects are minimized. Then, regular follow-up annually.

Sometimes, after symptoms have been relieved for an extended period, you and your healthcare provider may choose to evaluate whether you can safely discontinue your antidepressant and try taking a "drug holiday." Sometimes your symptoms can return, and you and your provider may choose to change your medication or dose. As with any medication, it's important to have a responsive, attentive healthcare provider and to promptly communicate all medication problems and changes.

Psychotherapy

People sometimes struggle with choosing whether to treat depression by engaging in psychotherapy. Some folks are adverse to psychotherapy because they have had, or know someone who has had, a negative experience with it. Some don't believe psychotherapy will help, they don't want to talk, they're too busy, or they are too ashamed.

There are many types of psychotherapy. How to choose? Again, talk to people. You will probably be surprised to learn that someone you know has seen a therapist they've liked. Get recommendations from people you respect. Interview several therapists to find someone you think may be a good

fit and you can afford. After you have selected a therapist, show up, and, when it gets rough–which it may–don't quit.

Social Engagement

Reaching out to people with depression is a top priority. The AzHTC study found that having social support decreases the risk for depression by 80% and being employed decreases the risk by 84%. Fortunately, the bleeding disorder community is a well-organized network of support organizations that promote social interaction, education, and self-reliance. Many HTCs currently implement effective screening, education, and interventions for depression care and management. Regionally and nationally, there is a focus on improving comprehensive care and expanding psychosocial support. The psychosocial program at the AzHTC in Tucson includes screening all patients for depression and anxiety at every comprehensive clinic visit. Our screening includes two questionnaires and a short clinical interview, scheduling a follow-up appointment for people who need and want further help, and providing education regarding treatment options both in and out of the HTC.

Many people with hemophilia have said summer camp changed their lives, giving them a supportive peer group and a sense of self-worth–much needed by young people with a bleeding disorder. One mother reported her son's perspective was changed by being a camper, and later a counselor, at Dream Street (a camp for kids with serious medical conditions, mostly cancer). Each year a few kids failed to return to camp because they had died. Rather than feel sorry for himself, her son felt lucky that he "only had hemophilia." Volunteering at summer camp also contributes to feelings of self-worth. Service to others is a great way to enlarge our perspective and possibly alleviate feelings of depression.

Here's some good advice from patients who participated in the HERO study: live life as normally as possible, keep active, get involved in the community, and educate those around you.

Coping Skills

Our ability to cope with stress, anxiety, and depression starts with acknowledging and accepting our experience in each moment. More advice from patients who participated in the HERO study: enjoy life, communicate openly, "embrace" hemophilia, and "get into" treatment.

Parents have the enormous responsibility of raising healthy children. This is sometimes compounded by the existence of a chronic illness like hemophilia. They have the equally enormous responsibility of letting go of these same children–and helping them achieve successful independence. Children cope with developing into productive members in their families, schools and communities, and, finally, in the larger society. We all have to learn how to productively negotiate emotionally and socially from the time of infancy into adulthood. Learning how to transition through life stages and within varied roles is a skill that constantly needs to be honed. We don't always get it right, but with an open mind, we can always learn. Developing the skills necessary to make conscious choices and strategizing to make desired changes in our lives is a process that takes a willingness to tolerate hard times and emotional upheavals, as well as awareness and practice.

Depression care is a team effort with the individual as the leader. Get educated about depression. Get screened. Healthcare providers need to improve screening, follow up with findings and medication prescriptions, and collaborate with patients and other healthcare providers. Patients need to show up and challenge themselves to do the work. Remember, change can be difficult. Participate in proper treatment and don't give up until you get it right.

Chris's Outcome

Balancing recovery and pushing himself to reach his goals requires Chris Bombardier to process a broad range of positive and negative emotions. He attributes his initial and sustained recovery from depression to his wife's support, the resources at his HTC, and finding his passion for the outdoors. He finds his time in nature "good for his soul." He engaged in psychotherapy, became active in the hemophilia community, and challenged himself to set and achieve goals.

Chris hopes that other people with hemophilia will find relief from depression by talking about their experiences and finding the strength to acknowledge their condition and move on. Chris has learned that it's okay to struggle with his feelings of anger, frustration, and guilt. With proper self-care, these feelings are no longer overwhelming.

Maria Iannone is a licensed professional counselor at the Arizona Hemophilia and Thrombosis Center (AzHTC) in Tucson, Arizona, where she has worked for nine years. She treats adults, children, and families. She has developed a comprehensive mental healthcare management program for patients with hemophilia at the AzHTC and engages in psychosocial research projects. She is the lead author of the peer-reviewed article "The Prevalence of Depression in Adults with Hemophilia," and she wrote the nationally disseminated NHF Collaborating in Care module on depression and anxiety. Maria completed her graduate study in counseling psychology, an internship at the Blake Foundation in which she specialized in the assessment and treatment of children and the use of parent/child psychotherapy, and an internship in the Psychosocial Oncology Program at the University of Arizona Cancer Center, in which she specialized in assessment and treatment of breast cancer survivors. Maria draws from both her clinical experience and previous biomedical research experience.

If several of your family members have depression, your loved one with an inhibitor might be more susceptible to depression when the responsibilities, pain, and limitations of the disorder become too much.

"I'm trying to hold it together / Head is lighter than a feather"*

"I have felt hopeless and sad," reflects Sam, "questioning many things. Sometimes I felt like letting myself go–thinking, what makes you think you're so special? I've never thought seriously of ending my life, but I have let myself go, like not taking care of myself."

Karen realizes that all of her children react differently when depressed. "John never got overly emotional; he would become very quiet, not engaged. He'd escape into video games and books. He struggles with ADD, and has some serious anger issues. Nick tries hard not to be depressed, to see good in everything. He's always been social and talkative. But when he was little, he just seemed sad. And the two youngest would cry. Sometimes it would seem like for no reason."

Karen knows that one depression trigger is weather. "All four boys have a seasonal, cyclical depression. Charlie would wake up and cry and cry; he couldn't articulate it. Everything felt wrong. Sean has gone through the same thing."

People's depressive symptoms and triggers may differ. One thing to monitor is how long feelings of depression persist after the trigger has passed. Is your child still depressed long after a bleed has resolved? Long after he has rejoined his favorite activity following a period of inactivity? Identifying depression triggers may help you cope.

"Keep holding on..."*

Though depression is a serious health condition that can't be willed away or ignored, it can be successfully treated. Once symptoms are recognized, you may be able to avoid common depression triggers–or better manage those you can't control.

Sam tries to build his coping skills. "I joined a gym and started working out, and now it's my most constant form of coping. It gives me a reason to get out of my home, to be productive, and probably it releases hormones and allows me to work toward goals."

Because he lives in an area with limited sunlight in the winter, Sam made some minor adjustments to help ease depressive episodes: "I felt I was missing vitamin D, so I take supplements. I bought a clock with nature sounds–bonfires, rainstorms, crickets. And I use its built-in lighting to mimic sunlight."

Sam also learned that his thinking was exacerbating his depression. "I had to realize that when I constantly ruminate about things, my thoughts would go in vicious circles. I wasn't being rational. I was asking some big questions in life." For example, Sam wondered why people suffer–a question with no simple answer. "Maybe one should question less when possible, and sometimes you understand much more."

When Tim had a kidney bleed for three weeks, George thought his son needed a distraction. Tim wasn't clinically depressed, but George felt he might be at risk. "We bought him a puppy, which turned out to be a good coping mechanism: the puppy distracts from the pain and boredom, gets Tim to play with him, to care for something else…and he uses the puppy to meet girls!"

Karen says her sons have learned to "ride out" their depressive episodes. "When a bleeding episode, with all its pain, is over, so is usually any depression. The only one that isn't true for is Nick because he never is without a bleed or out of pain."

Nick had to use a lot of pain medication, leading to fears of addiction, but he found healthy activities. "Music was a huge coping strategy," says Karen. "The times he gets depressed now is when he can't play guitar due to bleeds. He's so limited in physical activities to cope, so…music has become his distraction, his release."

Seeking Professional Help

Not all young people with inhibitors can find healthy coping mechanisms. Don't hesitate to enlist professional help. Your HTC has qualified nurses and social workers, and can refer you to psychologists who can offer expert guidance. At some point, your child may need to be evaluated for depression.

"I approached the college psychologist to ask for help," says Sam, "and he referred me to other professionals until I met with the psychiatrist I am with now." Sam is realistic: "My doctors have never said I will overcome it, but with each episode I know at least that this too shall pass. It's a flavor of life, in a way. I go to therapy, and I do have medication."

Inhibitors may not cause depression, but certainly they test the limits of a young person's emotional and psychological health, especially if there is a genetic predisposition to depression.

Having an inhibitor means having limits. Sam advises, "Recognize your limits. You can find ways around those limits. And you really have to take care of yourself." Parents of a child with inhibitors should talk to HTC staff about symptoms of depression and possible triggers, and they should monitor their child periodically. Sometimes, we focus so much on treating the bleed or the inhibitor that we overlook a child's internal struggles. The psychological aspect of inhibitors should always be considered alongside the medical.

* "Coming Undone" by Korn, released as a single February 21, 2006, from the album *See You on the Other Side*, Virgin/EMI, produced by the Matrix, Jonathan Davis.

YOU... from page 6

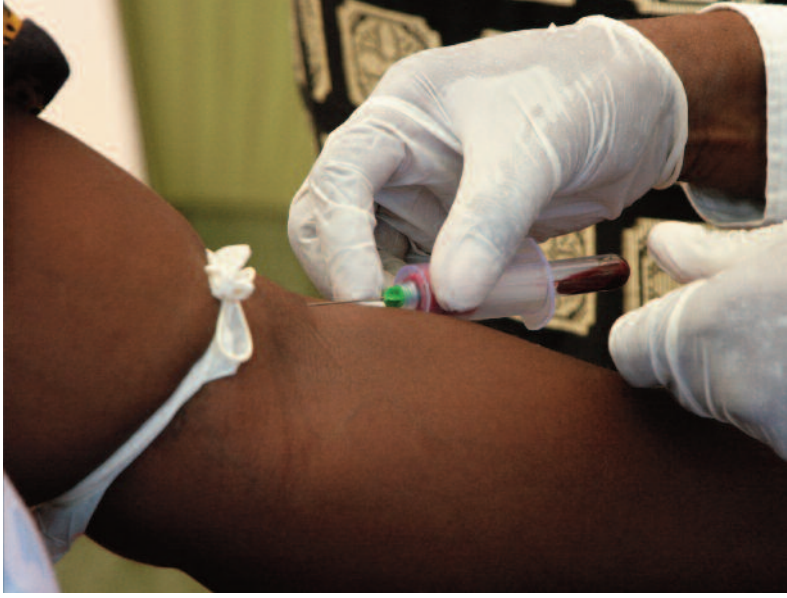
studies on a large patient sample using the same product). The Bayesian analysis method requires only three blood draws, recommended at 4, 24, and 48 hours post-infusion for a factor VIII analysis–much more convenient for patients and HTC staff![2] Unfortunately, this method isn't available at all HTCs because the computer software needed is not commercially available. Also, Bayesian analysis can't be used for the new prolonged half-life products because the population PK data for those products is not yet available. It's hoped that the Bayesian analysis method will become more common in future, as the software and necessary population PK data becomes available and HTC staff become more familiar with its use.

How many different parameters are measured when PK tests are performed? There is no set number of tests done when performing PK. In some cases, a physician may only be interested in one parameter, such as half-life; but a pharmaceutical company conducting a clinical trial may test more than a dozen parameters to gain a thorough understanding of how the drug is processed in the body. Typically, the results of about seven different parameters are reported in most PK tables found in PIs. Here, we'll look at one PK parameter you may already know something about: half-life.[3]

Half-life ($t_{1/2}$)

In PK tests of clotting factor, half-life is the most commonly reported PK parameter–and, for you, probably one of the most important ones. Half-life is also the most easily understood PK parameter because it's measured in a familiar unit: hours. There are several different types of half-life, but most PK reports list what's known as *terminal* or *elimination* half-life ($t_{1/2}$). That's the amount of time for the concentration of factor in plasma to drop by one-half. PIs usually list the average half-life of factor for adults aged 16 and older. For standard factor VIII concentrates, the half-life is about 12 hours. For standard factor IX concentrates, the half-life is 18 to 24 hours.

If you're contemplating switching products, perhaps to a prolonged half-life product, then the half-life of the product as shown in a product insert PK table allows you to compare the half-life of various products. This may help you choose a product. Otherwise, the average half-life of factor listed in a PK table is not much use to you. Why? Because you're not average! There is wide variation in how each of us processes a drug–so, for instance, the half-life of factor in your body will rarely match the average. More important is your *individual* PK, or how *your* body processes a drug over time. Your individual PK is not a single measurement or parameter; it's a series of measurements of several parameters. And these parameters, taken as a whole, describe how your body processes a drug. It's all about YOU: no two individual PKs



are the same. For example, in a child, it's likely that none of the PK measurements will match those in a PK table of average adult PK measurements. Here are a few considerations that can affect the half-life of factor in your body:

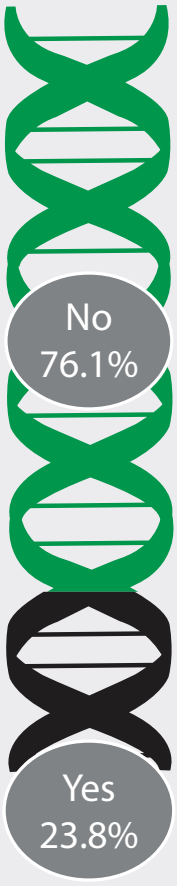
- **Inhibitors** have a dramatic effect on half-life. If you have an active high-titer inhibitor, the half-life of factor may be measured in minutes. But also know that even after you have been tolerized–your immune system desensitized to the presence of factor–you may still have very low-level inhibitors that can shorten the half-life of factor.
- **Age** significantly affects half-life of factor. The younger you are, the faster you clear or remove factor from the bloodstream, and the shorter the half-life of factor in your system. For factor VIII, babies may have a factor half-life only 50% or less than that of adults. The half-life of factor slowly increases as children get older, and at age 16 they're often approaching the average half-life listed in PK tables. The half-life of factor slowly continues to increase until at age 60, some people may have a factor VIII half-life of 20 hours or more.
- **Liver disease**, such as chronic hepatitis C infection, reduces clearance of factor, resulting in an increased half-life.
- **Blood type** influences half-life. People with blood type O have lower levels of von Willebrand factor (VWF), a protein that helps protect factor VIII. With less VWF, type O people clear factor faster, resulting in a shorter half-life. In people with blood type AB, factor tends to have a longer half-life.

Your individual PK, and in particular, the half-life of factor in your system, is important to know: to make sure you're being dosed correctly, and when planning a prophylaxis schedule with proper factor coverage. Yet most people with hemophilia have not had PK testing done, and many don't know the average half-life of their factor brand as noted in its PI. When you don't know your individual PK measurements, you're being dosed by guesswork–based on your weight and the average

2. S. Bjorkman and P. Collins, "Measurement of Factor VIII Pharmacokinetics in Routine Clinical Practice," *Journal of Thrombosis and Haemostasis* 11 (2013): 180–82. 3. Other PK parameters will be discussed in future issues of PEN.

Not OK to forgo PK!

"I have had (My child has had) pharmacokinetic testing."



From a total of 176 respondents nationwide to a survey emailed by LA Kelley Communications April 28, 2015

half-life of your factor product. As already noted, for children, the half-life of factor is likely to be significantly shorter than the average for adults, requiring children to have higher doses and/or more frequent infusions to maintain the target factor level.

Research has also shown that there is no direct relationship between weight and factor dose. Obese people have a smaller blood volume than non-obese people who are the same weight–and because most infused factor stays in the blood, this means that when factor is dosed by body weight, an obese patient will probably receive more factor than is needed to achieve the same factor level as a non-obese patient. Dosing according to your individual PK would eliminate these problems and could potentially reduce factor use while reducing breakthrough bleeds.

Did you answer yes to any of the questions at the beginning of this article? If so, have you had a PK test done? Talk to your hematologist about whether PK testing is right for you. And if you're thinking about switching to a prolonged half-life product, talk to your hematologist early. Discussing your intention to switch to a prolonged half-life factor product will benefit you, and possibly other people with hemophilia. Why? Because we need more data about prolonged half-life factor products.

Many physicians see the transition from a standard half-life product to a prolonged half-life product as an optimal time to do PK testing. Performing PK around the time of your switch will allow you and your doctor to see how your body processed your old factor, and how well the new prolonged half-life factor is working–vital information needed to design a prophylaxis schedule around your individual PK.

Richard's Review... from page 5

A Massachusetts historical marker now acknowledges the site as "Appleton's Pulpit." Refusing to apologize, Samuel was imprisoned in November 1687. He petitioned in January for his release due to his age and weakness, but wasn't freed until March 1688, when he posted a 1,000-pound bond.

In 1689, during the coup of crown-appointed Governor Andros, Samuel and other leaders in the Massachusetts Bay Colony put Andros on a boat to the island prison in Boston Harbor. Colonial revolutionaries 100 years later simplified the opposition to taxes with the slogan "No taxation without representation." But it's important to remember that the ideas for the American Revolution began long before 1776: to be properly recognized, Ipswich adopted the motto "The Birthplace of American Independence 1687."

Samuel Appleton served on the judiciary. He was a deputy to the Massachusetts General Court from 1668 to 1681. As a member of the Council of Assistants from 1681 to 1686, Samuel attended the examination of accused witches in Salem on April 11, 1692. His role may have been minor; he isn't always listed as one of the seven judges. And apparently he did not serve as a judge in any of the trials that executed 20 alleged witches in 1692. On May 2, 1693, the first Supreme Court convened in Ipswich to try Andover residents charged with witchcraft. As a judge at that hearing, Samuel cleared everyone accused of witchcraft, ending the infamous witch trials and demonstrating his rationality. During the hysterical witchcraft proceedings in Salem, Oliver Appleton was a 15-year-old with hemophilia living at home in Ipswich.

The story of Major Samuel Appleton reveals essential information about colonial America. Some of our defining principles that we cherish today were sown by the colonists years before the revolution for independence. We need to honor those colonial leaders for their contributions, and remember that Major Samuel Appleton also raised a son with hemophilia.

As I See It... from page 3

Ribavirin). I was told that I would be very sick throughout the process. I did research online, and after reading what people had to say, of course I was under the impression that my life was practically over. I read about liver transplants, and how most people don't live much longer after a transplant. I spent most of the next few weeks randomly crying and feeling scared. I told myself I would just file for disability because I couldn't keep a job with hemophilia, and now with this, I would be as good as dead.

I started the treatment, and just as the doctors said, I was very sick. I mostly slept all day and hid in my dark room, where I would occasionally play video games, and then I'd come out for a quick snack. I tossed and turned in my bed, always feeling like my head would explode or that I needed to vomit. I didn't shave or get a haircut, and I was as pale as the walls in my room. Simply said, I felt hopeless.

Halfway through the treatment, something started to change for me mentally. Although I wasn't dying, I really did experience the feeling of someone telling me that my life was at risk and that my time was limited. Something very powerful happens when you feel like you haven't much time. You start to think of your legacy. How would my two young sons look at my life if I died today? How do I want to be remembered? Do I have a purpose?

I woke up one day feeling better than average, and I had time to soul search. It was like a light bulb went on in my head. I finally realized my purpose was to use my life experiences and struggles to help as many people as possible in the bleeding disorder community. It was time for the world to listen to me, and I was going to create awareness about what we go through. I knew this wouldn't be easy, but I was dedicated and full of purpose.

I knew if I wanted to be a leader in my community, then I had to start living my life by example. From that day forward, I dedicated myself to being compliant to my infusion regimen, becoming extremely fit, and volunteering in the community. I started surrounding myself with people who would help me grow, and segregated myself from people who tried to bring me down or didn't believe in me. After dealing for so long with failed relationships, panic attacks, random crying, and even contemplated suicides, it was my opportunity to rewrite my book–and this time, I want the world to read it.

I'm still on my journey to becoming the best me possible, but I'm definitely on the right path. I'm growing every day, and I will never make excuses for why I can't do something. I've accepted my past as a blessing that allows me to reach out and relate to others. To me, hemophilia isn't a handicap, it's my reason why. My purpose.

Luis Andres ("L.A.") Aguayo is 28 and has severe hemophilia B. He lives in St. Louis, Missouri, with his fiancé Amanda and four children. L.A. works full time as a patient service representative in the bleeding disorder community and enjoys volunteering for the Gateway Hemophilia Association. L.A. is currently in a competition to make the cover of Men's Health Magazine and represent the bleeding disorder community as the 2016 Men's Health "Ultimate Guy." His motto is "See you at the top!"

PROJECT SHARE
It's time to give back

Fighting the Insidious Pseudotumor

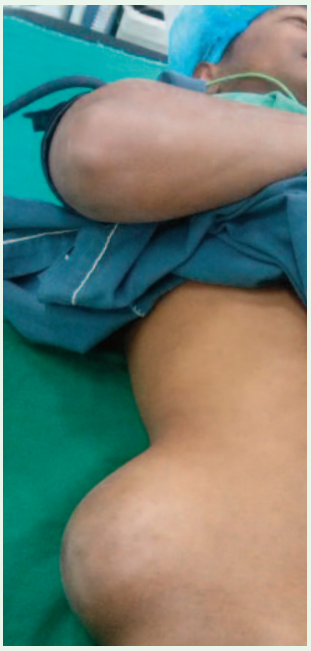
When visiting Nepal in September 2015 to assess the needs of the bleeding disorder community after the April 2015 earthquake, I met Buddhilal Shrestha, or BL, age 24. He has factor IX deficiency and participated in a meeting of the Youth Program. He confided his huge problem: pseudotumors, which are dangerous masses of blood vessels that grow unrestrained when repeated bleeding is not controlled. Though BL had surgery six months earlier to remove them, they grew back.

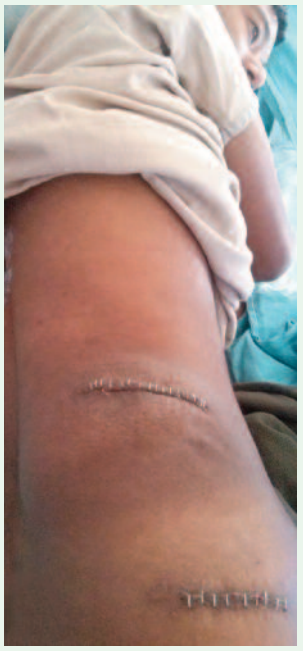
Pseudotumors are rare in developed countries. BL could not work as a teacher because of his pain. He needed $1,000 for another surgery: "I can collect $200 from my friends and from loans, but the remaining amount is difficult to collect. In post-earthquake Nepal, everyone is financially devastated."

Project SHARE offered the money, and with a factor donation from Biogen, BL had his operation in May. Dr. Bhaskar Pant, the surgeon, wrote, "I have removed all three pseudotumors and BL is doing well post-op. He is on continuous factor infusions as required."

BL is deeply grateful to his surgeon, his parents, Biogen, and Project SHARE.

Laurie





US Factor Brands by Company and Type

Manufacturer	Recombinant Product			Plasma-Derived Product		
	FVIII	FIX	Inhibitor	FVIII	FIX	Inhibitor
Baxalta	Advate Recombinate Adynovate	Rixubis		Hemofil M	Proplex T Bebulin VH	FEIBA VH
Bayer HealthCare	Kogenate FS Kovaltry					
Biogen	Eloctate	Alprolix				
CSL Behring	Helixate FS Afstyla	Idelvion		Monoclate-P Humate-P	Mononine	
Emergent Biosolutions		Ixinity				
Grifols				Alphanate	AlphaNine SD Profilnine SD	
Kedrion				Koate-DVI		
Novo Nordisk	Novoeight		NovoSeven RT			
Octapharma	Nuwiq					
Pfizer	Xyntha	BeneFix				

Baxalta is now part of Shire.
Recombinate is a first-generation product.
Kogenate FS and Helixate FS are second-generation products. They are the same product.
Advate, Adynovate, Afstyla, Alprolix, BeneFix, Eloctate, Idelvion, Ixinity, Kovaltry, Novoeight, Nuwiq, Rixubus, and Xyntha are third-generation products.*

*There is no consensus yet on what constitutes a prolonged half-life product. Some standard half-life products have the same half-life as some products marketed as prolonged half-life. The half-life of a product may vary widely from patient to patient. Knowing your individual half-life is important; have a pharmacokinetic (PK) test to determine your individual half-life and discuss with your HTC hematologist which product best meets your treatment needs.

In the May issue, we inadvertently left out Alphanate. This chart corrects that omission and shows all current products licensed for sale in the US.

headlines

industry

Plasma Predictions

With the goal to double Octapharma's production capacity over four years and increase overall operating efficiencies, the company will invest $447 million in 35 projects, including a new pilot plant in Vienna and capacity expansion at each of the company's four European fractionation plants. Meanwhile, Grifols will invest $360 million to expand manufacturing capacity for its plasma-derived products to meet expected growing demand through 2028–2030. **Why this matters:** Despite the influx of recombinant products, there is still significant need for plasma products worldwide.

For info: *IBPN* April 2016

Hemophilia A Innovation

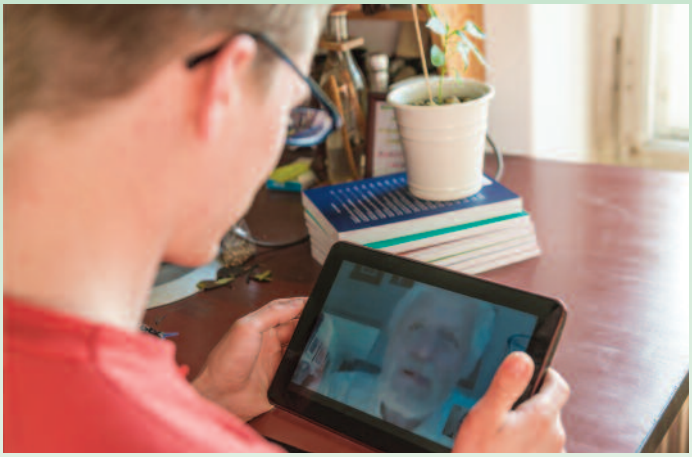
Another new hemophilia A drug–the sixth in the last two years–has been approved by the US FDA. CSL Behring's Afstyla is a recombinant, single-chain product indicated for on-demand treatment and control of bleeding episodes, routine prophylaxis to decrease the frequency of bleeding episodes, and perioperative management of bleeding in children and adults with hemophilia A. Afstyla is intended for intravenous dosing two to three times per week, and has a half-life of 14.2 hours. **Why this matters:** Afstyla is the first single-chain product for hemophilia A.

For info: www.cslbehring.com

Gene Therapy Hope

BioMarin Pharmaceutical Inc. reports that the phase 1/2 clinical trial of its adenovirus-associated virus vector (BMN 270) for a hemophilia A gene therapy treatment produced encouraging data. Initial data released by the California-based biotech company show that two high-dose patients saw levels of factor VIII above 50%, and five out of six high-dose patients show factor VIII levels above 5%. BMN 270 could potentially reduce or eliminate the need for infusions of factor VIII. **Why this matters:** BMN 270 is designed to address the underlying genetic defect that prevents the expression of functional factor VIII.

For info: www.biomarin.com



Job Hunting 101

Novo Nordisk is offering free career counseling to people with hemophilia and other bleeding disorders, aged 18–65, and their caregivers. The program is a two-hour time commitment split up over three phone calls/Skype sessions with a career counselor to help with resumes and interview skills. **Why this matters:** Your chance of securing a job improves with assistance from experts who can help you focus and refine your search and skills.

For info: www.mynovosecure.com

world

The Little Country That Could

Sri Lanka, a country of 21 million, now imports $12.1 million in therapeutic plasma products (as of 2012) including plasma-derived factor VIII and IX. **Why this matters:** Though many developing countries claim to not purchase factor products because of cost, Sri Lanka has shown that it's possible to secure a health budget for these items.

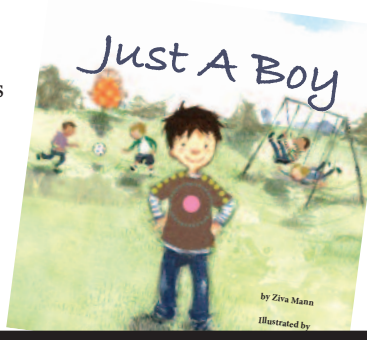
For info: *IBPN* April 2016

New from LA Kelley Communications

Just a Boy is back!

A little boy's fear about needlesticks is soothed by his wise mother, who helps him explore creative, fun ways to manage the initial needlestick pain. By Ziva Mann, parent of a child with hemophilia. Free to families.

For info: www.kelleycom.com



nonprofit

X-Men!

Leading X is a weeklong back-country adventure for young people with hemophilia that takes place in a tandem sea kayak or the hull of a canoe. Learning the fundamentals of navigating and traveling for a week by boat, and camping along the way, will challenge participants physically, emotionally, and mentally. Programs in September and December. **Why this matters:** The program teaches leadership skills and personal responsibility development, and promotes community bonds.

For info: info@gutmonkey.com

Inhibitors Are in Tents

Inhibitor Family Camp

October 7–10, 2016

Victory Junction

Randleman, North Carolina

Inhibitor Family Camp offers a full weekend of education, support, and fun designed for children with hemophilia and active inhibitors. **Why this matters:** This is the only hemophilia camp specifically for children with inhibitors, and is geared toward the entire immediate family. Sponsored by Novo Nordisk.

For info: www.comphealthed.com

Disaster Relief

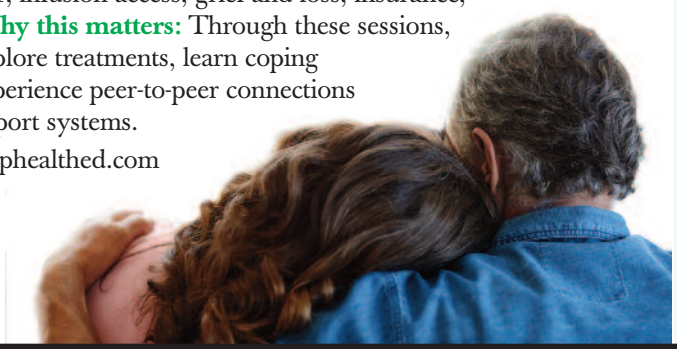
After the Shock

September 9, 2016

Location TBD

An inhibitor diagnosis can be traumatic for parents of a child with hemophilia. After the Shock is a new two-day workshop that will cover inhibitors 101, infusion access, grief and loss, insurance, and stress relief. **Why this matters:** Through these sessions, participants can explore treatments, learn coping techniques, and experience peer-to-peer connections to build strong support systems.

For info: www.comphealthed.com



advocacy

Danny's Dose

Darlene Shelton, grandmother of five-year-old Danny, who has hemophilia, has started an advocacy campaign in Missouri called Danny's Dose. Missourians with rare medical conditions need the right to receive lifesaving medication in an emergency. Currently, patients who are required to keep their lifesaving meds on hand cannot have those meds administered by medical first responders, such as paramedics and emergency room doctors, who are not initially in possession of the meds. **Why this matters:** HB 2665 would change the laws regarding the powers and duties of regional EMS medical directors, to allow these directors to make regulations for special medical needs.

For info: www.dannysdose.com

New Products Keep Coming

The US FDA has approved Kovaltry®, the latest hemophilia product on the market. Bayer's new recombinant factor product is an unmodified, full-length factor VIII compound for treating hemophilia A in children and adults. The approval is based on results from the LEOPOLD (Long-Term Efficacy Open-Label Program in Severe Hemophilia A Disease) clinical trials, which supported Kovaltry's approval for routine prophylaxis. **Why this matters:** NHF has expressed support for new products to create greater choice for US consumers.

For info: www.bayer.com

soundbites

- Kedrion Biopharma received FDA approval to package **Koate®-DVI** with Mix2Vial™ needle-free transfer device.
- Baxalta's **Vonvendi**, the first recombinant factor product for adults with von Willebrand disease, is now available.
- **Biogen** plans to spin off its hemophilia drug business as its own publicly traded company.
- Baxalta has been bought by **Shire**, an Irish pharmaceutical company, making Shire the world's largest pharmaceutical company.

Inbox... from page 2

THERE ARE CHILDREN AND MEN all over the world who go without treatment. Can you imagine not having the means to help your child? That's exactly what these parents must feel. When Gage was diagnosed, I was given the book *Raising a Child with Hemophilia*, written by Laurie Kelley. I don't know that I would've made it through without that book! If you want to be inspired, check out Project SHARE, a program that gives donated factor to people living with bleeding disorders all over the world.

Lyndsay Elam
KENTUCKY

Project Share

HERE IS A PICTURE OF JOSEPH when he is receiving the crutches you provided. The father is so thankful, and Joseph too. He said, "The wood crutch can be disposed of now." His shoulders and neck are now safe with your support. Many blessings!

Agnes Kisakye
UGANDA

inbox

Everything that irritates us about others can lead us to an understanding of ourselves.

– CARL JUNG

When you talk you are only repeating what you know. But if you listen, you might learn something new.

– DALAI LAMA

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