Parent Empowerment Newsletter

LA Kelley Communications, Inc.

PEN

CELEBRATING OUR 25 ANNIVERSARY

inside

Danelle Humphreys and family

When Prophy *Isn't Enough*

Laurie Kelley

It's a story no one wants to hear, and no parent can bear. A young man with hemophilia, on the brink of adulthood, living independently and attending college, runs into a group of troublemaking friends he used to hang with at a local bar. He doesn't want to go back to his friends' way of life. Words are exchanged. He gets into a fight, gets hit in the head. He goes home to bed, and never wakes up. Should he have gone to the emergency room when struck in the head, even while on prophylaxis?

Misunderstandings abound about prophy's power. Major traumas aren't our only worry when it comes to prophy's ability to protect our children. Danelle Humphreys realized that her son Jaxon, age seven, was still getting a lot of bleeds, even while on prophy. Sometimes the bleed resulted from an injury, and sometimes Danelle didn't know how it had happened. Jaxon would have a swollen knee, then a swollen ankle–and he doesn't have an inhibitor. Danelle admits, "Prophy has not been the total security blanket we thought it would be."

Why do hemophilia patients bleed while on prophylaxis? Does prophy lull us into thinking we're safer than we really are? As revolutionary as prophy has been in normalizing life for people with bleeding disorders, it's not fail-safe. We need education, awareness, and vigilance to ensure that our children and young adults do not misunderstand prophy's power.

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welcome

Laurie Kelley

I get a lot of ribbing when I travel because I'm always taking "biobreaks." I prefer to call these "prophylaxis." If you've traveled to the places where I often go–rural villages in Africa, mountain roads, slums–you'll know it's best to grab facilities whenever and wherever you can. You never know when you'll see another!

Prophylaxis means different things to different people. In the vernacular, of course, a prophylactic refers to birth control. When I discuss prophylaxis with those outside the bleeding disorder community, I invariably get smiles or snickers. Merriam-Webster defines prophylaxis as "measures designed to preserve health (as of an individual or of society) and prevent the spread of disease."

In the bleeding disorder community, prophylaxis means regular infusions to help prevent bleeds. But I think we sometimes believe it means prevention of all bleeds. We wish! Our feature article explains why prophylaxis doesn't always live up to our expectations. Just as no prophylactic is 100% effective, so it is with prophylactic infusions.

And when prophy doesn't help, read Paul Clement's article on pain management–it's not just for those with inhibitors.

Prophy has revolutionized life for people with bleeding disorders. Read about Barry Haarde's upcoming fourth ride across America, and also about Chris Bombardier's stunning summit of Carstensz Pyramid in Indonesia, his fifth summit on the way to conquering the Seven Summits.

We hope you enjoy this issue of PEN! Time for a biobreak.

My prophylaxis: outhouse in rural Kenya, on the farm of a family with hemophilia

inbox

Happy 25 Years, LA Kelley!

I JUST READ YOUR "HOW IT ALL BEGAN" STORY. I remember those early PEN days–it was my lifeline. My son was born a few months before yours, in 1987, and we had one year of ignorant bliss before his accurate diagnosis. Talk about life changing! I still have those first few articles I wrote for PEN and your first book, *Raising a Child with Hemophilia*. I can truly say "I remember when." Best regards to someone who will always remain in my heart.

Rita Epstein
NEW YORK

WORDS ARE NOT ENOUGH TO EXPRESS THE GREAT PRIDE I HAVE FOR you and this 25-year journey. I feel that I have been like a little bird looking over your shoulder all this time. A tiny part of me feels a part of your success.

Barbara Chang
CALIFORNIA

I JUST READ PEN'S BIENNIAL BLEEDING DISORDER RESOURCE GUIDE, and I'd like to thank you for the support and recognition of Inhibitor Family Camp and Lifelines for Health. And job well done on an extensive directory of resources!

Eric Lowe, Chief Operating Officer
Comprehensive Health Education Services, LLC
MASSACHUSETTS

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Cross-Country Cycling? It's Haarde!

Laurie Kelley

Texan Barry Haarde, 49, is about to make history again! From May 31 to June 21, he's riding across the US to raise $55,000 and 130 new sponsorships for Save One Life, a nonprofit that provides financial assistance to families with bleeding disorders in developing countries.

America by Bicycle will provide technical support to Barry during his journey. The ride is sponsored by Baxter Healthcare International, Biogen, and Alliance Pharmacy.

I founded Save One Life in 2001, and we now support over 1,200 children and young adults in 12 countries through individual sponsorship, micro enterprise grants, and college scholarships. I spoke with Barry recently about the upcoming ride.

LK: You've done three cross-country trips to raise money for Save One Life. How will the next one be different?

BH: It will be the longest and highest. Wheels for the World IV, dubbed Piles of Miles, will total over 4,000 miles by the time we reach Portsmouth, New Hampshire, on July 21 after leaving San Francisco on May 31. The tour route will reach an elevation exceeding 11,000 feet while crossing the Rocky Mountains in Colorado.

Elite athlete: Barry Haarde rides cross-country for Save One Life

LK: How do you prepare for such a challenging trip?

BH: Cycle! The amount of training varies from year to year, depending on weather. This winter has been rainy, so many of my weekend workouts have been indoors, which is never as effective as getting out on the real bike for 100 miles or more. I also sustained a minor knee injury last year resulting from overuse, so I took a lot of time off at the end of last year to mend

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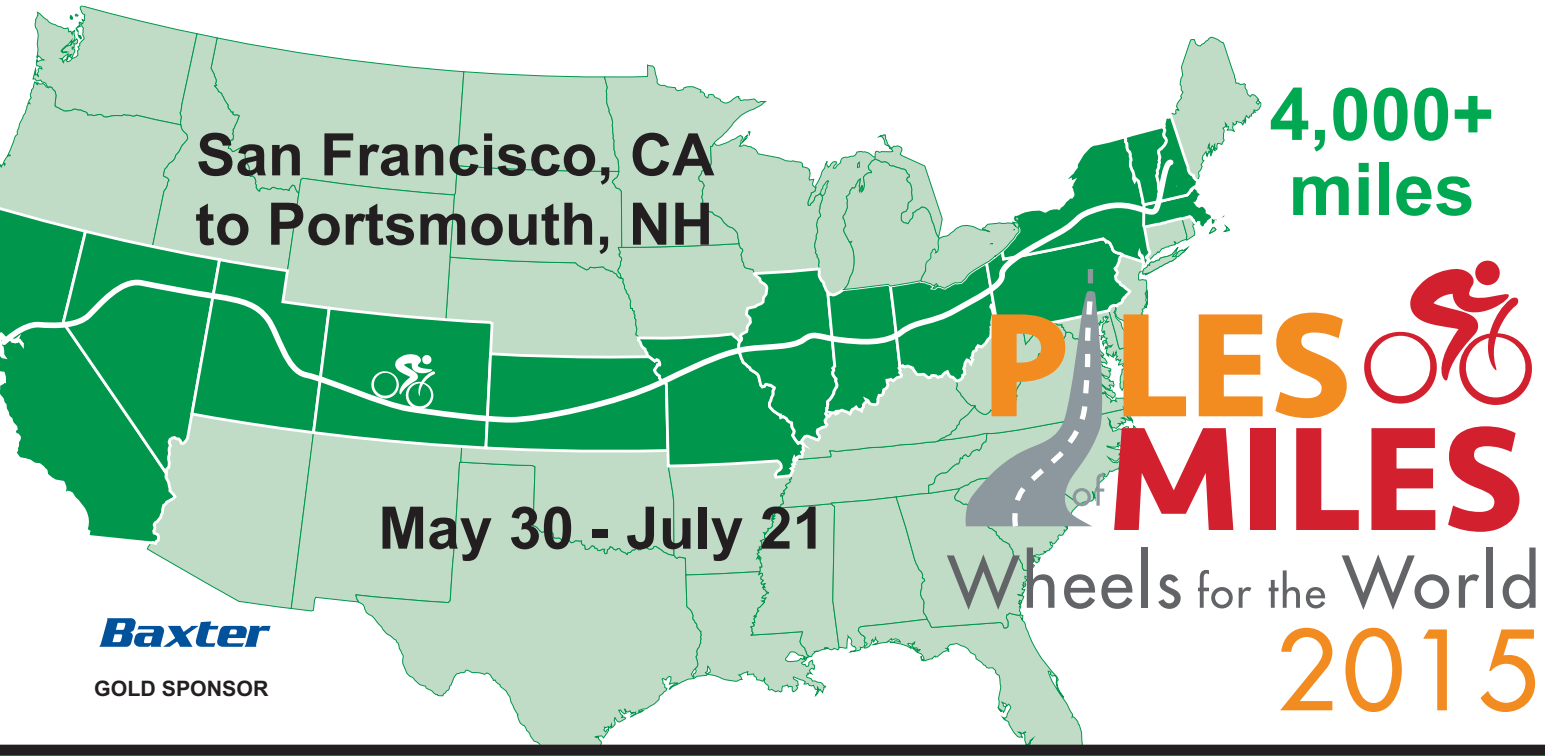
"I suppose what I've done represents what's possible if one really puts one's mind to it."



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How to Use Pain Meds Safely

Part 3

Paul Clement

If you have hemophilia, your *acute* (short-term) pain is usually caused by bleeding that leads to swelling in joints and muscles. By contrast, *chronic* pain (lasting several months or more) is usually caused by arthritis in joints, a result of repeated bleeds that have damaged the joint's cartilage. This is a common problem for many people with inhibitors.

The two types of pain, acute and chronic, require different treatment approaches and different pain meds.

Treating mild to moderate acute pain is usually manageable with over-the-counter (OTC) acetaminophen, or with OTC or prescription-strength NSAIDs. To treat severe acute pain, you may need to use an opiate[1] (morphine, codeine, fentanyl, oxycodone), or an NSAID plus an opiate, for a short time.

Treating chronic pain is different. In this last of our three-part series on the safe use of pain meds, we take a look at opiates.

Opiates for Chronic Pain

Chronic pain is a disease state in itself. It can be destructive and debilitating, harming our general well-being. People with inhibitors frequently suffer from chronic pain due to repeated and prolonged joint bleeds. Unlike acute pain, chronic pain often doesn't respond to OTC drugs. Even high-dose, prescription-only NSAIDs may not reduce the pain; and when used for extended periods, these drugs pose a significant risk of bleeding complications and other serious side effects.

So for moderate to severe chronic pain, opiates are the drugs of choice. Opiates are prescription-only drugs, sometimes called narcotics. They have some advantages: unlike NSAIDs and acetaminophen, opiates have no ceiling dose–the dose beyond which there is no additional analgesic effect. They don't damage the kidneys or liver, don't cause gastrointestinal bleeding, don't increase your risk of heart attack, and don't interfere with blood clotting.

But opiates do have side effects. Opiates depress the central nervous system (CNS) and gastrointestinal (GI) system. Side effects may include nausea, dizziness, drowsiness, twitching, constipation, urinary retention, bladder spasm, itching, and respiratory depression (slowed breathing). Except for constipation, most of these side effects go away after you take the medicine for a few weeks. But if opiates are abused or taken in combination with other CNS depressants such as Xanax or alcohol, the results can be fatal.

Still, in spite of their potential side effects, opiates are effective and safe for people with hemophilia when taken as directed.

You may worry about the long-term effects of opiates on your child with inhibitors. And your physician may also have fears–or even incorrect information–about the risks of addiction. Unfortunately, many physicians are poorly informed about treating chronic pain. As a result, chronic pain is generally undertreated and poorly managed.

Tolerance, Dependency, Addiction: What's the Difference?

Misunderstanding about opiates often centers on confusing the meaning of three terms:

- tolerance
- physical dependence
- addiction

Tolerance occurs when the same dose of a drug becomes less effective over time. Normally, opiates are prescribed at the lowest possible effective dose to start. Over time–weeks to years, depending on the person–opiates may become less effective, as your body gets used to the drug's presence: you have developed tolerance to the drug. To maintain effectiveness, the dose must be increased. With opiates, this can be done several times because

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1. Opiates or opiate drugs originate from naturally occurring alkaloids found in the opium poppy plant. Though similar to opiates, opioids are actually synthetic drugs that produce opiate-like effects.

Linda Weaver's Studio

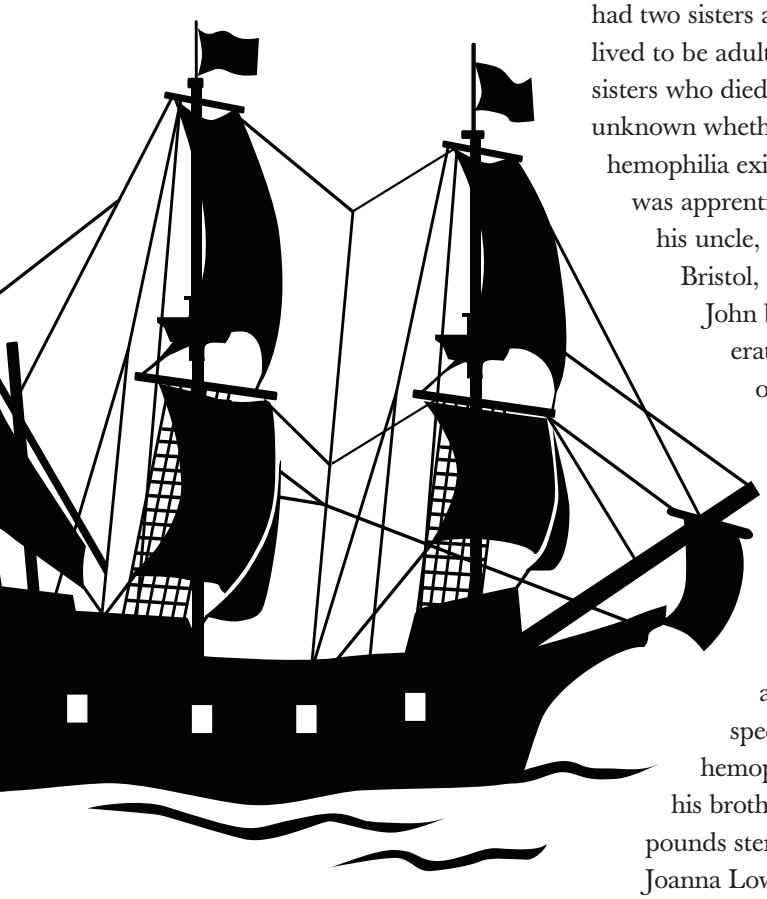
Richard J. Atwood

Traveling with Hemophilia: John Oliver

Have you ever thought of traveling overseas?

A great benefit of current hemophilia treatment is the freedom to safely travel. This was not always possible before the use of factor concentrates. Now, with your passport and credit card, medical ID, letter from your hematologist, factor concentrate and ancillaries, you can travel to most destinations in the world.

Suppose you want to travel across the Atlantic from England to America.



Today, you could take a six-hour direct flight from London to Boston. Now compare that to the voyage of John Oliver (1613–1642?), the first recognized person with hemophilia to travel across the ocean–almost 400 years ago. Newly married in 1639, John left England to settle in the Colonies. An act of bravery without factor!

John Oliver was baptized on May 15, 1613, in the parish church of St. Stephen in Bristol City, England. The eldest child of James Oliver (1586–1629) and Frances Cary (1590–1635), John had two sisters and two brothers who lived to be adults, and possibly three sisters who died as children. It's unknown whether a family history of hemophilia existed. At age 16, John was apprenticed for eight years to his uncle, Walter Stephens of Bristol, a mercer (textile dealer). John belonged to a multigenerational extended family of prosperous merchants.

By 1639, John had finished his apprenticeship and received his inheritance after both parents died. His younger brother James died that year at age 22, fueling current speculation that he had hemophilia. John received his brother's inheritance of 50 pounds sterling. After marrying Joanna Lowle (later spelled Lowell) at age 26, John packed their belongings. Then, accompanied by his in-laws, he and Joanna traveled probably by wagon to London, where they all boarded a ship called the *Jonathan*.

About 100 feet long, with a capacity of 200 to 300 tons, the *Jonathan* had two or three small cabins for important passengers, plus a hold for 100 passengers (and possibly room for cattle on deck). A passenger list has never been published for this voyage, but with a little research, I gathered the names of over 50 people on board. We don't know exactly what John paid for his voyage. From court records for other passengers, we know that a regular adult fare was 5 pounds, and a cabin cost 17 pounds, plus 8 pounds 10 shillings for one group's luggage, and even more for food.

Sailing under Master John Whetstone, the *Jonathan* departed London on April 12, stopped briefly in Southampton, and arrived in Boston Harbor on June 23. A voyage across the ocean at that time was expected to take six weeks. The *Jonathan's* trip lasted over ten weeks, indicating bad weather or other problems. We know that some passengers aboard the *Jonathan* died at sea, from childbirth complications, infant illnesses, and possibly infectious diseases. Sanitary conditions were impossible to maintain, and food supplies were limited.

John traveled in a party of 17 led by his father-in-law Percival Lowle

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Prophy: The CliffsNotes

First, let's review what prophylaxis is–and isn't. Widely used in the US as a treatment regimen for hemophilia,[1] prophy is the scheduled infusion of clotting factor with the goal of keeping factor levels consistently above 1% to prevent spontaneous bleeds, especially joint bleeds, and reduce the risk of long-term joint damage.[2]

Because factor starts breaking down as soon as it's infused, less and less factor is available over time to initiate the clotting process. To keep factor levels high enough to prevent spontaneous joint bleeds, prophy requires regular infusions, up to three times per week with standard factor (not extended half-life). This is in contrast to on-demand therapy, in which factor is infused when a bleed is suspected or already known to be happening. With on-demand therapy, factor levels often drop to zero between infusions, providing no protection against future bleeds.

There are different types of prophylaxis:

Primary prophylaxis: infusions given routinely before any bleeding has happened. Some children start on primary prophylaxis shortly after birth. By keeping factor levels always above 1%, primary prophylaxis essentially converts a person with severe hemophilia into one with moderate hemophilia. For many people, this is usually enough to prevent most joint bleeds not caused by trauma.

Secondary prophylaxis: started after a child has had a few joint bleeds, but before a target joint develops.[3]

Tertiary prophylaxis: started after a child bleeds repeatedly in the same spot and has established a target joint.

Event-related prophylaxis: done before specific or challenging events, such as snowboarding, basketball, daylong or faraway field trips, or extended airplane travel.

A child on prophy typically experiences few bleeds, and some children experience none. That's great news: we're preserving our children's joints. Rania Salem's ten-year-old son has been on prophy since age two days. "He hardly knows what a bleed is," she reports. "I hope he never knows what a life of joint bleeds is. He has no target joint, and no pain."

Rania Salem and son

Despite these upsides to prophy, there are concerns. One is medical: prophy doesn't prevent all bleeds. And one treatment regimen doesn't meet every person's needs.[4] Another concern is psychological: it can be challenging to teach your child why he is given infusions when he doesn't bleed, and in some cases has never had a bleed. How will a child recognize and treat a bleed when he has limited or no experience having a bleed? Will growing up nearly pain free and bleed free compromise his safety when he reaches adolescence? Will he skip a prophy dose, thinking that he'll be fine?

When Pain Is Your Teacher

Basketball great Michael Jordan once said, "Learning's a gift, even when pain is your teacher." Pain was the heartless headmaster for many years before the advent of prophylaxis.

Prophy slowly became the preferred treatment option in the US following the 1992 publication of a 25-year study in Sweden on the effects of prophy on preventing joint damage in hemophilia patients. Before this, prophy wasn't really an option offered in the US. Children who suffered bleeds were treated on demand, as soon as families could diagnose the bleed and infuse the child. Although by the late 1970s, factor concentrate and home care delivery were available, some families were not covered by insurance for home delivery, or could not yet home infuse. These families had to bring their children to the hemophilia treatment center (HTC) for each bleed, wasting precious minutes and even hours getting the treatment they needed. During that time, the child continued to bleed, increasing the pain and severity of the bleed.

Pain taught us many lessons in those days. When parents were infusing their children, they often explained hemophilia at the same time. Children could make an immediate connection between an activity, being injured, and having a bleed. Young people with hemophilia learned to detect their bleeds right away, often describing a tingling feeling–an aura–with increased warmth and swelling in the affected area. They learned to equate certain activities with subsequent bleeds.

1. According to the CDC Universal Data Collection System, in 2011, 55% of people in the US with severe hemophilia were on prophylaxis. 2. MASAC document 179 (2007), www.hemophilia.org. There are several regimens for primary prophylaxis, but most US regimens call for maintaining factor levels always above 1%. If you have severe hemophilia A, this usually means about three factor infusions per week using standard factor (not extended half-life). If you have severe hemophilia B, this means only two infusions per week using standard factor (not extended half-life). 3. A target joint is an area of repeated and regular bleeds, generally with more than 4 bleeds in the same joint within six months, or more than 20 in a lifetime. 4. The dose used for prophy varies widely between facilities and in different protocols—some call for infusing to 30% recovery and others 100%. Coppola, Antonio, and Massimo Franchini, "Target of Prophylaxis in Severe Haemophilia: More than Factor Levels," *Blood Transfusion* 11.3 (2013): 327–29.

"Before prophylaxis," revealed one teen during an interview for the book *Teach Your Child about Hemophilia*,[5] "I was always conscious of getting a bleed. If something hurt at the end of the day, I was always nervous that it might be a bleed. When you are not on prophylaxis, you think everything is a bleed."

With the advent of prophylaxis, we could happily prevent many bleeds and pain. Our children finally could have a more normal lifestyle, participating in many physical activities and traveling. Fantastic. But have we become too comfortable in this new lifestyle?

Victims of Our Own Success?

Overall, prophy is praised by most families. Sarah Mir says, "I love prophylaxis, and it has definitely reduced bleed and bruise incidence in my child." Keeping factor levels above 1% seems to protect most children from spontaneous joint bleeds and maintain healthy joints. But could we as a community become victims of our own success?

Sarah Mir's son


BDAI executive director Bob Robinson

Bob Robinson, executive director of Bleeding Disorders Alliance Illinois, points out that as prophy has become mainstream, visits to HTCs have dropped off. "When you're on prophy, if there are no problems, you may only go once a year to your HTC. That's a lot of responsibility for an HTC in one visit. It may not give enough time to know what's happening with a patient, or to educate patients. What if patients don't tell the truth to the hemophilia team about risky activities? Might we be compromising comprehensive care [by not making use of the HTC on a regular basis]?"

Fewer visits to the HTC mean fewer teaching opportunities. And prophy might provide a normal life for many years–unless bleeding happens unexpectedly. Young people with hemophilia might not turn to their HTCs for advice, simply because they have lost touch with them. Transitioning young adults, who leave their pediatric HTCs for adult HTCs, may disappear from the system altogether. And young adults may not be aware of the benefits of being seen at an HTC.[6]

"The downside of prophy for me," says HL Campbell, an adult female with von Willebrand disease type 3, "is that I see less of my HTC. I tend to diagnose my own bleeds without medical intervention."

And surprisingly, a few HTC staff members may not understand that prophy doesn't cover every bleed. Danelle phoned her HTC to report a bleed in her son Jaxon, "and they told us he was on prophy and he shouldn't have bleeds! Sometimes he'd have an injury, and sometimes we didn't know how he got a bleed. He didn't have an inhibitor. We finally took our logbook to show our HTC that despite prophy, Jaxon was bleeding once or twice a month. You'd think being on prophy, he would have zero bleeds.[7] Every person bleeds differently."

5. Laureen A. Kelley, *Teach Your Child about Hemophilia,* LA Kelley Communications 2007. 6. A study of 3,000 hemophilic males funded by the CDC documented a 40% decrease in mortality and a 40% reduction in bleed-related hospitalizations among men who used an HTC at least once in the three-year study period. Baker, Judith, et al., "A Model for a Regional System of Care to Promote the Health and Well-Being of People with Rare Chronic Genetic Disorders," *American Journal of Public Health* 95.11 (2005): 1910–16. 7. This is a common misunderstanding among parents.

Parents also fall victim to prophy's charm: they may start believing that prophy protects from everything. Sarah Mir notes, "When my son bumped his head, I called our HTC. I told my hematologist, 'But I infused a couple of hours ago,' when he told me to infuse ASAP. Then I realized it's incorrect to assume that prophy makes my child exactly like other kids. Despite prophy, some things are still an emergency for him that are not for other kids."

"Prophy's not perfect, and doesn't protect against all bleeds," reminds Dr. Ellis Neufeld, medical director, Boston Hemophilia Center. "We tell our patients when they are on prophy, they technically have mild hemophilia."

For families, two problems with prophy emerge: (1) bleeding while on prophy, and (2) the mindset of young adults who may believe they are fully covered by prophy and don't need extra doses, who take increased risks, or who don't know how to diagnose bleeds. For young adults, being on prophy much of their lives has reduced their ability to detect bleeds because they lack experience.

Enter Microbleeds

Even while on a prophy regimen established by your HTC, your child can still suffer from bleeding. One source of bleeding is *microbleeds*.

Microbleeds are tiny bleeds into joints from the capillaries, the smallest blood vessels.[8] They don't produce the typical signs and symptoms of a bleed. Microbleeds are usually self-limiting: only a minuscule amount of blood leaks out of the blood vessel before the clotting system kicks in and stops the bleeding. That's why they go unnoticed. Over years, these tiny undetected bleeds may contribute to changes in the joint cartilage, making the joint feel stiff or achy. Microbleeds cause inflammation and, eventually, arthritis.

Why doesn't prophy always work to stop microbleeds?

First, understand that prophylaxis, as used in the US, is not designed to stop all bleeding, just spontaneous joint bleeds. So microbleeds are always a risk. Second, microbleeds are now believed to occur in everyone, hemophilia or not. But in people with hemophilia, a microbleed is likely to bleed just a little longer than it would in someone without a bleeding disorder, especially if that person has a low factor level just before the next scheduled infusion.

There's no way to eliminate microbleeds, but we may be able to decrease their number and duration, and reduce their impact on joint health. How? By increasing factor levels circulating in the blood. This might mean infusing more than your child's usual dose for prophy, which is often set to raise factor levels to 1%.

How did the 1% factor level become our goal for prophy? This is called the *trough level*, which means that at its lowest point between infusions, the level of factor in the blood would be close to, but not fall below, 1%. But studies have shown that in many cases, a 1% trough level is not adequate to completely prevent spontaneous joint bleeds in prophy. Current research shows that in some people, 15% to 20% of factor VIII activity levels are needed to adequately prevent bleeds.[9]

1% versus 15%. That's a huge difference. Research–and some parents' experience–suggests that should we be infusing higher doses in prophy to prevent bleeding. This raises another question: Do you know what your child's actual trough level is?

Why Prophy Falls Short: Half-Life

Prophy's effectiveness depends on following your HTC's prescribed dosing regimen. But effectiveness also depends on how quickly your child uses up infused factor: the *half-life*. Half-life is a measure of how long factor lasts in the bloodstream after being infused: in other words, the time it takes for one-half of the clotting activity to disappear. The half-life of factor VIII is about 12 hours, usually a little shorter in children. This means that although 100% of the factor VIII is available when infused, the amount available steadily decreases to only 50% in about 12 hours. And, as the factor continues to degrade, about 50% of the remaining factor VIII is lost every 12 hours. So after 24 hours, about 25% is available, and so on. Factor IX has a longer half-life, about 24 hours.

What does all this mean? Even when your child is on prophy, his factor level doesn't stay consistently high. It drops steadily after an infusion, and that's why he needs repeated doses. The trick is to find the right dosing regimen for your child, one that provides a sufficiently high trough level for him. Several studies have shown that half-life varies widely among patients and age groups, even with the same severity level. More and more, we're learning that a prescribed prophy regimen is not one-size-fits-all.[10]

To know the specific half-life of factor in your child, he needs to have a *recovery study* (also called a pharmacokinetic study, PK, or half-life study). If your child's recovery study reveals a very short half-life, then he'll need a higher-than-normal factor dosage or more frequent infusions while on prophy. But most people haven't had recovery studies to show how long factor lasts in their system. This study is sometimes not ordered by the HTC when a child is put on a prophy regimen.

Danelle admits, "We've never done a recovery study; our HTC has not suggested it. We should know how long factor lasts for Jaxon. Not everyone is the same."

8. For an in-depth look at microbleeds, read Paul Clement, "Joint Disease, Prophy, and Microbleeds: Are We Getting It Right?" *PEN* 24, issue 2 (May/June 2014). 9. Messier, S. P., D. J. Gutekunst, C. Davis, et al., "Weight Loss Reduces Knee-Joint Loads in Overweight and Obese Older Adults with Knee Osteoarthritis," *Arthritis and Rheumatism* 52 (2005): 2026–32 (doi: 10.1002/art.21139). 10. Valentino, L. A., V. Mamonov, A. Hellmann, et al., "Randomized Comparison of Two Prophylaxis Regimens and a Paired Comparison of On-demand and Prophylaxis Treatments in Hemophilia A Management," *Journal of Thrombosis and Haemostasis* 10 (2012): 359–67.

Ashley Gregory, mother of 17-year-old Nicholas, recalls his 2013 evaluation by a physical therapist at their HTC: "She found a loss of range of motion in his shoulder. He had never complained of a bleed there! He was referred to an orthopedist, who said, 'Well, he has hemophilia! You can expect this!' And they ignored it. We went to NHF's annual meeting that year, and I attended a breakout session about prophy. They discussed microbleeds and shorter half-life. We took Nicholas back to our HTC, and learned his half-life is only 6.5 hours! So all these years, we'd thought everything was fine on prophy and it wasn't."

Ashley Gregory

One prophylaxis clinical study demonstrated that although trough level is important, it isn't the only thing to consider when designing a prophy regimen. The amount of time spent near peak levels (the highest achieved factor level on prophy) between infusions is also critical. For many people with hemophilia, the initial dose of factor needed to maintain a 1% trough level is calculated based on weight and on an average half-life for the factor being used–but, as studies have shown, neither of these calculations may be accurate.

The bottom line? Some clinicians are using seat-of-the-pants estimates for initial dosing of their patients, and then adjusting the dose upward if the patient has multiple "breakthrough" bleeds–bleeds that happen while on prophy. As a result, some patients are dosed inappropriately to begin with, and then have several joint bleeds before their factor dose is adjusted upward; these patients may suffer preventable joint damage.

"At our HTC, we think prophy's all about the half-life," says Dr. Neufeld. "Almost all our severe patients are on prophy. We do PK testing, and pay close attention to half-life. We try to customize prophy for each individual. We got one kid to switch to low dose daily during his sports season. We also make patients get their PK checked before they switch to extended half-life products. The half-life gets better as a child gets older. So as a child matures, your hematologist can change the regimen to fit the child's need."

The Invincible Teen

Prophy may not be enough when your child becomes a teenager. This is when the medical concerns of prophy meet the psychological.

Pete Wells, a man with hemophilia, recalls being a teen not on prophy. He reminds us, "Teens will test the limits whether on prophy or not, and whether they have hemophilia or not. That's what adolescence is all about. Even if they are on prophy, they *will* skip days."

Prophy has given teens and young adults with hemophilia a chance to live more normal lives, and to pursue dreams and activities, some involving higher-than-normal risk. There are champion cyclists, mountain climbers, and karate masters with hemophilia. There are students traveling the world, living in exotic places. But there are also some who take recklessly dangerous risks: drinking and driving, doing sports without proper precautions, traveling without enough factor. Why do they risk their health this way?

The HERO study, funded by Novo Nordisk Inc.,[11] discovered that despite 50% prophylaxis use, and despite high patient-reported perceived control of their disorder, bleeding occurred about one to two times per month for

11. Forsyth, A., M. Gregory, D. Nugent, et al., "Haemophilia Experiences, Results and Opportunities (HERO) Study: Survey Methodology and Population Demographics," *Haemophilia* 20, issue 1 (Jan. 2014): 44–51 (doi: 10.1111/hae.12239).

Prepare, Prevent, Poke

Prophylaxis helps reduce bleeds, but it doesn't prevent all bleeds. Your child may have spontaneous breakthrough bleeds or bleeds from trauma. Unfortunately, it may take only one major bleed into a joint to set the stage for degenerative joint disease, with effects that may not show up for several years. Here's how to minimize the risk of joint damage:

- Stick to the prescribed prophylaxis schedule. Don't skip days.
- Tailor your infusion schedule to meet your needs. If your child participates in a sport, infuse on practice days to have higher factor levels on those days.
- Always infuse in the morning so factor levels will be highest during the day when activity levels are highest.
- Request a recovery study if your child experiences breakthrough bleeds; he may need a higher dose of factor.
- If your child has a bleed, *treat early and aggressively with factor*.

young adults on prophy. Many of the study's young adults reported participating in intermediate- and higher-risk sports and recreational activities. Prophy has become a safety net for young adults who want to be more active and adventurous. Yet these young people are also experiencing more bleeds. Why?

The HERO study notes that more research is needed. One cause of the increased bleeds may be the way young adults perceive themselves and prophylaxis. Some perceptions are based on experience with bleeds: people who have had bleeds think differently than those who never bled while on prophy. Interviews with over 20 adolescents for *Teach Your Child about Hemophilia* uncovered three general patterns in how adolescents understood prophy and bleeds: in the book, we call these invincible thinking, complete thinking, and limited thinking.[12]

> **Invincible thinking** develops in adolescents who rarely experience bleeds but may have had several in the past. These teens believe that being on prophy will prevent all bleeds. "I haven't had a problem with my knee, so I wouldn't expect a bleed to develop in the joint, but if I banged it especially hard, it would probably bruise," reported one teen.

Ashley recalls, "We purchased tickets for a concert one Friday night. Nicholas does prophy every other day, and the entire week was uneventful. On Friday, a prophy day, he said, 'I have a bleed.' So I asked, 'How long has this been going on?' Since Monday! 'Why didn't you tell me?' He's 16! He replied, 'Well, I'm on prophy, and I shouldn't be having a bleed. I felt all these prophy doses should fix it.'

A teen who shows invincible thinking may know what a bleed is, because he's had a few experiences, but when he gets a bleed, he won't have expected it. He believes that factor will completely protect him from bleeds, and he won't expect a bleed to occur even after an injury.

> **Complete thinking** develops in an adolescent who has had more than just a few bleeding experiences. He can identify a bleed and explain what happens inside a bleeding joint. He understands that prophy keeps his factor levels high enough to prevent a bleed from getting worse, or even from starting, but it doesn't protect him from all bleeds. He knows that prophy is a preventive measure. "If I get a major bleed," shared one teen, "I have factor stored in my body from using prophylaxis, which will help to treat the injury faster by having it in my body than the time it takes to mix and then infuse."

> **Limited thinking** is apparent in an adolescent who has never had a bleed. His understanding of hemophilia comes from educational resources alone, and not from direct experience. This teen will have little understanding of bleeds. Prophy is done simply "because I have hemophilia." Routine infusions are accepted as a way of life, with limited thinking about their purpose.

"My biggest fear," worries Vanessa Stowers Flora, parent of a child with hemophilia, "is that boys who have only known prophy don't really know when they bleed. And as teens, they may not be safe, despite everything we teach them. Face it, boys learn through experimentation!"

Vanessa Stowers Flora and family

12. Order *Teach Your Child about Hemophilia* at www.kelleycom.com. Free to families with hemophilia.

Before his adoption at age three, Kelly Cartwright's son with hemophilia had bleeds while not on prophy. "Because he had many painful bleeds prior to starting prophy," Kelly says, "he knows how factor helps him. I think he's more compliant with treatment because he knows what life is like without it. He also knows when a bleed is starting, even when I can't see any signs, and he communicates that pretty well. I suspect that he would not be as compliant or helpful in treatment if he had never experienced the painful effects of untreated bleeds."

Does Ashley's son Nicholas understand bleeds now? "I think he understands, but at the same time, there's a level of denial. I don't know if it's a maturity thing, though he's a junior counselor at camp."

Surprisingly, invincible and limited thinking in a teen can also be learned from parents. One mother writes confidently, "Prophylaxis has been successful–it has allowed him to live without hemophilia. Why does he need to know about it?"

Why do our children need to know? Consider breakthrough bleeds, and the fact that our young men will someday be completely responsible for a disorder that, in some cases, is a mystery to them. This is enough to sound a warning to parents of teens on prophy: Interview your son, or ask your HTC staff to interview him. Find out what he knows and what he doesn't know. Encourage him to learn. Learning about his disorder is a necessity. As a young adult, he must rely on his knowledge of his body to take good care of himself independently.

Dr. Neufeld agrees. "Some kids who've never bled due to prophy may go off to college, and actually need to experience at least one or more bleeds to understand why they should never skip a dose or why they should time their activities to their prophy regimen. They might play Frisbee or touch football late in the afternoon on the second day on prophy with factor VIII. By then, they really have hemophilia again. Prophy doesn't keep levels up all the time. We've heard from our most compliant and educated families that this happens. You can tell teens to be compliant, but they don't hear it like you're saying it!"

"Prophy is not a cure."

Bob Robinson believes that we are victims of our own success. "We have information on bleeds and how to detect them, but we have to read it and teach it. Parents have to be more vigilant about teaching their children about potential bleeds. Prophy is not a cure. I feel like I'm on a soapbox, but our organization will keep teaching about bleeds."

Teaching about bleeds may happen naturally, when a child is experiencing one. But if a child on prophy hasn't had a bleed, does teaching take place? Many parents admit that they don't talk much to their children about bleeds or hemophilia because "they haven't had any." One parent comments, "He doesn't completely understand what hemophilia is all about. He really doesn't experience problems or bleeds." This parent needs to find the right moment to sit down and discuss bleeds and hemophilia.

As parents of children with hemophilia, we are continually challenged with educating our children. If your child is on prophy, that challenge may be greater. Pain was once the teacher, but now parents are.

"We really had to push and stay vigilant," says Danelle, "to tell our HTC we want more done [to prevent bleeds]. I see other kids who are severe and on prophy, and they never have a bleed. Some HTC staff get stuck in cookie-cutter thinking: he's moderate, and this is what it says in the books, so that's what we'll do. We didn't want that to happen to him."

In Ashley's experience, "the upside of prophy is that we are not in hospital; we do our own infusions. Life has settled into

predictable, convenient living with hemophilia. When our HTC upped Nicholas's dose, he had fewer bleeds, but he still gets breakthrough bleeds."

Sarah stresses, "I still wouldn't say there is a downside to prophy. It's just that you need to realize it has limitations, especially as they apply to your own unique case."

Prophy's sometimes subtle limitations aren't as obvious as its immense power to improve our children's quality of life. Don't deny your child prophy if it can help him, but don't go on autopilot either. If your parental radar tells you something isn't right–your child has breakthrough bleeds, a medical professional tells you he shouldn't bleed, or your teen starts taking risks–get a second opinion. Dig for more information, and ask our community for help.

Bob emphasizes the value of education. "I didn't know that young man who died, but I went home that night and cried. We don't want to lose anyone. We will keep educating at our family events in Illinois about breakthrough bleeds, microbleeds, and prophy, and hope that parents teach their children in turn."

As I See It... from page 3

and recharge for this year. My work schedule and travel for various hemophilia events have also taken a toll on my training, but I hope to get enough miles in before heading to San Francisco to get me back in shape.

LK: What do you think about on the road each day?

BH: I focus mostly on road conditions and the scenery, scouting for nice photo opportunities. I spend time thinking about how improbable it is that I can do these transcontinental tours at all, given my initial poor life expectancy. I was born in 1965, when the average lifespan for a person with hemophilia was around 30. Then came an HIV diagnosis in 1985, and a liver cirrhosis diagnosis in 2007. I think a lot about the thousands of people with hemophilia who have died from the same set of medical circumstances that have defined so much of my life. I lost a brother to hepatitis C and a brother-in-law to AIDS, so I think a lot about them and what they would think if they were alive to see me complete three cross-country bike tours. It's something I'll never know and that affects me very deeply.

LK: Did you ever imagine that you'd one day be called an elite athlete?

BH: I'd have to say no. In addition to the three Hs, I also have a 15-year-old total knee replacement and suffer from peripheral neuropathy. It still surprises me that I'm able to pull it off, and of course it has required a lot of adaptation and overcoming to reach this point. But I suppose what I've done represents what's possible if one really puts one's mind to it. Overcoming the stigma and false limitations of chronic illness has proven to be a pretty powerful motivator, so it helps to have a kind of fanatical determination to overcome one's circumstances and make a statement.

LK: What made you get involved with Save One Life?

BH: Before my first ride, I devoted considerable thought to which organization I would try to do the ride for. I knew I wanted a hemophilia organization, but I didn't want to choose one of the three national organizations because I didn't want to be criticized for playing favorites. Save One Life is respected by everyone in the community, and its goals and objectives are universally accepted. I plan to do all future cross-countries for Save One Life as long as the rides continue to raise sufficient funding levels.

LK: How much money have you raised so far for Save One Life?

BH: Over $150,000. Our sponsors have included Baxter Healthcare International, Bayer HealthCare, Biogen, as well as several home care companies including Alliance Pharmacy and Matrix Health Group. We also rely on lots of grassroots donations, primarily from hemophilia community members. I've set a goal of someday raising $500,000 before I wrap it all up. I think that would make a pretty good day's work!

LK: Do you think you'll ever take this amazing fundraiser global by cycling in other countries?

BH: I'd love to do some overseas tours, especially if we could hold one in a country where Save One Life provides programs. Obviously, there are logistical considerations involved with this kind of event, such as support for the ride along the route and availability of medical facilities in the event of an accident. I've set a goal of riding through every state in America (we've already completed 35 of the 50 states), so maybe when we finish that effort, we'll turn our attention to other countries.

To contribute to Barry's ride and support Save One Life, please visit www.SaveOneLife.net

Piles of Miles 13-State Challenge

opiates have no ceiling dose. But if you continue to develop a tolerance to higher and higher levels of a particular opiate, then the physician will need to switch you to another opiate, because the use of high-dose opiates increases the risk of dangerous side effects such as respiratory depression.

Physical dependence will cause withdrawal symptoms such as sweating, rapid heart rate, nausea, diarrhea, and anxiety if the drug is suddenly stopped or the dose is lowered too quickly. Physical dependence is often confused with addiction, but *dependence isn't addiction*: it's a normal reaction to opiates. Anyone on opiates for more than a few weeks is usually considered dependent. To avoid withdrawal symptoms, the dosage must be decreased slowly over time, a process called *tapering*. Suddenly stopping medications that cause dependency (going "cold turkey") can be life-threatening. Always consult your healthcare professional before stopping any opiate you have taken for more than a few weeks.

Addiction is a medical diagnosis, characterized by behaviors that include impaired control over drug use, compulsive use, continued use despite harm, and craving. Addiction usually causes quality of life to deteriorate.

Although just under half of people with hemophilia and chronic pain have taken short-acting opiates, only about a quarter take long-acting opiates to control their pain.[2] Many people refuse opiates, fearing addiction–a fear constantly reinforced by the media. But this concern is mainly unfounded: several large retrospective studies have determined that opiate addiction among chronic pain sufferers is rare, with only 1% to 5% becoming addicted.[3] Even people who are more susceptible to addiction–who suffer from depression, who have abused alcohol, or who suffer from post-traumatic stress–can often take opiates safely under the close supervision of a pain specialist.

Because most people with inhibitors will have chronic pain due to joint damage, it's essential to understand the differences between tolerance, physical dependence, and addiction. Don't let misinformation or fear prevent you from getting adequate pain treatment.

Managing Chronic Pain: The Multimodality Approach

Although opiate painkillers may be highly effective in reducing pain and helping to improve quality of life, they are not a panacea. There's no magic pill to make the pain go away without side effects. Managing chronic pain is an ongoing process: the goal is to take the lowest possible dose of pain medication that will effectively reduce your pain and allow you to function normally. Lower drug doses mean fewer side effects. To accomplish this, you and your pain management team should use the *multimodality* or multidisciplinary approach.

A successful multimodality pain management plan may include medications, plus additional or adjunct therapies. Adjunct therapies are often called CAM, or Complementary and Alternative Medicine. The key word is *complementary*: CAM is used along with conventional medicine. There are many different types of CAM, including biofeedback, relaxation therapy, massage, music therapy, behavior modification, hypnotherapy, and stress management training. Pain specialists are familiar with CAM and can help you design a pain management plan specific to your needs.

Don't try to develop a plan alone. You need the expertise of specialists. If you're lucky, your HTC has a pain clinic with physicians who understand chronic pain and can help you develop a plan. If not, you can request a referral to a pain clinic at a nearby teaching hospital. Surprisingly, fewer than 10% of people with hemophilia seek the guidance of specialists in pain management. Most, almost 60%, receive their pain meds from hematologists.

Using Opiates Safely

When taken as directed, opiates are safe. The main risk of opiates is overdose resulting in respiratory depression. Here are recommendations for using opiates safely.

- Get a prescription for a Naloxone auto-injector (brand name Evzio) if you are taking high-dose opiates.[4] This

2. Witkop, M., A. Lambing, E. Kachalsky, et al., "Assessment of Acute and Persistent Pain Management in Patients with Hemophilia," *Haemophilia* 17:4 (2011), 612–19. 3. Fishbain, David A., Brandly Cole, et al., "What Percentage of Chronic Nonmalignant Pain Patients Exposed to Chronic Opioid Analgesic Therapy Develop Abuse/Addiction and/or Aberrant Drug-Related Behaviors? A Structured Evidence-Based Review," *Pain Medicine* 9:4 (May–June 2008), 444–59. 4. Various opiates have differing effects and differing potencies. In an effort to make comparisons, opiates are often compared to the effects and potency of morphine in a unit called a *morphine equivalent*. High-dose opiates are usually classified as greater than 120 mg of morphine equivalents per day.

autoinjector works like the EpiPen® many people carry for severe allergies, and the drug reverses the effects of opiate overdose almost instantly.

- To prevent accidental overdose, use a weekly pillbox to help you keep track of meds you have taken.
- Never use an old or expired opiate from which you have been tapered. You may have lost some or all of your tolerance to the drug, and taking an old prescription may result in overdose.
- Never take any opiate prescribed for another person. That person may be tolerized to the drug and be taking high doses, which could be fatal to you. Also, various opiates act differently and have different potencies. For example, fentanyl is 80 to 100 times more potent than morphine, and unlike other opiates is measured in millionths of a gram (micrograms or mcg) instead of thousandths of a gram (milligrams or mg). Taking what may seem like a small dose of fentanyl may be fatal.
- Never take an opiate with any other CNS depressants such as alcohol, or with benzodiazepines such as Valium (diazepam), or with barbiturates such as phenobarbital. These combinations can cause respiratory depression and possibly death. Combining CNS depressants with opiates is one of the most common causes of death from prescription opiate overdose.
- Opiates often work for a shorter time in younger patients and for a prolonged time in elderly patients. Elderly patients are also at higher risk of respiratory depression by opiates.
- Talk to your pain management specialist about what to do for breakthrough pain. Never double up a dose of long-acting opiates to control breakthrough pain; this can result in overdose.
- If you have been prescribed a short-acting opiate to take for breakthrough pain in combination with your long-acting opiate, take it exactly as instructed by your doctor to avoid an accidental overdose.
- Most side effects of opiates go away after taking the drug for a few weeks. But the most common side effect, constipation, does not. If you are prescribed an opiate, have a plan in place and a drug prescription to treat constipation before leaving your doctor's office.
- Store your drugs in a safe place, and never share them with anyone.

People with hemophilia and inhibitors are at high risk of developing arthritic joint damage as children, and joint replacement may not be an option until later in life. This doesn't mean you must suffer pain every day. If your pain impacts your quality of life, preventing you from sleeping through the night and participating in daily activities, then consult with a pain specialist to develop a plan to get your pain under control and your life back on track.

Richard's Review... from page 5

(1571–1665), an importer and merchant from Bristol. Lowle was accompanied by his wife, his two married sons and their families, his two married daughters and their families, plus business associates and apprentices. This was the beginning of the prominent Lowell family pedigree in New England. A town in Massachusetts would later be named for them.

Soon after arriving in Massachusetts Bay Colony, John and his wife settled in Newbury, about 35 miles north of Boston. The couple bought house lots including arable lands, meadows, marsh, orchard, and fences from Stephen Bachelor and Christopher Hussey for 120 pounds.

John Oliver became a merchant of imported goods from England, probably working from his home. In 1640, he was admitted as a freeman[1] and his daughter, Mary, was born. The next year John was chosen to serve as an appointed commissioner on the General Court in Newbury.

John died in late 1641 or early 1642, probably from complications of his hemophilia, leaving an estate worth 420 pounds in lands and goods. In 1645, his widow Joanna married Captain William Gerrish, another merchant who had sailed from England in the Lowle party. In 1656, 16-year-old Mary Oliver, a hemophilia carrier, married Major Samuel Appleton Jr., from a prominent New England family in Ipswich, Massachusetts. Their marriage started the extensive Appleton-Swain family tree of hemophilia A in Massachusetts.

Today, we are often critical of air travel. I certainly rant about a long list of complaints at the airport: high cost, poor service, lack of leg and elbow room, inadequate bin size, rude passengers, extra charges, security checks, long delays. Still, we eventually reach our destinations. To appreciate how we travel in this century, consider what John Oliver had to endure during those ten weeks he was aboard a ship–without factor. Today, we can bring factor on board and infuse when needed. Yet some complaints about traveling persist: like John Oliver, we also have to pay extra for luggage and food. But don't let that hinder your travels abroad. Just carry the proper supplies, and enjoy the trip.

1. To qualify as a freeman, a male citizen had to be a respectable member of the Congregational church. After taking an oath as a subject of the Commonwealth government, the freeman then had the right to hold office, vote, and use the title Mister. A freeman was usually someone of sufficient means to be a home and land owner.

headlines

nonprofit

Eradicating ABC's Genetic Flaw

ABC's show *Secrets and Lies* called hemophilia a "nasty byproduct of incest" in the episode "The Sister" airing Sunday, March 15. March is Hemophilia Awareness Month. NHF, HFA, many chapters and independent organizations, and the hemophilia Facebook community immediately fired off responses to ABC, asking for an apology and retraction. **Why this matters:** Through intense advocacy by our community, ABC removed the offensive content and re-aired the show.

For info: www.hemophiliafed.org
www.hemophilia.org

Victory!

Inhibitor Family Camps are designed to provide education along with fun activities in a relaxed atmosphere that helps inhibitor families establish meaningful bonds. **Why this matters:** Until this program was created, inhibitor families often felt unable to participate in regular hemophilia camps due to their unique needs.

Victory Junction
Randleman, NC
October 16–19

For info:
www.comphealthed.com

INALEX COMMUNICATIONS

Come Together, Right Now

Inalex Communications is a national nonprofit dedicated to meeting the emotional and informational needs of people living with bleeding disorders. Inalex develops and distributes educational materials and presents programs in a straightforward, inspiring way. **Why this matters:** Some families benefit from interactive, in-person workshops as well as print material.

2015 Inalex Workshops

Northern Ohio Hemophilia Foundation, Cleveland, OH July 11
Virginia Hemophilia Foundation, Richmond, VA October 3

For info: www.inalex.com

Top This!

Chris Bombardier, a 29-year-old man with hemophilia B, made history again by becoming the first person with hemophilia to summit Carstensz Pyramid, the largest mountain in Oceania. This is the fifth victory on Chris's Seven Summits Quest. The month-long journey took Chris to Indonesia, where the final leg of the adventure consisted of ziplining across a huge chasm, and then slogging though a dense jungle and swamp. **Why this matters:** Chris helped raise awareness of hemophilia during Hemophilia Awareness Month, and also promoted Save One Life, a child sponsorship nonprofit that helps children with hemophilia in developing countries.

For info:
adventuresofahemophiliac.com
www.saveonelife.net

Chris Bombardier summits Carstensz Pyramid

LEOPOLD: Clinical Trial for Royal Disease

The FDA accepted Bayer HealthCare's Biologics License Application (BLA) for BAY 81-8973, a plasma- and protein-free recombinant factor VIII concentrate (proposed name Kovaltry™) for treating hemophilia A in children and adults. Kovaltry will be an upgrade of the currently marketed Kogenate® FS and will be produced with no added components of animal or human origin. A clinical trial called LEOPOLD (Long-Term Efficacy Open-Label Program in Severe Hemophilia A Disease) evaluated BAY 81-8973 in adults and children. **Why this matters:** Prophylaxis with BAY 81-8973 two or three times weekly reduced median annual bleed rate (ABR) by 97% compared with on-demand therapy, confirming the superiority of prophylaxis over on-demand.

For info: www.bayer.com

Jeffrey Leiken, life coach for HEROPath

We Can Be Heroes Just for One Day

Life coach Jeffrey Leiken offers coaching and peer support to teens and young adults with bleeding disorders to help them excel in daily life and chart a path forward. The program was developed in response to findings from the HERO (Hemophilia Experiences, Results, and Opportunities) initiative, the largest international study on the psychosocial impact of hemophilia on patients and loved ones. Funded by Novo Nordisk Inc. Applications due by June 15 for two workshops:

July 31–August 2 (ages 20–25)

Aug 7–9 (ages 16–19)

Why this matters: Leadership training helps teens and young adults manage their lives and also become advocates in the bleeding disorder community.

For info: mynovosecure.com

Be Secure

Novo Nordisk Inc. launched NovoSecure™ on March 26. The program is open to patients with hemophilia A, hemophilia A or B with inhibitors, factor VII deficiency, acquired hemophilia, Glanzmann's thrombasthenia, or factor XIII deficiency. Enrollees can apply for a variety of programs, including a competitive scholarship program, life coaching with HeroPath™, career counseling, and insurance support. **Why this matters:** The program replaces SevenSECURE® and is open to qualified patients regardless of product choice.

For info: 844-NOVOSEC
mynovosecure.com

Financial Support for Wilate Users

Octapharma USA announced Octapharma Co-Pay Assistance Program, a new financial support program for US patients currently receiving or with a prescription to receive Wilate. The program offers eligible patients a maximum of $6,000 annually for copay, coinsurance, and deductible expenses associated with the treatment. Patients must have commercial insurance to participate. **Why this matters:** Patients can apply regardless of financial level and ability to pay.

For info: www.wilateusa.com

Advanced Manufacturing Enhances Safety

Kedrion Biopharma's Koate® DVI, used to treat hemophilia A, is now being manufactured through a process that enhances its safety and purity. The manufacturing process involves applying a polyethylene glycol (PEG) depth filtration step during purification. Studies of the new manufacturing process showed viral reduction levels improved in six of seven viruses tested; reduction levels were unchanged in one of the seven viruses. **Why this matters:** Because all plasma-derived factors are associated with a risk of viral transmission, companies like Kedrion Biopharma routinely improve their processes in all areas, staying alert to new and improved methods to reduce even theoretical risks to patients.

For info: www.kedrion.com

Got Choice? Now there's Novoeight

Novo Nordisk's new recombinant factor VIII product has just been approved for sale in the US. Novoeight® undergoes a five-step purification process. It has the highest storage temperature for the longest period of time compared with other rFVIII products–up to 86°F for 12 months. It can be kept at that temperature for up to four hours after reconstitution, giving it the longest postreconstitution storage time. **Why this matters:** Novoeight was tested in the guardian™ trials, one of the largest and most comprehensive clinical trial programs of a recombinant factor VIII to date, where it was shown to be safe and effective with zero inhibitors confirmed in 213 previously treated patients with hemophilia A.

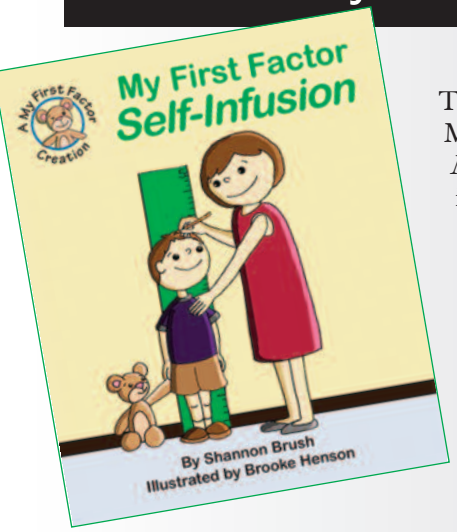
For info: www.novoeight.com

First Recombinant VWD Product Coming

Baxter International has submitted a Biologics License Application to the FDA for the approval of BAX111, the first highly purified recombinant von Willebrand factor (rVWF) in clinical development as a treatment for patients with von Willebrand disease. **Why this matters:** If approved, BAX111 will be the first recombinant replacement treatment for VWD, offering an important new option in treating patients.

For info: www.baxter.com

news from LA Kelley Communications



The tenth book in our My First Factor series is coming! *My First Factor: Self-Infusion* introduces the concept of self-infusion to toddlers by comparing it to some other "big-boy" activities he will do one day.

For info: www.kelleycom.com

soundbites

Nomoreinhibitors.com is a **blog** dedicated to inhibitors by a mother who has struggled with them.

Brazil's Federal Ministry of Health authorized the purchase of 180 million IU of factor VIII. Brazil is the sixth most populous country on earth.

Baxter Healthcare will divide into two companies in mid-2015. The biopharmaceutical division that produces factor will be **Baxalta Incorporated**.

Alprolix®, Biogen's extended half-life recombinant factor IX product, is being used in almost 25% of hemophilia B prophylaxis, according to Marketing Research Bureau.

Diplomat Pharmacy, Inc., the nation's largest independent specialty pharmacy, is acquiring BioRx, LLC, a specialty pharmacy and infusion services company.

Matrix Health Group has purchased Factor Support Network, an independent specialty pharmacy.

Biogen has made an investment deal to develop **gene therapy** for hemophilia A and B.

Obizur® is a new recombinant factor concentrate indicated for treating **acquired hemophilia A**.

NHF's new address: 7 Penn Plaza, Suite 1204, New York, NY 10001

gene therapy

Gene Therapy: To the Nines

Baxter International announced that six adult patients with hemophilia B have been treated in an ongoing phase I/II open-label trial with BAX 335, the company's investigational gene therapy product. In the two highest dose groups, factor IX activity levels of about 10% or higher were seen in two patients, who also experienced no bleeding events after receiving a recombinant adenovirus (rAAV) vector carrying the gene that encodes a special high-activity version of factor IX. One of these patients showed elevated liver enzyme levels, indicating an immune response, which is being treated with oral corticosteroids per the study protocol. No patients have developed factor IX inhibitors to date. **Why this matters:** Promising clinical trials show that gene therapy might make a person with severe hemophilia into one with mild hemophilia.

For info: www.baxter.com/press

Inbox... from p. 2

inbox

Project SHARE

THANK YOU FOR GIVING SO MUCH OF YOURSELF OVER THESE past 25 years! What an amazing impact you have had and continue to have on so many people throughout the world. Thank you for using your inspiration to inspire so many others, including our family. Congratulations!

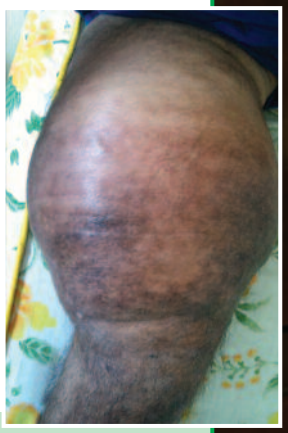
Wendie Chadd
CALIFORNIA

YOUR GIFT OF FACTOR HAS SAVED A YOUNG BOY'S life in China. While I was visiting the hemophilia families, he was brought in with a head bleed. He received the factor needed to stop the bleeding in time. He's 16 years old and doing well. Thank you for this gift. I hope at some point in the future, your factor supplies will increase and the gifts of factor will keep coming.

Steven Riedle
INDIANA

IT IS OVERWHELMING THAT WE HAVE SUCH WONDERFUL, precious friends and supporters of our patients. Project SHARE's help is often lifesaving. You really understand the challenges confronting our people with hemophilia. Your last shipment allowed surgery for a lady with severe type 3 von Willebrand disease. Thank you and God bless you.

Dr. Margit Serban
ROMANIA



I'M WRITING YOU THIS LETTER IN GRATITUDE. I RECEIVED THE FACTOR VIII ON February 25 at HAPLOS Foundation Office in Manila, Philippines. This was an unexpected blessing, because my left knee was swollen, measuring 24 inches in diameter. Project SHARE's support is of great help in relieving the symptoms. I hope that you continue your advocacy in helping patients suffering from hemophilia.

Juan P. Suarez Jr.
THE PHILIPPINES

On behalf of Little Children of the Philippines, headed by our active nurse Peter Janguin and the blood brothers in Dumaguete, we thank Project SHARE for responding to our factor requests. The products were distributed to the recipients, including me. This product adds more minutes and hope to our lives. Thanks to Laurie, Zoraida, and the rest of the Project SHARE staff.

Joseph Robert Maquiling
The Philippines

Thank you so much for funding a new wheelchair. I just went to the store to buy it, and it will be delivered tomorrow. Thank you! I have new legs! So happy.

Chandra Galih Permana
Indonesia

Today is the first day of the Lunar New Year, the year of sheep (or goat) in my country. Happy Lunar New Year to your family, your colleagues, and your organization. I wish you prosperity, health, happiness. Today I was informed by Project SHARE that I am to receive a new factor donation. I'm extremely happy. It's such a great New Year's gift for me.

Le Huu Hung
Vietnam

Parenting Moment

Tell me and I forget. Teach me and I remember. Involve me and I learn.

— *Benjamin Franklin*

It is one thing to show your child the way, and a harder thing to then stand out of it.

— *Robert Brault*

OUR DEEPEST THANKS TO PEN'S CORPORATE SPONSORS

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Pfizer

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www.hemophiliavillage.com

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Visit Your HTC Annually!

Meet NAVA, your new best friend

Like a best friend, Baxter's NAVA program will be your...

Guide who provides personalized service, connecting you with resources when you need them.

Mentor who can share insights, thoughts, and experiences about life with a bleeding condition.

Partner who provides one-on-one coaching to help you plan and achieve your goals.

Baxter's NAVA program is free for anyone whose life has been touched by a bleeding condition, regardless of treatment.

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Which way next?
Navigating life with bleeding conditions

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