Parent Empowerment Newsletter

LA Kelley Communications, Inc.

PEN

30 years anniversary

inside

Meet Your Child's Joints

Paul Clement

Joint disease is still the most common complication of bleeding in severe hemophilia. Repeated bleeding into joints eventually leads to *hemophilic arthropathy*—a degenerative joint disease caused by the slow deterioration of cartilage in the joint, resulting in a painful form of arthritis and eventual destruction of the joint. To try to prevent joint disease, a new treatment protocol for hemophilia—prophylaxis, or "prophy"—was started in the US in the mid-1990s. First pioneered by Sweden decades earlier, the goal of prophylaxis was to prevent spontaneous joint bleeds (bleeds not caused by trauma) by infusing clotting factor one to three times a week, enough to always keep some factor circulating in the bloodstream. It was hoped that prophy would greatly reduce or even prevent joint disease. Prophy promised that children with severe hemophilia could mature into physically active adults, free of the crippling effects of arthritis caused by bleeds.

Yet some young men who have been on prophy all of their lives still have joint bleeds and are showing some signs of degenerative joint disease, sometimes in joints where they haven't reported any major bleeds. But isn't prophy, along with other general healthy habits, supposed to prevent that? Is there something about prophy that we're not getting right?

Anatomy of a Joint Bleed

To understand how joint disease progresses, it helps to review what happens when a joint bleeds. A joint is where two bones meet. There are three main types of joints: some are immovable, for example the fibrous joints in the skull; some are slightly movable, for example the spine; and others are freely movable, for example the knee or hip. In hemophilia, it's the freely movable joints in the body, also called *synovial joints*, that are most likely to bleed.

Synovial joints include the elbow, knee, and ankle. These joints are surrounded by a tough, thick sheath of connective tissue called a *joint capsule*, which helps stabilize the joint and also seals and isolates it from surrounding tissues. Lining the inside of the capsule is a very thin layer called the *synovial membrane*, or *synovium*, which is normally clear and colorless.

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welcome

I had an x-ray once for a chronic back issue that had developed in my 40s, and the doctor asked if I had been in a car accident. Well, yes, decades ago, at age 20. Nothing much had happened: I rammed into a car at an intersection (blinded by the truck next to me) and hit my head on the steering wheel. What did that have to do with anything?

As you'll read in our feature, everything. Some of the injuries we sustained through life come back to haunt us—and hurt us. I enjoyed a childhood and young adulthood free of bone breaks or medical problems. I could swim, run, climb trees, ride motorcycles, and bike without even being aware of the risks. Now that I'm in my 60s, it's a different story. A broken toe, broken thumb, severely sprained ankle… And each morning when I get out of bed, my feet hurt, making it hard to walk at first, and I hobble around until they warm up and work properly. Sounds like someone with a bleeding disorder, except I don't have a bleeding disorder.

In our feature, Paul Clement introduces you to your joints in an in-depth, comprehensive way that you might not have read before. He explains the anatomy of the joint and the many perils faced by joints with hemophilia. You'll learn why even prophylaxis may not be the protection we think it is. And you'll learn about an insidious threat: microbleeds.

Read Cazandra Campos-MacDonald's article on inhibitors and joints. And learn about the joys of joint replacement, from the experiences of a young hemophilia leader in Fiji. Finally, read what Michael Zolotnitsky, a physical therapist with hemophilia, has to say about what you can do to relieve joint pain and prevent damage. This is our joint issue! Read up, and take good care of your joints—at any age!

Laurie Kelley

inbox

It feels so odd reading those first two blog posts (PEN, February 16 and 23, 2019). I could have written the same thing concerning our son's first bleed. Of course, I wasn't reading *Peter the Great* at the time. We didn't find out the diagnosis until last August, right before his third birthday. Your website, books, and newsletter have been so helpful in navigating our new normal. He can now tell us what factor is: "It stops my bleeding." I have no doubt this is because of your resources.

Amee Gould
Arkansas

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In the past, it was incorrectly believed that only men could have hemophilia, and women with the gene were labeled asymptomatic "carriers." It's now recognized that women are not just carriers of hemophilia, but can also have hemophilia and experience symptoms if less than 50% of their factor is active. Most diagnosed patients are male. For editorial simplicity in PEN articles, when we refer to a person with hemophilia, we may alternately use "he," "she," or "they."

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Kunaal Mark Prasad

Man on a Mission:
How Joint Replacement Changed My Life

In 2017, at age 23, I was hospitalized in one of three hospitals that treated hemophilia in Fiji. This was when Fijians with hemophilia only had cryoprecipitate and fresh frozen plasma to treat their bleeds. Factor concentrate was accessible only by the rich and those who had families overseas.

After an x-ray, I was told that I needed a total left hip and total right knee replacement if I wanted to continue walking. The orthopedic surgeon gave me two years tops before I would be confined to a wheelchair permanently. Hearing those words felt like a death sentence, knowing that I'd never be able to get factor, let alone surgery. Commercial factor wasn't possible in Fiji, and our family's financial state wouldn't allow it. I was in desperate need of help, and the desire to change the deplorable situation for my country's hemophilia community ignited me.

Fast-forward to 2018. I got in touch with humanitarians in the US hemophilia community through Facebook, and with their help and mentorship, I managed to start Fiji's first non-profit for people with bleeding disorders. With the excitement and passion I felt to help others in the community and make lasting change, I'd forgotten what the doctor had said about time running out for me.

Of course, I would remember it whenever I suffered knee and hip bleeds—up to four times a week. The bleeds were affecting my studies and work in the new organization. I still hadn't graduated from high school, because I'd missed so much school.

The US humanitarians convinced me I needed surgery before continuing my work and studies. They arranged for me to travel to India, to Vellore Christian Medical College, a renowned hospital for hemophilia surgery. I had never traveled outside of Fiji.

On April 6, 2018, my mother and I flew to India after a month's delay from our initial flight bookings. Even though the US humanitarians had bought us tickets, the airline wouldn't give us clearance at first—because of my hemophilia! We had to advocate for ourselves and get proper medical forms submitted. But we did, and we soon arrived in India.

An MRI and x-ray were done again, and they revealed a lot of damage. My left hip and right knee both needed to be replaced. The simultaneous surgery was scheduled for May 3.

I was now looking forward to the surgery and felt mentally prepared. My friends said it was no big deal, that I'd be

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Cazandra Campos-MacDonald

Joint Damage:
The Aftermath of an Inhibitor

When a bleed occurs in a joint, it is being damaged. I remember a physical therapist saying this many years ago, during a workshop at a local bleeding disorder chapter event. At the time, I didn't give much thought to joint bleeds because my older son, Julian, who has severe hemophilia A with a history of an inhibitor, was very young and hadn't yet experienced this type of bleed. But I kept this comment by the PT tucked away in the back of my mind. When my second son, Caeleb, began having joint bleeds, those words came back to haunt me. Not only did Caeleb have more frequent bleeding episodes, he also had an inhibitor and developed two target joints.

Watching Caeleb endure extreme pain in his right knee and right ankle was very difficult. Because his inhibitor level was extremely high, his hematologist did not recommend immune tolerance therapy (ITT).[1] Treating Caeleb's bleeds with bypassing products and R.I.C.E.[2] therapy was the only option. During those early years of repeated bleeds into his knee and ankle, I knew that Caeleb's joints were being damaged. Still, I hadn't truly considered how the long-lasting effect of these bleeds would impact his life. I was too concerned with doing everything possible to stop his repeated bleeds.

Caeleb's ITT protocol of daily infusions with a plasma-derived factor product kept him bleed-free from 2015 to 2017. A three-year period of not bleeding is amazing when you have severe hemophilia with an active inhibitor. In 2018, Caeleb's hematologist recommended a new subcutaneous treatment that has continued to keep him bleed-free and has improved his quality of life without daily infusions. Despite a five-year streak of not bleeding, the aftermath of the damage to knee and ankle began to surface.

Over the past two years, Caeleb began having significant pain in his knee and ankle. The pain wasn't caused by strenuous activity; it simply began while he was walking. His pain is worse during the winter, but even during the heat of the summer, he often uses a crutch to get around. He hurt so much that our hematologist ordered an MRI to find out how much joint damage had happened from the earlier bleeds. The damage to Caeleb's knee revealed a spot where his bones rub together, causing debilitating pain. His ankle is in worse shape compared to his knee; I found this surprising because the majority of his joint bleeds have been in his knee. What can I do for him so that he won't hurt?

Helping a 14-year-old boy accept and deal with chronic pain isn't easy. While acute pain can be severe, it normally lasts a short time. Chronic pain lasts for several months or longer,

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1. Immune tolerance therapy is the administration of high, frequent doses of factor in an attempt to desensitize the immune system to factor VIII or factor IX infusions. The goal of ITT is that the body will "learn" to recognize factor over time and stop producing inhibitors. 2. R.I.C.E. (Rest, Ice, Compression, Elevation)

richard's review

Linda Weaver's Studio

Richard J. Atwood

Hemophilia and Boxing: Philip Nilon

Let's be clear: Boxing is a dangerous sport for everyone, but especially for someone with a bleeding disorder. Even once! The risk of a head bleed far outweighs any benefit from the exercise.

Ignoring this risk, some people with hemophilia attempt to box. One was Philip James Nilon (1937–1991) from Australia.

Nilon was mentioned several times in books and journals. C. B. Kerr, MB, a hematologist at the University of Sydney, mentioned Philip twice: in *The Management of Haemophilia* (1963), a small medical text that summarized the standard of care at the time; and in a 1964 article in the *Journal of Neurology, Neurosurgery and Psychiatry*. Kerr identified Philip as Case 7 or with his initials P. N. at a time before the privacy of medical information became protected by law. Anne Kearney, Philip's younger sister, wrote *The Billycart, the Boxing Tent, the Battle: Life with Haemophilia* (2013), a memoir of her brother. For his part, Philip used dismissal, denial, and deception while trying to lead a life of adventure.

Philip was born in Ungarie, New South Wales, and grew up in Sydney. He was the sixth of seven children. He had a maternal uncle and a maternal cousin with hemophilia. Philip received the diagnosis of moderate factor VIII hemophilia. As a child, he injured his left leg, causing permanent nerve damage and a lifelong limp. Just like other boys in Sydney, Philip built a "billycart," basically a fruit box on wheels with imprecise steering for rolling down hills as fast as possible. He was knocked unconscious when he tried to scoot his billycart under a moving semi-trailer. This accident, along with others, meant that Philip spent long periods confined to bed. There he developed his natural drawing skills that, as an employed adult, he applied to technical drawings.

Philip's sister described his treatment as receiving "bottles of blood" and occasionally requiring opening a vein for access. His hematologist documented therapy using plasma for factor replacement. Philip suffered countless cerebral hemorrhages, including a notable intracerebral bleed with recovery when only age 9, in 1947. Joint bleeds, especially in ankles and elbows, limited

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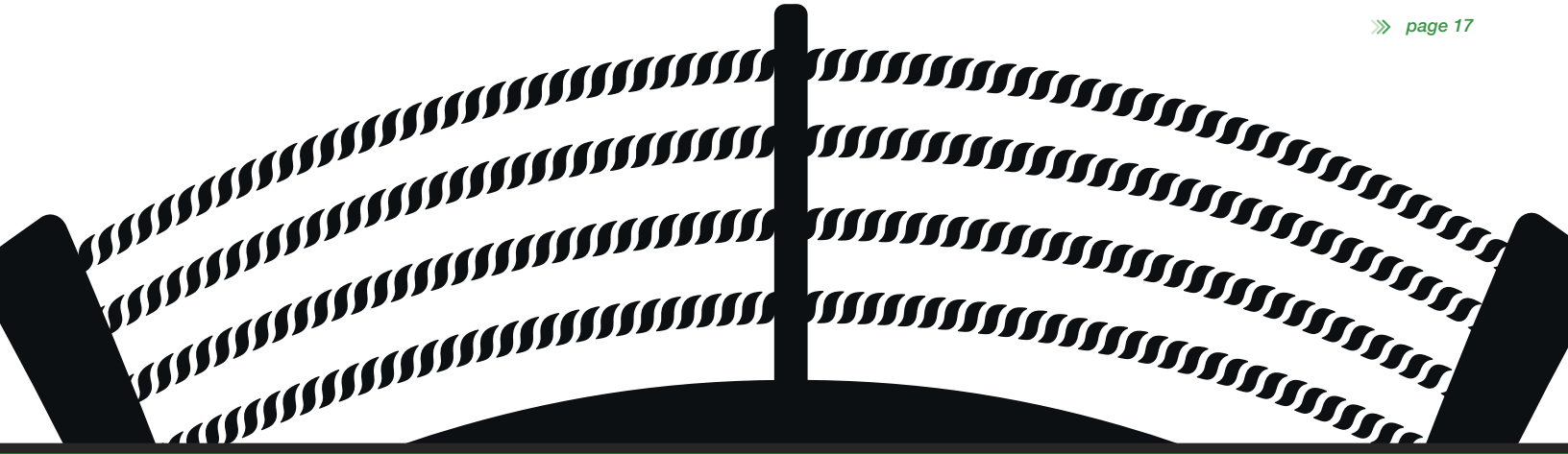
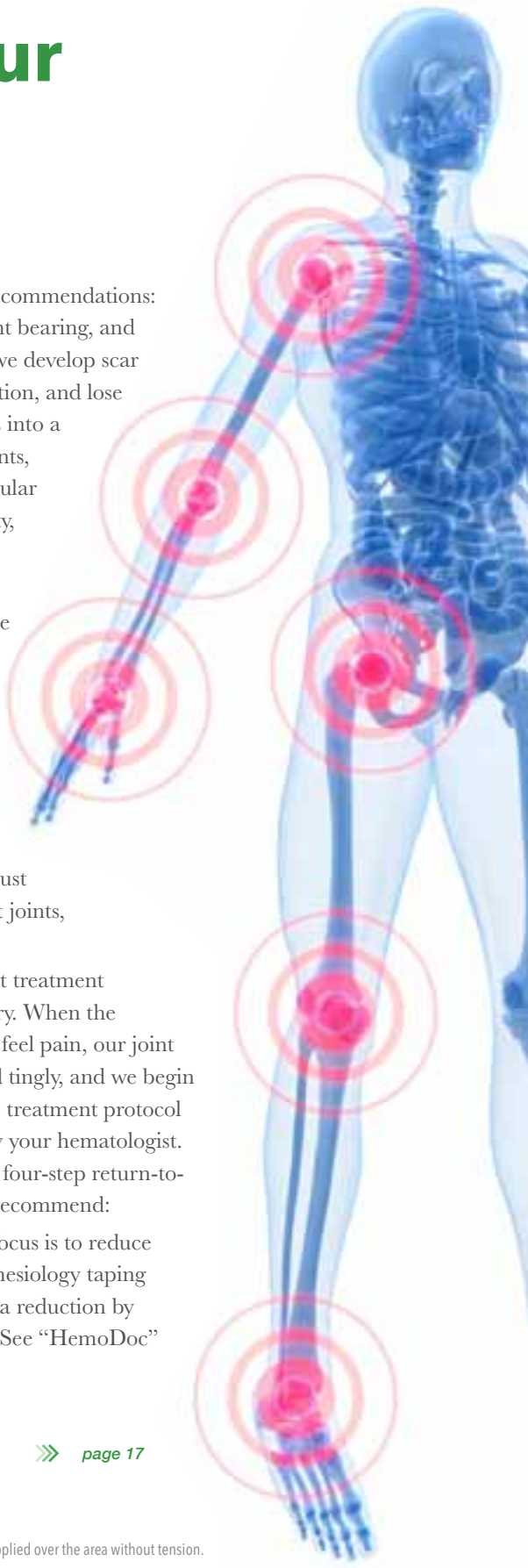


Bulletproof Your Target Joints

Dr. Michael Zolotnitsky, PT, DPT



Growing up with hemophilia, I endured frequent joint bleeds into my ankles and knees while playing basketball. I was told that those were my target joints because I continued to bleed into the same joints, and that ultimately, this would cause hemarthropathy. I was put in braces, and told to use crutches, ice, rest, and elevate. All good things, right?

Well, have you heard of Steph Curry, the all-pro basketball superstar? He continuously experiences ankle sprains that force him to miss games. In our community, we would say that Steph has an ankle target joint; but he doesn't have a bleeding disorder. So why do some people with a bleeding disorder get target joints, and others who experience similar injuries do not?

If an athlete has a low-level ankle or knee sprain, it takes 4–6 weeks for a ligament injury to recover. Recovery includes exercise to strengthen the lengthened ligament and exercises to stabilize the joint. A more intense sprain or strain takes 8–12 weeks to heal, with additional stability training recommended. Someone with a bleeding disorder has different recommendations: usually rest, avoid weight bearing, and ice. If this is all we do, we develop scar tissue, lose range of motion, and lose muscle mass. This turns into a negative cascade of events, because now that particular joint has limited mobility, stability, and flexibility.

When a joint is in a weakened state, it's more likely to be reinjured. After four to six injuries per year, we call this cascade a target joint. This is all preventable with the appropriate post-injury exercise regimen. We must "bulletproof" our target joints, but how?

Let's look at different treatment stages following an injury. When the initial injury occurs, we feel pain, our joint swells, it feels warm and tingly, and we begin to limp. First, follow the treatment protocol that is recommended by your hematologist. After that, consider this four-step return-to-activity protocol that I recommend:

Step 1: The initial focus is to reduce swelling, so apply kinesiology taping specifically for edema reduction by using the fan strip.[1] (See "HemoDoc" videos on YouTube.)

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1. A fan strip is a piece of tape that is cut in the shape of a fan. The head of the fan is placed above the area of the swelling, and four pieces are applied over the area without tension. This will allow a negative pressure gradient to occur to reduce swelling and improve circulation.

The synovium secretes a small amount of *synovial fluid*, a slimy, slippery liquid with the consistency of egg yolk. Synovial fluid coats the cartilage that covers the bone ends within the joint capsule, and serves as a lubricant to reduce friction between the moving bones. The fluid helps absorb shock; it also transports nutrients and oxygen to cartilage cells and the ends of the bones, and removes the cells' waste.

Friction in the joint is also reduced by the *articular cartilage*—the smooth, rubbery layer covering the ends of bones in the joint. Along with reducing friction, cartilage absorbs shock and evenly distributes forces—for example, your weight—onto the underlying bones. Unlike most other tissues, articular cartilage has no blood vessels, lymph tissue, or nerves. Instead of getting nutrition through the blood supply, like other cells do, cartilage cells get their nutrition by diffusion[1] from the synovial fluid. This is why exercise is important: moving your joints not only improves muscle strength that helps protect the joint against bleeds, but it also increases diffusion within the joint and helps your cartilage cells stay healthy.

Unfortunately, articular cartilage cells aren't often replaced when they die. This limits the healing capacity of cartilage in response to an injury. In other words, if you damage cartilage, your injury may not heal, and will probably get worse over time.

Joint bleeds (*acute hemarthrosis*) begin when one of the many tiny blood vessels of the synovium ruptures, spilling blood into the joint capsule. Untreated, the ruptured blood vessel fills the joint cavity with blood. Eventually, the pressure of the blood inside the joint capsule increases until it equals the pressure inside the blood vessel, so that the bleeding stops. In the first stages of a bleed, the joint may feel warm, bubbling, or tingling. Some people report feeling an *aura*, an unusual sensation in the joint when a bleed begins. As the pressure of the blood within the joint increases, the swelling joint becomes increasingly painful. Later symptoms of a joint bleed often include stiffness, warmth to the touch, reduced range of motion, and inability to bear weight.

During a painful joint bleed, a person will often hold the joint in a bent position (*flexion*), which is less painful. But if the limb is flexed for a long time, normal range of motion can be lost, and the joint may stay permanently bent in a *flexion contracture*. Before factor concentrate was readily available in the early 1970s, boys with hemophilia often spent weeks to months in the hospital, wearing casts, splints, or traction devices in an attempt to straighten a limb bent because of flexion contracture. This complication is now rare in countries where factor is easily available.

After a bleed has stopped, the body begins to remove blood from the joint. Cells in the synovium secrete enzymes that break down the blood, so it can be absorbed and removed by white blood cells called *macrophages*. These enzymes also irritate and inflame the synovium as well as the cartilage. It may take four to six weeks after a joint bleed for the blood inside to be completely removed. But some of the breakdown products of blood stay inside the joint, especially *hemosiderin*—iron from broken-down red blood cells—which stains the normally colorless synovium a brown or rust color. Chronic inflammation of the synovium, along with hemosiderin deposits, cause the synovium to proliferate, or overgrow and thicken, and also to grow more blood vessels. This sets the stage for more bleeds.

Bilateral synovitis: extreme swelling in the right knee results from little or no access to factor

An enlarged and chronically inflamed synovial membrane is called *synovitis*. Synovitis causes the joint to remain swollen and "spongy," even after treatment. Chronic synovitis contributes to more frequent bleeding into the joint, and this speeds cartilage damage, eventually causing hemophilic arthropathy, a crippling form of arthritis. Adding to these destructive changes in the joint, the muscles surrounding the joint often atrophy (weaken) because the patient uses them less, as a result of pain. Weak muscles provide less support for the joint, which also leads to more frequent bleeding. And the painful cycle of joint bleeds continues.

1. Diffusion is the random movement of molecules from an area of high concentration to an area of low concentration. For example, if you add sugar to your coffee and let it sit, the sugar, through the process of diffusion, will eventually reach an equal concentration throughout the coffee.

For several weeks after a bleed, a joint is susceptible to re-bleeding. Repeated bleeding into the same joint may produce a *target joint*—a joint that bleeds with increasing frequency and also bleeds spontaneously, with no apparent trauma. Repeated bleeding into a target joint further irritates the synovium, causing it to thicken and grow more blood vessels. It's a vicious cycle: the thickened and inflamed synovium bleeds more easily, causing more irritation and inflammation, resulting in more frequent bleeds.

Treatment for Chronic Synovitis and Joint Disease

Treatment with factor to prevent bleeds is called *primary prophylaxis*—a long-term preventive treatment approach where young patients (usually starting at age one or two) receive regular infusions of factor either before or after their first joint bleed. This regimen is often continued for life. Treatment for early stages of chronic synovitis usually involves *secondary prophylaxis* (often at higher doses than for primary prophy), usually for three to six months, and physical therapy.[2] The goal is to break the cycle of bleeding and allow the synovium to return to normal. If the synovium doesn't return to normal after this first secondary prophy program, the treatment may be repeated for another three to six months.[3]

What then? If you don't respond to secondary prophylaxis, then surgery is usually the next option. A surgical procedure called a *synovectomy* is performed to remove the overgrown synovium. This allows the joint capsule to grow a new, more normal synovium, usually within six months. A synovectomy may be *open* (large incision), *arthroscopic* (specialized pencil-thin instruments are inserted through a few small incisions), or *radionuclide* (a radioactive isotope is injected into the joint to kill the synovium). The goal of a synovectomy is to reduce the frequency of joint bleeds. When performed early, synovectomies often work to break the cycle of bleeds and slow the progression of joint disease. But it's important to remember that although a synovectomy may successfully reduce the frequency of bleeding in a joint, the procedure will not *stop* joint disease from progressing. Joint damage will continue, though more slowly, even without new bleeds.

Surgical intervention can't make your joint like new. It can't reverse joint damage already caused by repeated bleeds into a joint. And it can't restore lost range of motion. The major benefit of surgery is to reduce the number of bleeds, slow the progression of joint disease, reduce pain, and make your joint work better.

A factor infusion, depending on the dose, may raise your factor level to between 60% and 100%. As soon as factor is infused, the body begins removing it from the bloodstream. Within about two days, your level may be near 1%. Time to infuse again. The lowest factor level before the next infusion is called the ***trough***.

Preventing Joint Bleeds through Prophy

The only way you can prevent degenerative joint disease is to prevent joint bleeds.

Until a couple of years ago, preventing joint bleeds meant using primary prophylaxis with clotting factor. There are several protocols for primary prophy, but until recently, most US protocols have called for keeping factor levels always above 1%; in other words, a target trough of 1%. If you have severe hemophilia A and are using a standard half-life factor, keeping the trough above 1% usually means infusing factor about three days per week; if you have severe hemophilia B, two infusions of standard half-life factor per week. By keeping factor levels always above 1%, primary prophy significantly reduces—but does not eliminate—spontaneous joint bleeds in most people. Unfortunately, it may take only one major bleed into a joint to set the stage for slow degenerative joint disease, with effects that may not show up for several years.

Studies show that primary prophy has dramatically decreased joint damage in people with severe hemophilia without inhibitors. The first phase of the Joint Outcome Study (1995–2005), a randomized clinical trial funded by the US Centers for Disease Control and Prevention (CDC), found that primary prophy provided an 84% risk reduction in "structural bone disease"—in other words, a reduction in arthritic changes to the joint. The study also found that by

2. Secondary prophylaxis is a short-term infusion program usually begun after repeated bleeds into a joint. Primary prophylaxis is usually a lifelong infusion regimen begun before age two. 3. Unfortunately, once someone has developed chronic synovitis, secondary prophy often fails to break the cycle of bleeding, with only about 40% of patients showing clear improvement.

age six, 93% of the boys on primary prophy maintained normal joint cartilage with no defects detected by MRI of the elbows, knees, and ankles. This is compared to only 58% of the boys using on-demand therapy. But a later 2016 review, including an additional five years of data (through 2010), found that boys who started prophy after age four had reduced range of motion of their joints—meaning these boys now had the first stages of joint disease.[4,5] What gives?

One of the possible culprits of joint disease, even while on prophy, suggested over a decade ago is *microbleeds*. Microbleeds are tiny bleeds into joints that don't produce the typical signs and symptoms of a bleed. Because they go unnoticed, these are called *subclinical* bleeds. In animal studies, microbleeds did not cause an inflammatory response in the synovium, as do more serious bleeds. But it's believed that, over time, these tiny undetected bleeds may contribute to degenerative changes in the joint cartilage, making the joint feel stiff or achy. Whether microbleeds are responsible for joint damage over the long term is still unproven. Yet we now know that prophylaxis, as practiced in the US in the 1990s and 2000s, does not provide the best protection against spontaneous joint bleeds: many boys still bled while on prophy, resulting in joint damage. Now, this has started to change.

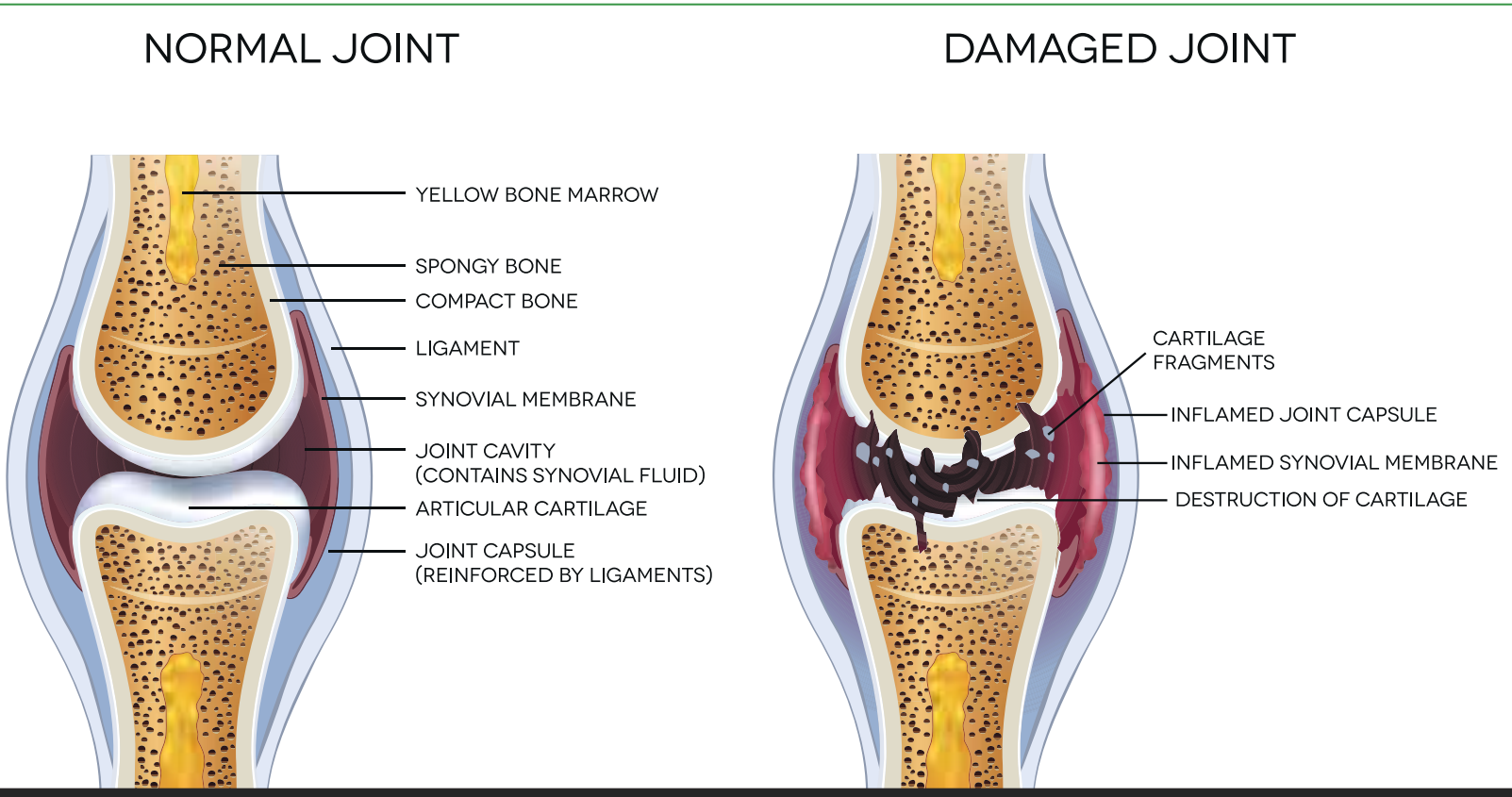
A New Prophylaxis Protocol

In the US, in the first two decades after primary prophylaxis began, the targeted trough level was usually 1%. But almost a decade ago, clinical studies showed that a 1% trough level is not enough to protect against joint bleeds, and that the absence of joint bleeding may be reached only when nearing factor VIII levels of 15%.[6] At the 2012 International Congress of the World Federation of Haemophilia (WFH), Mark Skinner, then WFH president, called on the hemophilia community to aim for a baseline replacement factor activity level of 15%, and the absence of joint bleeds for all.[7] His call for higher trough levels was heard, and levels used in primary prophy have increased over the past decade, but rarely to 15%. The high cost of factor has made increasing trough levels an uphill battle with insurance companies.

Trough levels in prophy using factor can be increased three ways: (1) Infuse more often (which most people don't want to do). (2) Increase your factor dose. (3) Use an extended half-life factor.

Studies have shown that higher trough levels decrease joint bleeds, but also that close monitoring of trough levels and peak factor levels is key when designing a prophy regimen. Why?

4. M. J. Manco-Johnson, J. M. Soucie, J. C. Gill, Joint Outcomes Committee of the Universal Data Collection, US Hemophilia Treatment Center Network, "Prophylaxis Usage, Bleeding Rates, and Joint Outcomes of Hemophilia, 1999 to 2010: A Surveillance Project," *Blood* 129 no. 17 (April 27, 2017): 2368–74. 5. Another study based on data from the CDC's Universal Data Collection (UDC) project found that female carriers with hemophilia often had reduced joint range of motion (indicating bleeding), regardless of age and clinical hemophilia severity: R. F. Sidonio, F. D. Mili, T. Li, et al, and Hemophilia Treatment Centers Network (2014), "Females with FVIII and FIX Deficiency Have Reduced Joint Range of Motion," *American Journal of Hematology* 89 no. 8 (2014): 831–36. 6. I. E. M. Den Uijl, K. Fischer, J. G. Van Der Bom, et al, "Analysis of Low Frequency Bleeding Data: The Association of Joint Bleeds According to Baseline FVIII Activity Levels," *Haemophilia* 17 (2011): 41–44. 7. M. W. Skinner, "WFH: Closing the Global Gap–Achieving Optimal Care," *Haemophilia* 18 (2012): 1–12.



Guidelines for Reducing the Risk of Joint Damage

- Stick to your prophylaxis schedule. Don't skip days! This is a problem with teens and young adults. Many teens don't know that a single major joint bleed can set them on the road to irreversible joint damage. Parents, before handing over to your child the responsibility of doing infusions, be sure to educate about joint disease and the importance of prophy!
- Tailor your infusion schedule to meet your needs. If you participate in a sport, infuse on practice and game days to ensure higher factor levels and more protection on those days.
- Always infuse in the morning so factor levels will be highest during the day when activity levels are highest. Don't infuse prophylactically at night.
- See your hematologist if you experience breakthrough bleeds. You may need a higher dose of factor, or you may have developed an inhibitor. Everyone metabolizes factor differently—a dosage that works for one person may not work for another.
- If you have a bleed, always treat *early and aggressively*. Never "wait and see" or wait until symptoms worsen before infusing. Early treatment reduces the risk of joint damage. Applying ice or compression bandages to a joint bleed may slow the bleed and help relieve pain, *but this does not stop the bleed and does not take the place of factor replacement therapy*.
- If you must visit a local emergency room, go prepared with a treatment letter from your hematologist stressing the need to infuse without delay and before any diagnostic tests are done.
- Stay physically fit. There is overwhelming evidence that strong, flexible muscles help stabilize joints and decrease the incidence of joint and muscle bleeds. (Check with your hemophilia treatment center [HTC] team before starting any physical fitness routine or resuming exercise after a joint bleed.)
- Watch your weight. Statistics from the CDC show obesity now affects about 20% of all US children and adolescents—triple the rate of just one generation ago. More than 70% of American adults are overweight, with 40% classified as obese. Obesity increases your risk of heart disease, high blood pressure, stroke, diabetes, cancer, and many other disorders. And it also affects your joints. If you're overweight, then your hip, knee, and ankle joints bear a heavier load, increasing your risk of joint bleeds—especially ankle and knee bleeds.
- Wear protective gear. When a toddler is first getting his "land legs," knee and elbow pads can help prevent joint bleeds caused by falling. As he grows and begins to participate in sports, he needs to wear appropriate protective athletic gear.

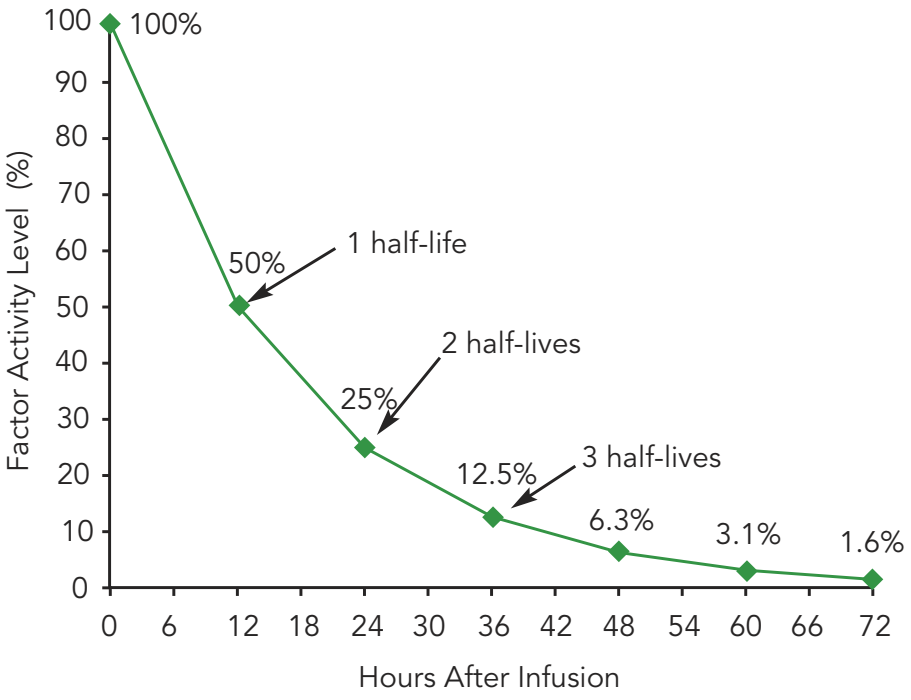
Because more time spent near peak factor levels gives more protection against bleeds.

This raises another question: Do you even know what your trough level is?

Most people might say, "Yes, my factor trough level is about 1% or more." But do you *really* know? The average half-life of a factor product listed in the package insert is not a good indicator, because the half-life often varies widely between individuals. In general, factor in children has a significantly shorter half-life than factor in older adults. For example, a factor VIII product with a 12-hour half-life may have a half-life of only 4 hours in a young child; in an older adult, it may have a half-life of more than 20 hours. And most people haven't had half-life studies (pharmacokinetic or PK studies) of how long factor lasts in their system because, in the past, PK studies were inconvenient for both patient and clinician: they required 9 to 11 blood draws over a period of three days. Newer "population" PK studies can mathematically estimate factor half-life with good accuracy based on only two or three blood draws (for factor VIII) taken in a single day, making the process of a PK study much more convenient.

For most of the past 25 years, initial dosing of factor was based on the patient's weight, the average half-life of the factor being used, and the target trough level—without knowing the patient's actual factor half-life. And then the dose was adjusted upward if the patient had multiple breakthrough bleeds. So some patients—those with a short half-life—started off being dosed inappropriately, and had several joint bleeds before their factor dose was adjusted correctly. They probably suffered joint damage as a result. PK studies were often ordered for patients having breakthrough bleeds,

Factor VIII Activity Levels Over Time After Infusion of Product with a 12-Hour Half-Life



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

but by the time a problem appeared, damage had already been done.

Factor dosing based on weight and on an average half-life for the product may not be accurate, especially for children or older adults. People with a short factor half-life will need a higher dose of factor, or more frequent dosing, to maintain the same trough level as someone with a longer half-life. With convenient population PK models now available for most factor products, it's recommended that everyone have a PK study done to determine their individual factor half-life.[8,9] Once your half-life is known, your clinician can more accurately dose your factor. Dosing factor based on PK results goes by various names: *PK dosing, personalized prophylaxis, individualized prophylaxis,* or *tailored dosing*. Whatever you call it, using PK results to personalize your prophy schedule can help reduce bleeds and use factor more efficiently, but the idea hasn't caught on yet in many healthcare systems outside the HTC network.

So you know your PK, and you're being appropriately dosed. But how do you and your physician increase your trough level, when insurance companies don't want to pay for additional factor? One way is through switching to an extended half-life factor product. The half-life extension for factor VIII products is modest when compared to the half-life extension for factor IX products, and ranges from 1.1 to 1.8 times that of standard factor VIII. For factor IX, the half-life extension is higher: from three to five times that of standard factor IX. This means that if you have hemophilia B, you can get a major benefit by switching to an extended half-life product, and you can extend infusion times as well as increase your trough level. A study of factor IX patients who switched to an extended half-life product indicated that they used one-third to one-half the factor they had used previously, but not three to five times less, as might be expected if they had only

8. Two PK software programs are widely available: *Web-Accessible Population Pharmacokinetic Service–Hemophilia* (WAPPS-Hemo), www.wapps-hemo.org; and *MyPKFiT for Advate* for patients age 16 and older who weigh more than 100 lb (45 kg), www.advatepro.com/us/mypkfit. 9. PK studies should be done several times during a person's life, because half-life usually increases as the patient ages. By the time the person is 18, the half-life should be close to the average half-life of the product being used.

Studies show that primary prophy has dramatically decreased joint damage in people with severe hemophilia without inhibitors. The first phase of the Joint Outcome Study (1995–2005), a randomized clinical trial funded by the CDC, found that primary prophy provided an 84% risk reduction in "structural bone disease"—in other words, a reduction in arthritic changes to the joint. The study also found that by age six, 93% of the boys on prophy maintained normal joint cartilage with no defects detected by MRI of the elbows, knees, and ankles. This is compared to only 58% of the boys using on-demand therapy. But a later 2016 review, including an additional five years of data (through 2010), found that boys who started prophy after age four had reduced range of motion of their joints—meaning these boys now had the first stages of joint disease. What gives?

used the extended half-life factor to extend the interval between infusions.[10] This suggests that the patients not only increased the interval between prophylactic infusions, but also increased their trough level. Note: Insurers are watching all this carefully, and are concerned about another finding of the study: even though consumers used fewer units of factor on extended half-life products, the yearly cost of the factor almost doubled.

Because of the modest increase in half-life of factor VIII extended half-life products, when compared to factor IX products, it's harder to increase the interval between infusions *and* increase your trough level. If you have hemophilia A and want to increase your trough level using an extended half-life product, you'll probably need to keep your same infusion schedule (as with standard half-life factor) or only slightly increase the interval between infusions, to get the benefit of extended half-life toward increasing your trough level.

10. J. Tortella Bartholomew, José Alvir, Margaret McDonald, et. al., "Real-World Analysis of Dispensed IUs of Coagulation Factor IX and Resultant Expenditures in Hemophilia B Patients Receiving Standard Half-Life Versus Extended Half-Life Products and Those Switching from Standard Half-Life to Extended Half-Life Products," *Journal of Managed Care & Specialty Pharmacy* 24 no. 7 (2018): 643–53.

Alternative to Standard Prophy Regimens?

Now we have a new option for prophylaxis without factor: Hemlibra®, a non-factor therapy.[11] Hemlibra is the first of the novel hemophilia therapies on the market, with others in the pipeline. Hemlibra is not a factor product, but a genetically engineered antibody that mimics the function of factor VIII. For many people with high-titer inhibitors, this therapy has been nothing short of a miracle. Inhibitor patients are at great risk of joint damage due to their inability to use standard factor concentrates. To treat bleeds, they must use bypassing agents such as factor VIIa or an activated prothrombin complex concentrate, both of which are less effective at stopping bleeds than standard factor concentrate. As a result, these patients often bleed longer and suffer more severe bleeds, causing the development of target joints and frequent joint bleeds.

Hemlibra essentially converts severe hemophilia A into mild hemophilia, dramatically reducing bleeds. And in people with hemophilia A without inhibitors, it has also been more effective in preventing bleeds than prophy with factor. Also, it provides a steady level of protection: there are no peaks and troughs, as with factor therapy. Other novel non-factor therapies in the pipeline, including concizumab (anti-tissue factor pathway inhibitor, or TFPI) and fitusiran (RNA interference agent that targets antithrombin), are also subcutaneous therapies that would be used prophylactically and could be used not only for hemophilia A but also for hemophilia B, with and without inhibitors. And it looks like some people might be able to do away with prophylaxis entirely: a gene therapy for hemophilia A awaiting approval by the Food and Drug Administration (FDA) is expected to be available later this year.

The bottom line?

Personalized prophylaxis with higher trough levels, extended half-life factor, novel therapies, and gene therapy may all prevent spontaneous bleeds—and microbleeds! This would finally deliver on the original promise of prophy: that children with severe hemophilia can look forward to maturing into physically active adults, free of the crippling effects of arthritis. And that's when we get it right.

11. Hemlibra was approved for prophylactic use in people with hemophilia A and inhibitors in October 2017, and for use in people with hemophilia A without inhibitors in November 2018.

As I See It... from page 3

running around within a week. The doctor told me what to expect and explained all the risks. But the day before the operation, I had a massive panic attack.

I asked my orthopedist lots of questions about the surgery: How would my life be after the surgery? Could I look at my original joints after the operation? After all, they were my joints being replaced by foreign bodies!

The doctor said he would take photographs during the surgery. I had negative thoughts about prosthetic joints. In fact, I was scared of them. I had a mental battle with myself about whether to go through with the surgery. Half an hour before the actual operation, I calmed down and went for it.

The hardest part for me was after surgery. This was my first operation, and in truth, I had no idea what to expect. I wasn't prepared for post-surgery. No one had warned about the amount of pain I'd feel. My rehabilitation was extremely painful, and I was in hospital for about four weeks. I was scared to put my foot down. I'm not sure if the pain was real, or in my mind. I had regular prophylaxis for two weeks followed by an on-demand schedule.

I remained in hospital care for another three weeks, but as an outpatient. And we were in a country where we did not speak the language. Thank goodness the nurses, doctors, and staff spoke English, but getting around Vellore was a challenge!

Going back home, I had a lot of struggles. My house was not equipped for me on my crutches. I began to think it had been a bad idea to have the surgery. It took a lot of motivation from others to convince me that surgery had been the right decision.

On a positive note, after four months, for the first time I could walk around my house, town, and school without having a bleed, let alone crutches! Not only could I walk, I could run! All this without pain or discomfort. It was such an achievement. And all this happened because of the generous hearts in our community, the specialists in India, Hemophilia Federation (India), and the supporting friends, mentors, families, and loved ones.

I still have a problem with stairs, but currently, my main challenge is physical therapy. When I went for my first PT at the local hospital close to home, I was their first hemophilic patient, and they didn't know what to do. So I started learning and doing my own rehabilitation through the exercise guides that I received in India.

Before surgery, life was depressing and surrounded by lots of obstacles. Now I look forward to life. I have school to complete, and an organization to run, to help folks just like me in the community and the world.

The world is my oyster! I am now on a mission!

Kunaal Mark Prasad is president and founder of the Fiji Hemophilia Foundation, which is being considered for accreditation by the World Federation of Hemophilia. The foundation has received assistance from Save One Life, including mentoring, funding, and factor.

Headliners

NONPROFIT

Safety Summit

Hemophilia Federation of America (HFA) and National Hemophilia Foundation (NHF) co-hosted a Safety Summit in Washington, DC, January 29–February 1. The summit responded to community concerns about a series of drug safety reports in 2019. Attendees included 85 patients, and representatives of HTCs, manufacturers, specialty pharmacies, and federal health agencies. **Why this matters:** In the 1980s and '90s, many people in the bleeding disorder community died from contaminated plasma-derived products; the community continues its role as safety watchdog.

For info: hemophiliafed.org

Talking 'Bout MyBDC

My Bleeding Disorder Community is a registry of de-identified aggregate data on patients with bleeding disorders. "De-identified" means that personal identifying information has been removed. MyBDC is managed by NHF. About 350 people are enrolled, including 165 patients. To enroll, patients take a baseline survey, then update surveys yearly, helping researchers look for bleeding patterns. MyBDC will help identify the community's research priorities and encourage participants to be active partners in healthcare. **Why this matters:** This community-powered registry will help researchers understand what it means to live with a bleeding disorder and how current treatments, therapies, and policies affect us.

For info: hemophilia.org

Hot Fun in the Summertime

NHF's Bleeding Disorder Conference
August 6–8, 2020
Atlanta, Georgia

Three days of educational sessions, networking opportunities and access to the Exhibit Hall. Registration includes entrance to Opening Session, Awards Luncheon, and exciting Final Night. Kids' Program for children under age 12. **Why this matters:** This is one of the best venues to learn about hemophilia, von Willebrand disease, and other bleeding disorders.

For info: hemophilia.org

Defending the ACA

HFA joined with 19 other patient and health advocacy groups to file an *amicus curiae* brief with the US Supreme Court, urging the Court to expedite review in the case of *Texas v. United States*. This case is the latest court challenge to the Affordable Care Act. The Court turned down the ACA defenders' request for expedited review on January 21. But three days later, the Court also turned down the opposing parties' request to delay submitting their briefs in the case. So it's still possible that the Court will consider hearing the case during this session, ending in June. **Why this matters:** An *amicus curiae* brief is filed by a person or organization to present arguments in addition to those presented by the immediate parties. The ACA continues in effect while the case is pending; patient advocates are committed to protecting Americans' access to affordable, quality healthcare.

For info: hemophiliafed.org

MANUFACTURER

New Extended Half-Life Therapy

Novo Nordisk's Esperoct®, a glyco-PEGylated B-domain deleted factor VIII protein, is now available in the US to treat adults and children with hemophilia A. Esperoct is a recombinant extended half-life factor VIII replacement therapy. Phase III clinical trials showed a 1.6-times better half-life in adults and adolescents, and a 1.9-times longer half-life in children, compared to standard factor VIII products. **Why this matters:** Standard half-life treatments require multiple intravenous injections, but Esperoct helps people with hemophilia A maintain high factor VIII levels longer, reduce frequency of bleeding, and dose less often.

For info: novonordisk-us.com

SCIENCE

Gene Therapy: Cha-Ching

BioMarin Pharmaceutical estimates a $2–3 million price tag for valoctocogene roxaparvovec (Valrox), a hemophilia A gene therapy in phase III clinical trials. Results show significant improvements: the number of patients' bleeding incidents dropped to zero for several years after an injection. Chief Executive Jean-Jacques Bienaime said the eventual list price should be compared with annual costs of existing therapies and the lifetime cost of treatment, which BioMarin estimated at $25 million. **Why this matters:** If approved, Valrox would be the first gene therapy for hemophilia and also the most expensive drug in the world.

For info: biomarin.com

First to File

BioMarin has submitted the first biologics license application (BLA) for gene therapy for hemophilia. Valrox is a single-dose, adeno-associated virus (AAV) mediated gene therapy, for the production of factor VIII. The license application included an interim analysis of a phase III study and the three-year phase I/II data. The phase I/II study showed that two people did not experience improved levels of factor, as their factor VIII was less than 1 IU/dL. But the median factor VIII of seven patients was 20 IU/dL, and the median number of treatments due to bleeding was zero. **Why this matters:** BioMarin has officially ushered in the era of commercial gene therapy for hemophilia.

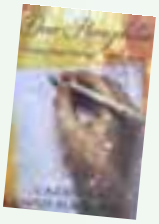
For info: biomarin.com

COMMUNITY

Hello Talk!

Hello Talk is a patient-focused program offered around the US to educate patients about their bleeding disorders. Topics like "Stepping Up—Individualizing Your Prophy Plan" will help patients learn what an individualized prophylaxis plan is and how to get started. **Why this matters:** Only part of the bleeding disorder community attends national conferences; these regional programs allow local families to participate, socialize, and be educated. Presented by Takeda.

For info: bleedingdisorders.com



Dear Hemophilia

Dear Hemophilia: Finding Hope Through Chronic Illness is a new book by PEN contributing writer Cazandra Campos-MacDonald. In the style of letters written to the disorder, Caz shares her experiences and emotions as a mother of two sons with hemophilia, one with severe inhibitors. Topics include pain management, surgery, depression, addiction, therapies, and Caz's Christian faith. **Why this matters:** Few if any books exist on inhibitors from a parent's experience.

For info: amazon.com

SOUNDBITES

- Medexus has acquired worldwide commercial rights to **Ixinity®**, previously marketed by Aptevo in the US for use in people age 12 or older with hemophilia B.
- At 52 weeks after one-time administration of etranacogene dezaparovec, **uniQure**'s investigational hemophilia B gene therapy, mean factor IX activity has been sustained at therapeutic levels in all three enrolled treated phase IIb study patients with severe hemophilia B.
- Sangamo Therapeutics has completed the transfer to **Pfizer** of its SB-525 gene therapy Investigational New Drug application.
- Roche subsidiary **Spark Therapeutics** presented clinical data on 15 adult hemophilia B patients using fidanacogene elaparvovec (previously SPK-9001), an investigational gene therapy; all patients demonstrated a marked reduction in bleeding frequency and factor IX concentrate.
- The US FDA published "Guidance for Industry on Human Gene Therapy for Hemophilia," defining **FDA recommendations** for manufacturers developing human gene therapy products for hemophilia treatment.

Sharon Meyers, EdD

- **Sharon Meyers**, EdD, is the new president and CEO of HFA.
- **Dr. Leonard A. Valentino** is now NHF's president and CEO; formerly, he was vice president of medical affairs at Spark, and senior medical director at Shire.
- The global hemophilia market is estimated to grow about 5.3% and projected to reach a market value of over **$17 billion** in 2026, according to Acumen Research and Consulting.
- By 2025, the **FDA** expects to be reviewing and approving 10–20 cell and gene therapies every year.
- **Aptevo Therapeutics** announced the first dosing of a patient in a phase IV study aiming to extend use of its prophylactic treatment Ixinity to children younger than 12 with hemophilia B.

Inhibitor Insights... from page 4

and is usually associated with a long-lasting condition—like degenerative joint disease. Sometimes Caeleb's pain isn't at the forefront of his daily life, but he now experiences days when his pain is constant. Most people don't live with pain as he does, and he accepts this while realizing that his "normal" is very different than most people's. It's when his pain gets to the point of affecting his daily life that the damage sustained as a result of his inhibitor takes center stage, even though he is not bleeding.

Caeleb's hematologist and orthopedist have both told him that he is many years away from even considering any type of surgical intervention. Because of his youth, surgery isn't in his best interest. The implants used in joint replacements have a limited lifespan, and younger patients end up needing multiple revisions as they grow—with each revision becoming increasingly riskier. Younger patients are more active and wear out the implants faster than an older adult would. The good thing is that Caeleb can still walk. He is no longer wheelchair-bound, as he was when bleeding regularly, and his daily activities keep him busy.

My goal is to keep Caeleb active and attending school despite any flare-ups. For Caeleb, these flare-ups come without warning. As he is walking, pain shoots through his knee and/or ankle, and he stops in his tracks, bending down to catch his breath. Sometimes it takes him a few minutes to compose himself before he can continue, but most often he needs to sit for a short time to let his pain calm down. I use several tools help him through times when he hurts.

Our PT recommended exercises to help strengthen Caleb's muscles. When the PT made his initial evaluation, Caeleb was stunned at how limited his range of motion was, particularly in his ankle. This was a key moment that continues giving him a goal to increase his range of motion. "I knew I had issues with my ankle," he told me. "I just didn't realize how bad it really was." Caeleb also insists on walking to and from school. When his pain is significant, I drive him to school, but he insists on walking as much as possible. He tells me that he wants to make sure that he continues moving forward.

Another tool in helping my son is medication, especially Tylenol®. Caeleb chooses not to take opioids; he never liked how he felt when using narcotics. He manages his pain with only Tylenol and R.I.C.E. While Caeleb was hospitalized, he took pain meds to get through his bleeds. He always complained about how he felt when taking morphine, which gave him relief while he waited for bleeds to resolve. I'm glad

he remembers the effects of prescription pain meds. Opiates, NSAIDS, and acetaminophen all carry risks; I just hope that when Caeleb does need to rely on stronger pain meds, we will talk about it and use them only as needed.

Perhaps the most effective tools, at least for Caeleb, are knee and ankle compression sleeves. After trying many types of wraps and braces, we finally found compression wear that works well on both his knee and his ankle. When he's doing a lot of walking or activities, these sleeves are needed to minimize pain and swelling. Sometimes Caeleb tries to avoid wearing them because he wants to forget that he has issues with his joints. But then, he often wishes he had worn his sleeves instead of being sidelined because of pain.

Although I can't go back and undo the damage, I can help my son look ahead and do what he can to keep his joints healthy. Preserving what's left of his joints requires a lot of work. Caeleb needs to be as active as his body allows, while using therapy and medication. His inhibitor is no longer the center of his life, but unfortunately it has left him with an all-too-familiar reminder of his past. A surgical intervention will be in Caeleb's future, but for now we are moving forward with a positive attitude. Each day is filled with moments where pain is not center stage, and for all of those moments I give great thanks.

Richard's Review... from page 5

his movement. He had a throat bleed at age 15.

When he was age 16 and six feet tall, Philip entered the Jimmy Sharman boxing booth at the Royal Easter Show. He sparred with an unbeatable professional boxer for ten bouts. Philip was knocked out cold without experiencing a brain hemorrhage, as confirmed by Prince Alfred Hospital records and by his hematologist. Surprisingly, there were no ill effects. Later, at age 23 in 1961, Philip had an accident, possibly while surfing. Doctors couldn't determine if he had a blow to the head, a spontaneous head bleed, or meningitis. Philip became delirious, then unconscious for a week due to suspected intracerebral and subarachnoid bleeds. When he recovered after plasma therapy, Philip had lingering aphasia with no memory of the event; he refused speech therapy.

Philip worked at Bennett & Wood, a transportation conglomerate in Zetland, where he applied his skills in the spare parts division. In 1983, he was the first patient with hemophilia to undergo a right knee fusion that resulted in no further bleeds. Then, in 1984, Philip was diagnosed with medically acquired AIDS after being treated for pneumocystic pneumonia. He continued to have cerebral hemorrhages. A right hip hematoma the size of a football was successfully treated with a dose of radiation. Philip rejuvenated his Catholic faith in 1990. Regrettably, his self-diagnosis of melanoma was medically confirmed, and the cancer spread to his spine, causing his death.

Philip Nilon was extremely lucky to survive numerous medically documented head bleeds. His hematologist provided the needed medical care. And his sister provided palliative care in her home at the end of his life. Because of its emotional content, Anne Kearney needed several attempts over 21 years to finish the memoir of her brother. Philip led an adventurous life, one that included an ill-advised boxing escapade.

YOU... from page 6

Step 2: Active range of motion of the joint can improve blood flow in a non-weight-bearing position. For the ankle specifically, you can trace the alphabet with your foot, make ankle circles, and do gentle towel curls.[2] This will reduce scar tissue adhesion and reduce the loss of range of motion.

Step 3: Now begin to strengthen the joints and ligaments by employing gentle resistance. It takes three days to lose strength, but six weeks to regain it, so for a low-level ligament sprain, I recommend performing these exercises three to four times per week, for six to eight weeks.

Step 4: Gently and gradually return to activity.

In my first 13 years of life, I was continuously in and out of the hospital for insidious joint bleeds. I began to exercise and took control of my own life. This is what inspired me to become a physical therapist. And for the past 15 years, I have not experienced joint bleeds, and I can say that I don't have target joints. My dedication and focus now are to help people affected by bleeding disorders.

We are just like normal people. We get hurt; our muscles and joints are weakened. If we don't take the appropriate measures to rehabilitate them, then we're more likely to reinjure them, just like NBA star Steph Curry. Joint injuries are preventable with appropriate workouts and mobility exercises. Allowing our muscles to regain their strength is possible, and will ensure improved overall joint health. Let's all bulletproof those target joints!

Dr. Michael Zolotnitsky is director of neurological rehabilitation at New Jersey Spine and Wellness in Old Bridge, New Jersey. He also has severe hemophilia A. He can be reached at 732-952-2292 and michael.zolotnisky@spineandwellness.com.

2. Towel curls strengthen the inner foot. Place a towel flat on the floor and use your toes to grab the towel and curl it toward you. Then use your toes to push it away from you. Increase resistance by placing a weight on the towel.

hemablog

Origins: Part 2

Laurie Kelley

Adapted from the second blog in a six-part series

It's our 30th anniversary of LA Kelley Communications! We've been publishing original books and newsletters on bleeding disorders since 1990, and started programs to help families struggling in developing countries. At first, we just wanted to help new moms and dads, but we grew to have global impact. We continue to assist families with bleeding disorders worldwide with educational and financial resources. Read HemaBlog for the whole story!

It was September 1987, and I was waiting to deliver my first child. I never went into labor, so we had to jump-start it, because I was two weeks overdue. I knew I was in for a long labor, so I grabbed my favorite book, *Peter the Great* by Robert Massie, which I had already read. My mother had given me the book nine months earlier; the author's son has hemophilia. Oh boy, would that make an impression soon. At the hospital, the nurses teased me as they saw me lying in bed in labor, reading this historical book, holding a yellow highlighter. "Studying for a test tomorrow?" one of them joked.

Our son was born by C-section, and the next day, the doctor came into my room with a puzzled look on his face. He had circumcised our son, and "It bled for about 30 minutes," he said, literally scratching his head. "In 30 years, I've never seen that." In the back of my mind, I heard myself say, *That author's son has hemophilia…*

The doctor stitched up our newborn, and when I saw him, he seemed fine. He was big—nine and a half pounds! We took him home two days later. One week later, around midnight, I went to change my son's diaper, and was shocked to see it saturated with blood. The entire diaper was red. I called the doctor, who said to bring him to the ER. Our first ER trip at 1:00 am, with me still recovering from a C-section. At that time, Children's Hospital in Boston was rather old and in need of repair. My husband went with our newborn into an exam room; they had me sit outside. I was crying to myself with no one around. Hearing my newborn scream for the next hour, two hours, was torture. My husband was excellent; he stayed with our son, talking to him, calming the situation.

The ER doctor seemed more worried about me. It was 3:00 am, I was in the ugly waiting room alone, still not feeling great from the birth. By 6:00 am, our baby was asleep, having survived the horrible stitching, and we headed home, utterly drained. We had not slept in 24 hours.

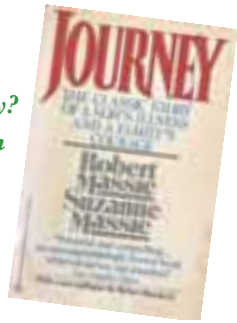
It would be a month before we got the news. Meanwhile, everything healed and life went on. Until the phone rang on a Friday afternoon in October. The voice of Jocelyn, a woman who would become our nurse and lifelong friend, was on the other end: "Laurie, this is Children's Hospital calling. We have the results in from the blood tests. Your son has hemophilia A."

Just like the author's son. The author of the book I was reading the night I gave birth. The book my mother gave me nine months ago…

I felt a rushing noise in my ears that made it hard to hear what Jocelyn was telling me. "Now, the clinic is closing for the weekend. If anything happens, if he bleeds, bring him in to the ER. We will need to give him an injection of medicine to clot his blood…"

While Jocelyn was talking, I looked at my fluffy-headed, blond-haired one-month-old, innocently asleep in his bassinet, wearing a onesie. He looked perfect. What was this woman talking about? This was like a jail sentence!

I knew how to fix this. I hung up on her. And felt instantly back in control.



Want to continue the story? Visit blog.kelleycom.com and read about Laurie's first clinic visit and more!

Laurie's baby with hemophilia

Laurie with her nurse and friend, Jocelyn

Inbox... from page 2

Celebrating 30 Years of *Raising a Child with Hemophilia*

ALWAYS SO GRATEFUL to you. At the time my son got diagnosed, there was hardly internet and no Spanish information. Your book *Raising a Child with Hemophilia* changed our lives forever. Thank you, and congratulations on those 30 years!

Fel Echandi
California

YOUR BOOK GAVE me calm in a storm swirling around me that literally was paralyzing sometimes! So grateful.

Shelley Clawson
Texas

JULY 21, 1995: My oldest son was born, and while we knew I was a carrier, no one in my town had the foggiest clue about testing. Fast-forward 11 months: he fell while with his grandparents, knocked out his bottom two teeth, and the official diagnosis was made. We were transferred to Cook Children's Hospital in Fort Worth, Texas, where I was given a copy of your book and tossed it in the trash can, saying something like, "I don't need a book on how to raise my child written by someone who has a few years' experience when I've been around hemophilia my whole life!" Number 1 advice: Learn to love your village and accept any help you can get. Thank you for all of your dedication, hard work, and research!

Melissa Howell
Michigan

THIS BOOK LITERALLY saved my son's life. I was a very young mother and got information from the Nashville chapter to learn about being the best medic and mother I could be. When Robby was in sixth grade, I kept him home from school because he was vomiting. I took him to a pediatrician, who looked in his ears, said it was red, treated him, and gave him phenergan. Robby continued to vomit on the drug; I thought that was odd. I pulled out *Raising a Child with Hemophilia* and there it was: cerebral hemorrhage. He was saved by the Grace of God. Thank you!

Patty Lybarger
Tennessee

I STARTED WORKING at Quantum Health Resources in the late 1980s. When your book came out, it was a mandatory read for all employees and new ones, forever. What a great eye opener! So grateful you wrote such a candid book for all of us to learn so many truths.

Diana Shugert Mumaw
California

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