WHAT IF THERE WAS A CURE FOR HEMOPHILIA?
Dear HFA Community,

As I write this, we’re in a time of change. Summer is officially over, fall is here, and kids are about a month or so into the new school year. This causes our routines to change. For parents, this usually means that it’s back to extra early mornings and perhaps a more ridged schedule with school start times.

Even bigger than those changes are the ones we’re seeing in the bleeding disorders community. We’ve seen the introduction of several longer lasting factor products with more set to launch in 2016. We’re talking about gene therapy again and even mentioning a really big word—CURE. Could this be on the horizon, something we see perhaps in our children’s lifetime? If so, what really does that mean?

I am constantly telling my son that his life is not defined by hemophilia. But on the other hand, so many of the choices he makes is because of it. As his caregiver, so much of my life is defined by hemophilia too. I’m his mother, but because of his hemophilia I’m more of a nurse than I ever imagined I would be. One component of our schedule that doesn’t change with the seasons is his prophylaxis infusions. For almost 11 years, we infuse at least every Monday, Wednesday, and Friday.

We’ve bonded over it. I say it’s “our thing.” So while I would gladly give it up today for a cure, I think I would miss that time together. Don’t get me wrong; our infusions dates are not like we’re going out for ice cream three times a week. They have often led to one or both of us crying, getting mad, or fussing. But it is “our thing.” We both individually have grown so much from those experiences and I think closer as mother and son.

How would our lives change if he didn’t have hemophilia? Maybe we’d actually go for ice cream three times a week to celebrate! I think it’s only natural to long for a cure for your child — or yourself. As you read this edition of Dateline, think about how that would really impact your life.

Warm regards,

Tracy Cleghorn
Board President

We’re talking about gene therapy again and even mentioning a really big word—CURE.”
gene therapy (noun): an experimental technique that uses genes to treat or prevent disease. In the future, this technique may allow doctors to treat a disorder by inserting a gene into a patient’s cells instead of using drugs or surgery. (source: Merriam-Webster)

Earlier this year, Xconomy, an international business and technology online publication, ran a story about hemophilia, the current products in the pipeline, and information about what gene therapy could mean for those living with a bleeding disorder. Xconomy interviewed HFA’s Executive Director, Kimberly Haugstad, about her thoughts as a leader in the bleeding disorders community and as a mother of a son with severe hemophilia, on whether or not gene therapy could finally be the answer that cures hemophilia. When we shared this article on our website and social media outlets, many others from the community commented on what a cure meant to them and how it could affect their lives.

With the permission of Xconomy, HFA decided to reprint this article on the following pages in Dateline. In addition, five community members looked into their crystal balls to share their perspectives on how the promise of a cure would change their lives. As you read this article, ask yourself the question what would a cure mean to you.
Ben Haugstad is 12-years-old and loves Taekwondo. He’s been doing it for six years, and soon he’ll be a black belt.

He also has a severe form of hemophilia. His body doesn’t produce the machinery needed to clot blood, and at any moment a bad tumble or a bruise could quickly turn into an emergency.

Three times a week, his mother Kimberly wakes up in the morning and injects Ben with drugs that, for a short time, help his blood clot. “I never thought I’d be a nurse,” she says.

These shots are expensive, about $2,500 a dose. But they’re also life-saving. They prevent cuts from becoming disasters, and ensure that spontaneous internal bleeds don’t seep into joints or organs and cause serious problems. Ben can live a mostly normal life. He does his Taekwondo, participates in gym class. He’s “private” about his condition, his mother says. He doesn’t talk about it or use it as an excuse to stay home from school and miss a test. He’s only had a little joint damage here and there.

“He wants to do what he can do,” Haugstad says. “We’re actually on a six week run [without a bleed] right now, so I’m pretty excited about that.”

Sometime in the near future, Ben’s tri-weekly infusions might become a thing of the past. With gene therapy, a modified virus carrying specific genetic instructions would be infused into Ben’s body and could give him the ability to clot blood for years, perhaps for life.

You’d expect his mom, the inadvertent nurse, to jump at the thought of it. But Kimberly has a much more measured response.

“When he was born, we heard loud and clear that it was going to be three years to a cure,” she says, and her skepticism is all the more notable because she’s also the executive director of the nonprofit Hemophilia Federation of America. In a sense she’s speaking for a lot of parents, not just herself.

Kimberly has good reason to be wary of promises. The idea of gene therapy for hemophilia has been around since the 1980s, and more than 15 years ago, the first hemophiliacs volunteered for tests. Yet no gene therapy product has come close to market.

Clinical failures and high-profile safety catastrophes in gene therapy trials turned hype to dust, and eviscerated most private investment in the early 2000s. Even with the current resurgence in the field, there are many questions to answer—how long will these therapies last? How safe will they be?—before Ben or any of the 400,000 or so people with hemophilia can count gene therapy as an option.

Beyond hemophilia, gene therapy is definitely back. Startups are forming again; some have gone public. Big Pharma is investing via partnerships and strategic alliances. One product is approved in Europe—the first in a Western country—for a rare liver disorder; another might help cure a crippling blood disorder, beta thalassemia.

Gene therapies for hemophilia are farther behind, with just one developer so far, Baxter International (NYSE: BAX), reporting the barest of clinical data. (Xconomy has learned more about those data, which we will describe later.)

Following Baxter are several more companies—see the box on page 5—and their clinical progress this year and next should be a touchstone for all of gene therapy. And hemophilia could prove to be the most competitive gene therapy race to date.
“The history of gene therapy really follows the story of hemophilia,” says James Wilson, the head of gene therapy research at the University of Pennsylvania, one of the field’s pioneers and most controversial figures.

Judging by the scrum of companies now with clinical trials or about to start, the story is about to add a wild new chapter. Seven groups have emerged so far with hemophilia programs. They are a mixed bag of big pharma companies protecting profitable franchises and smaller biotechs either working with the big companies or looking to one-up them.

What’s more, there are several scientific approaches and strategies involved, as well as the gamesmanship one might expect from a heated race.

“I think the competition is great,” says Wilson, who is also the scientific founder of the Washington, DC-based gene therapy startup RegenX Biosciences. “You know who’s going to really benefit from this? The patients.”

If it happens, that benefit would be a long time coming—even if patients today are better off than they were a generation or two ago. Until the 1980s, hemophiliacs who bled were rushed to the hospital and infused with a concentrated form of the “clotting factor,” or protein, that their bodies don’t produce: Factor VIII, for patients with hemophilia A, and Factor IX for those with hemophilia B.

Hospital stays could last for weeks or months if the bleed was severe, and patients understandably were overly cautious.

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**UPCOMING PRODUCTS IN DEVELOPMENT** (as of spring 2015)

**BAXTER INTERNATIONAL**

**Disease target:** Hemophilia B/A  
**Name:** BAX-335 (for hemophilia B; hemophilia A program undisclosed)  
**Vector:** AAV8  
**Therapeutic gene:** Padua mutant Factor IX  
**Program origin:** Chatham Therapeutics  
**Status:** Initial data from Phase I/II clinical trial of hemophilia B reported in February; more data expected in June

**UNIQUE**

**Disease target:** Hemophilia B/A  
**Name:** AMT-606 (for hemophilia B; hemophilia A program undisclosed)  
**Vector:** AAV5  
**Therapeutic gene:** Wild-type Factor IX  
**Program origin:** St. Jude Children’s Research Hospital, NIH  
**Status:** Started Phase I/II trial for hemophilia B in early 2015; data expected in the third quarter

**DIMENSION THERAPEUTICS**

**Disease target:** Hemophilia B/A  
**Name:** Undisclosed; hemophilia A program partnered with Bayer  
**Vector:** AAV, undisclosed  
**Therapeutic gene:** Wild-type Factor IX  
**Program origin:** RegenX Biosciences  
**Status:** Expects to start clinical testing in 2015

**SPARK THERAPEUTICS**

**Disease target:** Hemophilia B/A  
**Name:** SPK-FIX (for hemophilia B, partnered with Pfizer; hemophilia A program undisclosed)  
**Vector:** AAV, undisclosed  
**Therapeutic gene:** Padua mutant Factor IX  
**Program origin:** The Children’s Hospital of Philadelphia  
**Status:** Expects to begin Phase I/II trials in hemophilia B in the first half of 2015

**BIOMARIN PHARMACEUTICAL**

**Disease target:** Hemophilia A  
**Name:** BMRN-270  
**Vector:** AAV, Undisclosed  
**Therapeutic gene:** Wild type factor VIII  
**Program origin:** In-house, St. Jude Children’s Research Hospital  
**Status:** Expects to begin clinical testing in “early” 2015

**SANGAMO BIOSCIENCES/SHIRE**

**Disease target:** Hemophilia B/A  
**Name:** Undisclosed  
**Strategy:** Gene editing via zinc finger nucleases  
**Program origin:** In-house  
**Status:** Plans to submit IND in the second quarter of 2015

**BIOGEN IDEC**

**Disease target:** Hemophilia B/A  
**Name:** Undisclosed  
**Vector:** Lentivirus  
**Therapeutic gene:** Undisclosed  
**Program origin:** San Raffaele—Telethon Institute for Gene Therapy (TIGET)  
**Status:** Potential first trial in 2016

*Note: Since this article was published, Baxter International has changed their name to Baxalta.*
COMMUNITY PERSPECTIVES:
WHAT DOES A CURE MEAN TO YOU?

HFA asked several community members what a cure for hemophilia would mean to them and their families. These community members looked into their crystal balls to share their perspectives on how the promise of a cure would change their lives.

Morgan, teenager with hemophilia

A cure to me, means no more needles. It means no more medical bills to worry about when I'm older. No more worrying about what sports I might be able do, or doctors' appointments. Also, it means that I don't have to be in my room relaxing and hear my mom yell at me from the kitchen that I need to infuse. It also means no more blowing veins, finally! That is one of the most annoying parts. And it would mean no more internal bleeds.

If there were a cure one day, I think the community would still be strong. I believe we would still be together no matter what: celebrating the cure, even though some may not want it. But I think we would still have our annual meetings and events. We celebrate, grieve, and congratulate one another no matter what.

The way a cure would impact my family the most would be by not having all the medical supplies. Also, not having to travel to Boston every time I hit my head or something serious like that — it does get pretty annoying. I can count many times where I had to be taken to Boston just for bumping my head. (Okay, maybe they were more like slams on my head, but other than that, personally, I think that would be the most impacted.) It wouldn't really change our day-to-day life. Sometimes I feel like I don't even have hemophilia, except when I go to events and I am infusing. But it would probably cut back the time it takes me in the morning to get ready for school.

Morgan, who has severe hemophilia A, lives with her mom, dad, and twin sister in New Hampshire.

Worse, the infused factors came from donated blood samples and sometimes left hemophiliacs infected with HIV or hepatitis C.

The first breakthrough came when scientists genetically cloned Factor IX in 1982, and Factor VIII two years later. This led to the development of recombinant, or genetically engineered factors. The first was a Factor VIII product called Recombinate, from Baxter, approved by the FDA in 1992. These drugs completely changed hemophilia treatment. Not only did they end the risk of contaminated blood, they also paved the way for preventative treatment.

"Now you have teenagers [who] don't remember ever having a bleed," says Katherine High, the president and chief scientific officer of Spark Therapeutics (NASDAQ: ONCE), the former director of the Center for Cellular and Molecular Therapeutics at the Children's Hospital in Philadelphia, and a world-renowned hematologist.

For the roughly 20,000 patients with hemophilia A in the U.S., and the 3,000 or so with hemophilia B, it's become a chronic, manageable condition, albeit still stressful and expensive to treat.

About 60 percent of the hemophilia population has severe disease, according to the National Hemophilia Foundation. They have less than 1 percent of the necessary clotting factor in their blood, and so they have more bleeds and need bi- or tri-weekly infusions. Milder cases bleed and need treatment less often.

A few companies are working on incremental improvements to the protein replacement drugs, with versions meant to be used once a week or less, or that aim to help patients whose immune systems won't let them take current therapies. Alnylam Pharmaceuticals (NASDAQ: ALNY) is developing an RNA interference drug meant to be used even less often.

Beyond those improvements, gene therapy is shooting for long lasting solutions, perhaps even “one shot” cures. That’s the goal for many gene therapies, of course, not just in hemophilia. But the fact that even 30 years ago, hemophilia seemed to be the perfect application for gene therapy—and is still years away—speaks volumes about how hard the technology has been to harness.

For a long time, gene therapy seemed like science fiction. Microscopic viruses you’d think are dangerous are genetically engineered and used as little delivery vehicles, or “vectors.” Those vehicles are then packed with specific genetic instructions: go to this location and produce this protein. Or even, go to this stem cell and change its DNA, so every little baby cell that comes out afterward carries these genetic instructions too.
The promise is enormous. Find a disease you understand genetically—say, one known to be caused by a single faulty or missing gene—and engineer a long-lasting fix. Dozens of startups burst onto the scene in the 1990s, but they soon ran into technical challenges, especially around the viral delivery vehicles.

“It took time to figure out which vector systems are either the most easily used, or easy to make, or safest,” says Barrie Carter, the vice president who oversees gene therapy at BioMarin Pharmaceutical (NASDAQ: BMRN).

This was true in hemophilia, too. The disease has always been an ideal target for a gene therapy for a number of reasons. It’s monogenic (caused by a single mutation). It’s recessive (to fix it, a gene has to be added, rather than knocked out). And restoring only a little expression—some 5 percent of a normal person’s level of Factor VIII or IX—has a dramatic effect.

All those effects are easy to measure with a simple blood test. Along with cystic fibrosis, hemophilia was one of the first diseases tested with gene therapy. It was so ideal, in fact, that the pressure to use gene therapy became enormous. As The Scientist wrote back in 1999, “If gene therapy doesn’t work in hemophilia models, in what disease model will it work?”

In the late ’90s, the first wave of hemophilia gene therapy trials were beginning. High led one of the groups involved; she collaborated with an Alameda, CA-based gene therapy startup, Avigen.

High and her colleagues hadn’t focused on any specific technology. For viral vectors, “I tried everything,” says High, including retroviruses and adenoviruses, which are now largely antiquated delivery vectors due to safety and other problems.

According to Wilson, retrovirus wasn’t useful for hemophilia. It wouldn’t get into the liver, the body’s clotting factor production plant. And adenovirus, while adept at targeting liver cells and expressing genes there, wouldn’t produce a lasting effect. Worse, it threatened to set off a potentially dangerous immune response.

That threat became reality in 1999, when an 18-year-old Arizona teenager named Jesse Gelsinger became sick and died in a trial co-led by Wilson at UPenn. Gelsinger had a rare genetic disease of the liver called ornithine transcarbamylase deficiency, typically associated with infants, but he wasn’t sick. His condition was controlled with a restrictive diet and several drugs. The trial was to test the safety of a gene therapy that might ultimately benefit sick babies, and as the New York Times wrote in 1999, Gelsinger had volunteered knowing he wouldn’t benefit. But he paid the ultimate price. The gene therapy, delivered via adenovirus, triggered a wild immune system attack. He became jaundiced, suffered massive blood clots, and several organs failed. He died four days after treatment.

Wilson was soon at the center of a public and legal maelstrom. The FDA launched an investigation and suspended the trial, and later, the rest of UPenn’s gene therapy studies. Wilson became mired in lawsuits. Questions emerged about data that the investigators hadn’t initially reported from their research, including the fact that some monkeys were killed by these gene therapies in early testing. Wilson was also under fire for his ties to Genovo, the biotech that was funding much of UPenn’s gene therapy work (but not the Gelsinger study). Wilson founded Genovo in 1992, and both he and UPenn had an equity stake in the company.

“I was highly criticized, and under attack,” Wilson says. (Many years later, Wilson would write an editorial recounting the mistakes made, and lessons learned from the study, in Molecular Genetics and Metabolism.)

The damage reverberated through gene therapy, and companies in the field went into damage-control mode. Carter remembers how his former employer, Seattle’s Targeted Genetics, wrote a press release just to remind folks that it wasn’t using adenovirus. It got worse: Investors became skittish, the dot-com bubble popped, a slew of gene therapy startups crashed. In what seemed like a final blow to the field, four children in a French gene therapy study who were initially cured of a rare immune disorder later developed leukemia. One of them died in 2003.

Yet the maelstrom drowned out the fact that important progress was being made. A tool that’s become gene therapy’s most commonly used vector, the so-called “adeno-associated virus,” or AAV, was showing promise.

“This was the game changer,” Wilson says of AAV.

The name itself is a misnomer. AAV has nothing to do with adenovirus; its name came from scientists who discovered it on adenovirus lab preparations in the 1960s. It was smaller than adenovirus, and had no known role in any disease. Scientists made the first AAV vectors in 1984; the first AAV clinical trials, in cystic fibrosis, came in 1994 (run by Targeted Genetics). The continued on next page…
first hemophilia trials came five years later, run by Avigen and High’s group at the CHOP.

While nearly all for-profit activity in gene therapy ground to a halt after the bubble crash and trial deaths, High, Wilson, and others not only kept the field afloat, but helped make the advances that have led to the current hemophilia race.

Wilson’s path forward took a particularly odd turn. Shaken up and in no position to compete for NIH grant money after the Gelsinger fiasco, he went to an old mentor, Tachi Yamada, then the chief scientific officer of SmithKline-Beecham (now Glaxo-SmithKline).

A cure would mean a permanent end to hemophilia (and other inherited bleeding disorders). It would be life altering in so many ways, not just in the sense that there would be no more needle sticks, but in the security and relief it would bring. We’d truly be able to let our children be children. We wouldn’t be saddled with enormous medical debt nor experience lifetime joint issues. Life would be... normal.

The idea of a cure brings up many questions:

- If the cure were administered in-vitro, it would mean that only fetuses of known carriers would receive the treatment.
- Would every parent want the cure? What about their religious beliefs? Were the cure administered after diagnosis, the same question applies.
- Would insurance companies require a cure and no longer cover hemophilia as a chronic condition?
- Would hemophilia be a condition that is screened at birth in all infants? As we know, those with mild or moderate hemophilia may not develop symptoms for years.

Wilson wanted counsel, but he got more. “He said ‘I believe in you. I think you can do it. So how much money do you need?’” Wilson recalls. “I said ‘What do you mean?’ He said: [SmithKline-Beecham] would love to fund you in this endeavor.”

Wilson asked for $3 million to $4 million a year, Yamada made a phone call, and that was that. No grant application, no competition, no angst. Wilson got about $40 million from the big British drug maker over the next several years and went “subterranean.” He eschewed scientific lectures, he stayed away from awards banquets, and he avoided the press. “It was all about doing science,” he says.
High had her own brush with disaster. In the Avigen hemophilia study, a patient given an AAV gene therapy produced Factor IX for four weeks but then lost it, and enzymes in his liver spiked, which in some cases can mean inflammation or damage to the liver. In a post-Gelsinger world, with so many unknowns about gene therapy technology, that was particularly scary. Worse, High hadn’t seen this in animal studies; she was at a loss. “We didn’t know what was happening,” she says. “I still remember that as one of the most challenging times of my career. There was nobody to ask, no animal data to fall back on.”

The patient was being treated in Australia. High could only listen helplessly as reports came in twice a week. Slowly, to her relief, the patient’s liver function normalized, and he was never in mortal danger. But the FDA, on high alert after the Gelsinger case, put the trial on hold. When the trial resumed, it happened again to another patient.

Neither case was fatal, but Avigen had had enough and pulled out of gene therapy altogether.

That was a big problem: Avigen was making High’s vectors. So she went to CHOP CEO Steven Altschuler and pleaded for the hospital to set up, in-house, a clinical grade manufacturing facility. The decision wasn’t easy; the Gelsinger case was in litigation, and the sentiment around gene therapy was understandably negative. But High was adamant these problems could be solved. “I know a show-stopper if I see one; there’s not a show-stopper here,” she recalls telling Altschuler. “It’s always been my belief that if you can transplant an organ, you can transplant a gene.”

After a few days of thought, Altschuler sided with High, on one condition: she had to work on other genetic diseases too, not just hemophilia. The CHOP not only built manufacturing, it created an entire center for gene therapy. High recruited folks from Avigen, and one of them, Fraser Wright (now Spark’s chief technology officer), applied for and won an NIH contract to be the only federally-funded AAV manufacturing facility in the country.

“They had to basically build their own infrastructure to be able to manufacture and run their own clinical studies,” says Ken Mills, a former diagnostics executive who co-founded RegenX with Wilson (and through RegenX has also invested in Dimension Therapeutics).

The CHOP work led to a breakthrough for the problem that shut down the Avigen trial. Because most people have been infected at one point or another with the AAV variant High was using, the immune system recognized it, attacked it, and shut it down. That’s why enzymes in these patients’ livers were spiking. High began thinking of ways to combat this problem, like using steroids to stifle the immune response.

“Sometimes the way that I feel about my career is that I just keep walking along a list of problems, working my way to the end, and then starting back over again getting more refined solutions,” says High with a chuckle.

She also found a home for that variant—called AAV2—as a treatment for a childhood blindness called inherited retinal dystrophy. There was a sweet spot in the back of the eye, where the immune system couldn’t wash it out, and it only needed to have a small effect in a tiny area. That program, now known as SPK-RPE65—it inserts a healthy version of the RPE65 gene—led to the creation of Spark.

“That caused people to stand up and say, ‘Gee, these vectors can really do something that is clinically important,’” says BioMarin’s Carter.

With its SmithKline-Beecham funding, meanwhile, Wilson’s group stayed together and focused on finding better AAV vectors. “We became virus hunters,” he says, isolating AAVs from “whatever source we could”—monkeys, apes, humans—and screening them for differences.

They found about 150 variations, which would be named AAV7, 8, 9, and so on, and started turning them into vectors. (Wilson and Mills would later cut a deal with GSK for an exclusive license to these vectors to form RegenX.)

This flurry of vector work in Wilson’s lab is also part of the hemophilia story. One of Wilson’s post-docs, Lili Wang, had been studying hemophilia B using AAV2 in dogs, but the levels of Factor IX it produced were too low. Wang then tried one of the new variations, AAV8, in the same dogs, and the results were “20 fold higher,” says Wilson.

AAV8 also wasn’t as prevalent in humans as AAV2; perhaps it wouldn’t trigger immune system alarms. Wang and Wilson co-authored a 2005 paper in the journal Blood to share the results.

During this time, Wilson encouraged academics to use these vectors for their own research. High was one of them. Another was a group split between St. Jude Children’s Research Hospital in Memphis, TN, and University College London who were

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A cure for hemophilia can mean many things. In general, this sounds like a great thing, and it may well be for most part; but when asked what a cure means to me, a dad, and the only one in my house that may ultimately not have the disorder in some way, shape or form I have to put it into the context of the rest of my family. It also depends on just what is meant by a cure. Will it ultimately result in self-correction to normal factor levels or just higher-than-a-zero amount of circulating factor activity as long as it is therapeutic?

We have no idea yet the extent to which hemophilia has taken its toll on my oldest son who has battled an inhibitor for a decade. So yes, it would be wonderful for him to stop daily or multiple daily infusions. But it will not make him whole. It will not restore his joints and muscles that have been damaged from multiple bleeds that were difficult to stop.

When I asked my son if he would want to be free of hemophilia and inhibitors, the question is met with a torn response. Yes, no bleeding would be great, but when he reflects on the journey that we have been on so far, he realizes the positive impact on him of all the places he has been around the country, the friends he has met and keeps up with online, and the sense of being part of a bigger family. Even my not-quite-teenager can recognize the loss from just wishing hemophilia away. For both my wife and me, that family is a place we belong, where we don’t have to explain things, and we don’t have to try to fit in.

For my second son with severe hemophilia, it would be wonderful to not have to worry about whether we can catch a vein. To have the normal sibling issues as opposed to feeling left out since he doesn’t have his own wheelchair. It would mean being able to dream beyond a regulated set of allowed activities.

Perhaps the greatest hope for me lies in the next generation: for my grandchildren to have the possibility of never knowing a bleed or having to go down this road and for my daughters to not have to worry about the complexities and complications of life with hemophilia. It would mean no explaining to the local Emergency Department why they need to treat first, no fighting with the insurance companies about which pharmacy they use or figuring out how to pay for factor or all the other non-covered expenses, and no sitting in the ICU wondering if that bleed will ever stop.

But this all depends on what is really meant by a cure. So far this appears to be taking patients with severe hemophilia and promoting them to patients with mild hemophilia. While this sounds like another win for medical science, it will come with an enormous educational burden. How will local chapters maintain their funding to further education? With factor supply no longer in strong demand by the hemophilia population, what effect will this have on the supply chain for trauma situations? What happens to those for whom the cure does not work?

While there is a lot of exciting work on the horizon, there are many more questions than answers at this point. There are also a number of showstoppers that may prevent a cure from actually becoming a reality. We are a strong community. I have no doubt that we will find answers to these questions as well as many more that will be asked in the interim.

Eric lives in Virginia with his wife, Amy, and their two sons who have severe hemophilia (one with inhibitors, the other without), and two daughters. ••
intrigued by the UPenn dog study and wanted to try AAV8 for hemophilia in humans.

Wilson gave them access, and they ran a study with rousing results, which were published in the New England Journal of Medicine in 2011. The researchers—led by UCL’s Amit Nathwani—showed that an AAV8 gene therapy helped six patients with severe hemophilia B produce between 2 and 11 percent of normal levels of Factor IX. That might not seem like a big deal, but raising factor function to between 5 and 10 percent of normal turns a case of severe hemophilia into a mild one. “We believe that if you exceed 5 percent, you have a drug,” says UniQure’s (NASDAQ: QURE) CEO, Jorn Aldag.

As UniQure chief medical officer Christian Meyer says, such a seemingly small improvement could “eliminate” the risk of a spontaneous bleed. (UniQure licensed a genetic tool used in the St. Jude’s/UCL study for its own work.)

Four of the six patients in the study had been suffering from some 20 bleeding events per year before the treatment. The therapy ended those spontaneous bleeds and had lasted as long as 16 months at the time the study was published.

The results weren’t perfect, however. The therapies have now lasted as long as four years, but more than half the patients in the study have had to take a short course of the steroid prednisolone to fend off the type of immune response High first saw more than 10 years ago.

Still, the NEJM paper proved a gene therapy could get patients to “clinically important” levels of Factor IX through a simple injection into a peripheral vein, as Carter says. Mills remembers getting a number of phone calls, from investors and large pharma companies, trying to find the source of the data and where the technology came from.

“It was a huge turning point for the field,” Mills says.

Indeed, the race for AAV rights began. Here’s how all the entrants found their niche:

- Baxter is using AAV8 for hemophilia, which it acquired by purchasing Chatham Therapeutics. Chatham had licensed AAV8 from GSK/RegenX.
- UniQure is using AAV5 for hemophilia, which it licensed from the NIH in September 2011. In 2010, it grabbed rights to the therapeutic gene used in the St. Jude’s/UCL study.
- Spark is making its own AAV vectors in-house but won’t discuss details. It’s working with Pfizer on a treatment for hemophilia B.
- Dimension was formed by Fidelity Biosciences and RegenX in October 2013; the startup has a license to RegenX’s AAV vectors, and is teaming with Bayer on a gene therapy for hemophilia A.
- BioMarin licensed a hemophilia A program from St. Jude’s/UCL in February 2013.

The differences between these groups are very technical. Take vectors, for instance. UniQure is using AAV5, and its CMO Meyer contends it should stay in the body making protein for a long time because it’s less likely than AAV8 to provoke an immune response.

Then there are the genes. Some companies, like Baxter and Spark, are using mutant therapeutic genes that clot blood 8 to 12 times more strongly than normal. The original version was discovered in a young Italian man from the city of Padua. The proposed advantage: Patients can get a therapeutic effect with a smaller dose.

Others, like UniQure, BioMarin, and Dimension, are using genes that produce a normal amount of clotting factor. The proposed advantage: The results should be more predictable.

All of these arguments about the different AAV gene therapies for hemophilia are theoretical until they’re tested in people. There are many questions to answer: How durable will they be? If they wear off, would the body’s defense systems prevent a follow-up dose from working? How much factor expression is actually needed? Can they completely cure hemophilia, or just make it less severe? Will any safety issues crop up?

The door is open for other approaches. For example, one potential limitation is that AAVs might not last long in young children. As their livers grow, the AAV-modified cells might get washed out. This is an argument made by two companies using

“Hemophilia could prove to be the most competitive gene therapy race to date.”

Ben Fildler, Xconomy

continued on next page…
lentiviral vectors (Biogen (NASDAQ: BIIB)) and gene editing methods (Sangamo Biosciences (NASDAQ: SGMO), via a deal with Shire) for the disease. Both methods aim to create permanent fixes by passing genetic changes on to other cells. An AAV, by comparison, does its work as long as the cell it’s in stays alive.

“We think AAV vectors for gene therapy won’t provide persistent expression levels,” says Sangamo chief scientific officer Philip Gregory. “We can offer the ability to extend that long lasting [fix] right into patients who need it the most: newborns and small kids.”

Olivier Danos, Biogen’s head of gene therapy, said similar things a few months ago. Neither Sangamo nor Biogen has any human clinical data as of yet. The only glimpse from any of the competitors, so far, has come from Baxter, which last month produced its first human data—and just a very small sliver.

Here’s a summary of those data, according to Baxter R&D chief John Orloff.

- Six patients have been treated. The two at the highest two doses produced Factor IX levels of 20 percent (after five months) and 10 percent (after eight to 10 weeks). The patient at 10 percent, however, initially hit 25 percent of normal production before his liver enzymes spiked. Baxter responded with immunosuppressive steroids.

- The other four patients were treated more than a year ago at lower doses and have had “low expression,” according to Orloff. He declined to elaborate.

- Patients have been starting out with high factor expression before those levels drop and stabilize.

- All 16 patients in the study should be dosed this year; more data are coming in June.

- “It’s a small cohort obviously, we have more patients to treat, so the jury is still out,” Orloff says. “But the early data would suggest that we are seeing higher expression levels than what’s been previously reported.”

The St. Jude/UCL group, by comparison, published an update to their study in November showing that a total of 10 patients have maintained factor IX levels of between 1 and 6 percent over a median of 3.2 years after therapy. In dogs, positive effects have lasted a decade. The companies using AAV vectors for hemophilia view this as proof that they can produce a lasting, meaningful effect in humans. And more data are coming. UniQure has already started its first trial. BioMarin, Dimension, Spark, and Sangamo all could follow with their first studies this year as well. (Biogen is farther behind.)

But everyone acknowledges that there’s no telling when the therapeutic effects will wane, or if gene therapy in this field has really gotten over the hump.

“That’s one of the big questions that will have to be answered,” UniQure’s Meyer says of the staying power of an AAV gene therapy.

Haugstad takes that question very seriously. She worries that children with severe hemophilia will get a glimpse of life without needles, only to have it taken away.

“Maybe little Jimmy is 10 years old, he gets a shot, he’s good for 4 years, now he’s 14, and really is active normal young man—and [all of a sudden] he’s got severe hemophilia again,” she says. “What happens? How would we handle the psychosocial impact to families?”

It shows, despite all the progress that’s been made, just how far gene therapy still must go to get past one of its oldest nemeses. And that has Wilson, approaching his 60th birthday, feeling a bit reflective these days.

“I tell my wife that my career is starting at 60. That the field of gene therapy is now born. That it’s the beginning, it’s not the end,” Wilson says. “She said, ‘Well then, what have you been doing for 35 years?’”

His response: “Trying to figure it out!”

I feel there will always be a need for the community to stay close with or without a cure.”

Jennifer, hemophilia mom
COMMUNITY PERSPECTIVES:
WHAT DOES A CURE MEAN TO YOU?

Jeff, adult with hemophilia

A cure: it would be everything, and nothing. I have essentially mastered hemophilia, and with the current effectiveness and availability of factor, and given that it is well managed, I don’t see a need for my hemophilia to be cured. The damage and limitations I experienced happened long ago when I was young and when treatment was not as advanced. I might have hoped for a cure, but today, I really have no need.

As a community member and advocate for bleeding disorders, I am conscious that I am extremely fortunate to live as one of the one-third of hemophiliacs in the world who are privileged with access to factor. Too many of my blood siblings suffer with little to no treatment at all. A cure could grant them the opportunities and full lives that they are missing out on, that we enjoy, and in that light I can’t NOT want a cure. Even within our fortunate community here, where factor is readily available — if not extremely costly - many suffer from inhibitors or rare factor disorders, and the improvement in their lives would be so drastic and positive that for them, I again can’t avoid hoping for a cure.

A cure would have virtually no impact for me, and I would be likely to decline one. Hemophilia isn’t something I have; it’s part of me. It is among the many things that make me who I am. I was born a hemophiliac, and I will die a hemophiliac. I would miss our community and the many people within it whom I love and count as my family, though, I would celebrate their choice to be cured and revel in the lives they would go on to lead.

A cure would bring a complete paradigm shift in our community, and to some extent I have seen this happening already. When I was a child, we only met other bleeders at summer camp or the occasional chapter event. There was little-to-no awareness of our disorder among society. At most, we were a footnote in the AIDS story. We lacked today’s treatments and so, for my generation and those before, survival itself was still a major goal. Our need for a sense of belonging is what led to this community’s growth and strength.

Today, however, that need is not so strong. It still exists, but advances in treatment, advocacy wins, and our communal strength has changed the face of hemophilia. No longer are we frail kids with enlarged knees and bodies covered in bruises. Today’s hemophiliacs are strong and healthy. Where my generation sought to survive, a younger generation seeks to thrive, and with that, the deep, emotional need to connect with someone else who shares your daily struggle has diminished or vanished. Some participate in community events because they are there, but they don’t express the same sense of need that was once so prevalent. It is a tangible sign of success.

We wanted a future where hemophilia no longer dominated our lives, and looking around, I see signs that that future is near. As managing bleeding disorders becomes more simple and safe, we find success in the fight against inhibitors, and we find ways to get treatment to the world’s bleeders who lack it, I see our need for this community diminishing even further. Would that be sad? Certainly. Would future generations miss out on the amazing sense of family, strength, and purpose that we find in our community today? They would. But, the lives they will be living will more than make up for all of that, and that will be our greatest achievement.

Our collective story was born of great darkness. We banded together in response to a nightmare, and in each other we found strength and community. Whether it be a cure or advancements in treatment that provide us a practical cure, I believe we should embrace where we are headed, however different and scary that seems. However, when I consider the world without this community knowing that bleeders are living full lives without stress or struggle, the idea changes from frightening to exciting and something we should all look forward to.

Jeff lives in the state of Washington with his wife and is an active member of the bleeding disorders community.

“I think it goes without saying that a cure would bring with it a complete paradigm shift in our community.”

Jeff, adult man with hemophilia

Fall 2015 | Dateline Federation 13
A cure would be an amazing miracle for our family. Right now it seems like a dream, but we can’t wait for the day when it becomes a reality. We would be happy to give up infusing. The idea of no more huge boxes of factor and infusion supplies, no more pokes, no more worrying about medi-port health and the huge expense of it all is something we hope will someday come true. The older our son gets, the more aware he is that he is different, so being cured would make him feel more like everyone else.

A cure would also mean a lot less worry for the generations to come. Our son’s children and their children would not have the same struggles that we have today. Even if hemophilia were cured right now, we would still want to be part of the greater bleeding disorders community. Hemophilia has already been a huge part of our lives. It has been an emotional roller coaster that only others in our community can understand. Our local chapter has become an extended part of our family. When there is a cure, we will celebrate with them.

I feel there will always be a need for the community to stay close because with or without a cure there will still be children born with hemophilia. It is important to have a support group for parents when they experience the shock that we did when our son was born as the first in our family with severe hemophilia.

We live with hemophilia, however we have learned to not let it take over our lives. Our day-to-day activities wouldn’t change much if our son was cured as a child. He would still play with his friends, go swimming, and continue doing the things he loves. That being said, being cured of hemophilia would help relieve much of the stress we feel with the almost-constant worry about him getting hurt. Also without hemophilia, we would be able to give him more opportunities with sports, and would be able to travel with more ease.

With our son only being five years old, hemophilia affects us as parents more than it affects him. We have asked him how he feels about having hemophilia. He is very open to talking about it with anyone, and has said that he likes having hemophilia because it makes him feel special. It is a part of him that he is okay living with because he doesn’t know anything different. If asked that same question a few years from now, however, I believe he would give an entirely different answer. I hope that when we get to the point where he wishes he didn’t have hemophilia that we will be able to give him encouragement in knowing that improvements in treatments and eventually a cure are in his near future.

Jennifer and Chad live in Ohio and are parents of a five-year-old with severe hemophilia.
On The Horizon: What’s Next for Our Community?

By Dave Robinson, PhD, LMFT

As a father of two boys with hemophilia, I know firsthand that dealing with a bleeding disorder can be very taxing, expensive, and interfere significantly with everyday life. The focus of this section is to address where we are and contemplate where we may be going as a community. As with everything in life, there tends to be pros and cons to the various psychological, social and emotional aspects of living with a bleeding disorder.

On the horizon are new treatments and promises of a cure. At first look, most would feel that these changes are a good thing. However, change can be a difficult thing for many people. It has been asked, “If there were a cure would you take it?” The majority of the individuals asked this question say “yes.” There are some people, however, who when asked this question are slower to respond and others who currently say “no.” I believe that it is important to acknowledge that change, even if it is a positive change, does have its pros and cons.

As longer acting treatments, and ultimately, a cure, the bleeding disorders community experiences could include:

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Resulting in feelings of...</th>
<th>Positive Experiences</th>
<th>Resulting in feelings of...</th>
</tr>
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<tbody>
<tr>
<td>Bleeds</td>
<td>Fear</td>
<td>New Friends</td>
<td>Support</td>
</tr>
<tr>
<td>Treatments</td>
<td>Worry</td>
<td>Sense of Community</td>
<td>Caring</td>
</tr>
<tr>
<td>Hospitals</td>
<td>Loss of Control</td>
<td>Involvement in Local &amp; National Organizations</td>
<td>Connection</td>
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<tr>
<td>Doctors</td>
<td>Irritability</td>
<td>Learning to Self-Advocate</td>
<td>Teamwork</td>
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<td>Inhibitors</td>
<td>Sadness</td>
<td>Learning to Advocate for a Loved One</td>
<td>Accomplishment</td>
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<tr>
<td>Insurance</td>
<td>Isolation</td>
<td>Growing Through Difficulty</td>
<td>Unity</td>
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<td>Infusions</td>
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<td>(Individual &amp; Family)</td>
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On the horizon are new treatments and promises of a cure. At first look, most would feel that these changes are a good thing. However, change can be a difficult thing for many people. It has been asked, “If there were a cure would you take it?” The majority of the individuals asked this question say “yes.” There are some people, however, who when asked this question are slower to respond and others who currently say “no.” I believe that it is important to acknowledge that change, even if it is a positive change, does have its pros and cons.

As longer acting treatments, and ultimately, a cure, the bleeding disorders community experiences could include:

<table>
<thead>
<tr>
<th>Potential Positive Experiences</th>
<th>Resulting in diminished feelings of...</th>
<th>Potential Struggles &amp; Losses Associated w/ Cure</th>
<th>Resulting in...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longer Treatments</td>
<td>Fear</td>
<td>Social Support</td>
<td>Finding New Meaning</td>
</tr>
<tr>
<td>Fewer/No More Bleeds</td>
<td>Worry</td>
<td>Friendships</td>
<td>Finding the New Normal</td>
</tr>
<tr>
<td>No More Treatment Centers</td>
<td>Loss of Control</td>
<td>Local &amp; National Organizations</td>
<td>Finding Security (defined by what we know)</td>
</tr>
<tr>
<td>Overcoming Inhibitors</td>
<td>Irritability</td>
<td>Identity (no longer a person associated with a bleeding disorder)</td>
<td>Finding Joy in New Life</td>
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<tr>
<td>Fewer/No More Insurance Stressors</td>
<td>Sadness</td>
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<td></td>
<td>Isolation</td>
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We need to begin to adjust to the changes that are coming. We will need to find new meaning and work hard as individuals, couples, and families to make these important transitions during this exciting time. It is essential that we keep the lines of communication open and allow each member of the family to express their feelings and support each other. Change is part of life. Finding personal joy, family happiness, and adapting to our circumstances are important aspects to living well and finding ways to enjoy the journey—whether it be before the bleeding disorder, during the bleeding disorder or after the bleeding disorder. May we all work together to support one another as we look to the future with positive attitudes.

Dave Robinson is a licensed and practicing marriage and family therapist and director of the Marriage and Family Therapy program at Utah State University. He and his wife Jamie have 5 children (three sons and two daughters). Both his oldest and youngest sons have moderate Factor IX hemophilia.

Fall 2015 | Dateline Federation
On June 17th, HFA hosted its 2nd Community Fly-In. This annual event brings members of the community from all over the country to Washington, DC to meet with their congressional representatives and advocate on behalf of those with bleeding disorders. The members of Congress to be visited were picked based on their interest in particular legislation, their position on specific committees and/or their willingness to support our community, making these meetings incredibly effective. This year, community members were brought in from Massachusetts, Maryland, Maine, Michigan, Missouri, North Carolina, Pennsylvania, South Carolina and Tennessee.

The evening before, the incredibly enthusiastic group attending a briefing at HFA’s offices to learn about the policy issues they would be discussing the following day. This year, the policy agenda included:

**The Patients’ Access to Treatment Act:** the community asked members of the House to co-sponsor this important legislation requiring that an insurance company not charge more for a drug that they place on a specialty tier than they charge for the drugs that they place on their non-preferred brand tiers. This legislation ensures the affordability of specialty drugs.

**Nonprofits as Acceptable 3rd Party Payers:** because of a rule from the Centers for Medicaid and Medicare Services (CMS), certain Marketplace plans have stopped accepting premium assistance payments from nonprofits, such as PSI, that help our community. We asked that members of Congress sign on to a letter asking CMS to change this rule.

**Premium assistance is vital to ensuring our community can afford the insurance plans that will best cover their needs.**

**The Part D Beneficiary Appeals Fairness Act:** community members asked members of the House to co-sponsor this legislation that would create a process for drugs placed on a specialty tier in a Medicare plan. If a patient has no alternative drug available in a lower tier, it is important that they are able to appeal the decision to increase their out-of-pocket costs and keep their medication affordable.

For those with von Willebrand’s whose medication is covered under Medicare Part D, this legislation ensures a fair appeals process if medications are moved on to specialty tiers.

**Access to Skilled Nursing Facilities:** HFA raised awareness in Congress and supported NHF on this important initiative to make sure that those on Medicare are not turned away from skilled nursing facilities because of the high cost of factor.

As our community ages, it is vital that they have access to skilled nursing facilities.

Following a long day on Capitol Hill, the community attended HFA’s 2nd Annual Congressional Reception. The congressional reception brought together members of our community with members of Congress and their staff to learn more about our policy initiatives. We also honored members of Congress who have been particularly involved in health care issues with HFA’s Champion Award. This year, honorees included Senator Bill Cassidy, Congresswoman Diana DeGette, Congressman Cedric Richmond and Congressman Fred Upton.
Being an advocate is such an essential part of our community and many have seen over the years how effective a small yet organized group of individuals can be. We are grateful for the support of the community in making these events such a success.

Advocacy is truly in our blood!
Across the country, HFA has heard of many cases of patients and their families facing new limitations and restrictions from their insurance services like prior authorization, step therapy policies, and restrictions on which specialty pharmacy or pharmacy benefits manager (PBM) may be used. HFA speaks with individuals weekly who struggle to obtain needed exceptions to rules and policies from their service providers. Receiving temporary exceptions serves that particular family or situation but exceptions can be reversed without input or prior notice, and may only last a short time, needing constant renewal. Policy or rule changes provide more overall protection for the entire community. As a community advocacy organization, HFA recognizes the need to obtain policy changes for families with bleeding disorders. To do so, we need to present a unified request with multiple examples of how a current rule or policy is not effective or may possibly harm patients.

To address these concerns, HFA has developed Project CALLS [Creating Alternatives to Limiting and Lacking Services], a patient-centered initiative which invites members of the community to share their individual stories about insurance issues to help the entire bleeding disorders community. Project CALLS is flexible in accommodating those who wish to participate. Depending on their preference, participants may speak privately with a trained member of the HFA staff or complete an online form regarding their insurance concerns.

Through the gathering of these stories, HFA will identify trends and collate data to build a broad case for change then work with other advocates, insurance companies, pharmacies and other providers to request needed changes. The information may also be used to educate insurers, legislators, and human resource departments about more comprehensive, cost-effective ways to provide quality care for individuals with bleeding disorders.
Your Voice Really Matters!

Like our CHOICE survey, Project CALLS is the latest way that HFA is listening to our community’s needs. HFA has been able to turn the results of CHOICE into action with Project RED and our Bleeders’ Bill of Rights. Project CALLS is the next step in helping individuals with bleeding disorders to receive the best care possible.

SHARE YOUR STORY through this very important initiative and be a part of a community that cares!

To participate in Project CALLS, visit the HFA website: www.hemophiliafed.org/project-calls/ and share with others in the community.

Project CALLS is designed for individuals or families who have been:

- Denied services or have received an exception,
- Forced by an insurance company to “fail” on a product before being allowed to use the product of their choice,
- Mandated to use a pharmacy that is not meeting their needs, and/or
- Forced to go through a lengthy pre-/prior-authorization process.

- Ann LeWalk

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Date of preparation: 10/2015, NUW-004-CAD-B
Adult Men’s Connection and Support

By Lauren Neybert, MSW

HFA often hears that one of the most beneficial tools when living with a chronic disorder is to regularly connect with others sharing similar experiences. That’s why HFA is proud to sponsor the Blood Brotherhood Online Forum, a secure site for adult men with diagnosed bleeding disorders to meet other Blood Brothers from across the country. In this private format, men living with bleeding disorders have an opportunity to expand their support network and learn from each other. Join in the conversation today by registering at www.hemophiliafed.net!

What are the consistent topics you see on the forum?

**Tom:** The topics I enjoy the most are either on new product development and manufacturer news or personal patient experiences.

**John:** Topics change over time, however consistent topics include: joint health, treatments, replacements, fusions, braces, factor (prophylaxis vs. on-demand, product vs. product), as well as Hepatitis C and HIV. From time to time, posts will include dental issues, relationships, grief/loss, and depression.

**Steve:** The topics I refer to most often are ongoing Hepatitis C cures which are now advancing into genotypes beyond type 1. A number of my Blood Brothers have joint issues and I see some great discussion on the merits of various treatments or procedures.

**Reid:** The topics vary and are fun. We have topics on funny jokes, exercise, physical therapy, how you handle stress, or you can create a topic that interests you. There are no wrong answers and it is just for the guys. If you need to vent about a bad day, you can do so. The other guys in the community are supportive and understanding. Chances are if there is a problem among us, others have had it also.

What is the greatest benefit of logging onto the forum?

**Tom:** The greatest benefit is hearing the experiences of my peers. It’s a trusted, vetted community and I like hearing others experiences and comparing them to my own.

The History of the Online Forum

- **2007**
  - HFA Blood Brotherhood Online Forum launched.

- **2010**
  - 200+ registered participants.

- **2011**
  - Monthly live chats created.

- **2015**
  - 400+ registered participants.
  - 9490+ made from registered participants.
  - 777+ topics discussed.
John: Since this is a forum for adult men with bleeding disorders only, it is certainly the only place online where you can be assured you are being heard by other men with bleeding disorders. There are also no geographical boundaries. You can ask a question about whatever is going on in your life and there will be a score of ears hearing you that have been through the same or similar circumstances. Even if you do not find the answer you are looking for, you certainly get support.

Steve: I have benefited greatly from a few specific posts, especially one by a Blood Brother and his bad experience with amoxicillin. It seems that it tends to inflame the liver and can cause esophageal varices to misbehave. I was about to have oral surgery and when the doctor mentioned starting with amoxicillin, I remembered the post and had the doctor change the prescription. There is a great deal of excellent interchange of ideas and solutions.

Reid: We learn from each other on these forums. I can read of a problem that someone has and go, “ahhhhh... I have had that.” Then I can comment on how I dealt with it. I always enjoy connecting with the men whether it is reading posts or chatting. It is always beneficial.

Why do you think other men with bleeding disorders should participate in the forum?

Tom: The forum is a great way to meet people in the community without leaving your couch (and it’s even cooler if and when you meet those people in real life later on, say at a national conference). It’s an amazing resource for information. Everyone’s patient experience can be different, but a lot of times there are commonalities that can help you make decisions about your own care. Finally, it’s a good place to go for advice from people who are leaders in the hemophilia community.

Reid: I think other men would get so much out of the postings. Every time I post, someone else thanks me or recognizes that they have read my posts. Other men, especially those in isolated areas, will get the sense of belonging to the community. Many of us have mobility issues and are not able to attend meetings for one reason or the other so this can provide a way of connecting and belonging to a community of people with the same issues. We help each other by sharing our experiences.

*Disclaimer: HFA’s Blood Brotherhood Online Forum and these listed experiences are a collection of personal opinions and a representation of individual experiences. They do not represent HFA or its Board of Directors. This is not to be taken as medical advice or the official opinion/position of HFA, its staff, or its Board of Directors. Readers are strongly encouraged to discuss their own medical treatment with their healthcare providers.*

Our vision for innovation, brighter than ever.

For more than 60 years, we’ve consistently pursued advancements in the treatment of bleeding conditions.

Now, as Baxter’s BioScience becomes Baxalta Incorporated, this proven heritage—along with the advancements we’re making today to cultivate tomorrow’s developments—fuels our global vision and promise: Our relentless desire to make a meaningful difference in the lives of real people—one person at a time. This promise to you can be seen in all we do, and helps to make us the company we are today.
Listening to the Needs Of Women
By Janet Chupka RN, BSN

Throughout the CHOICE Project we heard from numerous women about their lack of access to the diagnosis and care they need as patients with bleeding disorders. Many women explained that doctors told them women can’t have hemophilia, or a bleeding disorder, and otherwise how providers were dismissive of their symptoms and pain.” — Wendy Owens, CHOICE Project Officer

That rather disturbing information Wendy gathered was the catalyst for HFA’s Blood Sisterhood program’s “Share Your Story” survey. Unfortunately, it was a consistent and unnerving refrain among the women who took the CHOICE survey: they were having difficulty being seen or receiving treatment for their bleeding disorder symptoms. Some women were even being denied care. This was reported by women utilizing Hemophilia Treatment Centers (HTCs) as well as women who sought medical care elsewhere.

This matter was naturally of great concern to HFA, particularly regarding HTCs. Starting in the fall of 2014, HFA reached out to the Health Resources and Services Administration (HRSA), to ask what requirements HTCs have to care for individuals diagnosed with a bleeding disorder. HRSA is an agency of the US Department of Health and Human Services, and the primary federal agency for improving access to health care and is responsible for the National Hemophilia Program and grant funding that supports HTCs.

HFA also wanted to clarify the needs of women and verify the CHOICE Project feedback. We launched the “Share Your Story” survey on the Blood Sisterhood pages of the HFA website on February 15, 2015. This short, 15-question survey provides women the opportunity to share their experiences in their own words about the care they have received in reaching diagnosis and treatment for their bleeding symptoms.

The following provides a summary of what we learned and what we have done with what we learned in the first six months of the survey collection.

The Data
HFA received 53 completed surveys from women in 26 states across the country. The average age of the women taking the survey was 40 years old, with the youngest being 14 and the oldest 70 years old.

Of the 53 women who completed the survey, five of them reported bleeding symptoms, but did not have a doctor-diag-

Survey Results: By The Numbers

- Number of women who’ve completed the survey: 53
- Number of states represented by survey respondents: 26
- Number of states in which denial of care is being reported: 8
- Number of women reporting denial of care from both HTC and non-HTC providers: 13
- Percentage of women reporting a doctor-diagnosed bleeding disorder: 90.6%
- Percentage of diagnosed women receiving treatment for their bleeding disorder: 60.4%
nosed bleeding disorder. The most common symptoms reported were: bruising, heavy menses, post-partum bleeding, nosebleeds and joint pain. Three of the women reported a family history of a bleeding disorder, one had no family history, and one was uncertain whether there was a family history.

The other 48 women did report receiving a bleeding disorder diagnosis from a physician.

The chart at right shows a breakdown of the diagnoses received:

Of the 48 women with a diagnosis, the following is a breakdown of the type of provider they see for regular care of their bleeding disorder:

- 39 Hematologist
- 5 Family Practice physician
- 5 None

Only 29 women reported receiving any type of treatment for their bleeding disorder. Nineteen of the 48 reported they did

continued on next page...
not have a treatment plan and do not currently receive any treatment for their diagnosed bleeding disorder.

What Did We Hear?
Many women did report receiving a diagnosis, getting good care and following a treatment plan which includes factor. However, others reported care that has been less than adequate and some women reported being refused care altogether. According to these 53 surveys, three women were denied care by local physicians and 10 women reported instances of refusal of care at HTCs across the country simply because they were women.

What Do Women Want?
In addition to asking women about their care, HFA also wanted to know what the needs are of the women across the country who experience bleeding disorder symptoms or who have a diagnosis of a bleeding disorder.

We heard overwhelmingly that women want more information and education about bleeding disorders. The majority of the women also stated that provider education specific to women with bleeding disorders is an unquestionable need. Other tools mentioned that women felt would be helpful in managing their bleeding disorders were: HTC uniformity of care, a social media connection, opportunities for social interactions and support.

What is HFA doing?
We have reported to HRSA all 10 of the instances where an alleged denial of care to women occurred at HTCs. HRSA has been receptive to this information and will be working with their Regional Coordinators on this issue.

Some of the women who took the survey found insurance issues to be an additional barrier to receiving quality care. Organizationally, we have created Project CALLS (Creative Alternatives to Limiting and Lacking Services). Project CALLS is an opportunity for the community to share their experiences with insurance issues while helping the entire bleeding disorders community. Through Project CALLS, HFA will collect stories from the bleeding disorders community across the country, collate the data, identify trends, and use the information to build a case for changes in the insurance industry.

Programmatically, HFA’s Blood Sisterhood program will continue to provide the education, support, and resources that women need to reach a diagnosis, and continue that support through the stages of their lives with a bleeding disorder. In 2015 we had 20+ local educational sessions of Blood Sisterhood happening at our local member organizations, as well as webinars, an improved website information for women, and a mobile app that allows women to track their menstrual cycles and bleeds and share that information with their health care provider.

We have added a new physician, Robert Sidonio, MD, MSc, as a medical advisor to our professional advisors team. Dr. Sidonio is passionate about addressing the needs of women with bleeding disorders.

We also are partnering with other organizations to raise awareness, particularly those that provide education and training to health care providers such as the Foundation for Women and Girls with Blood Disorders.

Looking Ahead
HFA plans to continue the “Share Your Story” survey and learn from women across the country over the next year. A more detailed report of the first year will be available in the spring of 2016.

We will also continue listening to women and collecting their stories through this survey and other means about the health care they are receiving. We will persevere in reporting to HRSA about women with a diagnosis who have been refused care at HTCs, as we continue to seek our overall objective of assisting women and raising a united voice for positive change that is felt by the women in our community.

1. http://www.hrsa.gov/about/
“Healthy Bodies Bleed Less” continues to be the mantra of HFA’s FitFactor program. It is our goal to get every community member at least considering the positive effects that physical activity and a healthy diet can have not only on their joint health, but also their overall health and sense of well-being. Through a collaborative agreement with the Centers for Disease Control and Prevention (CDC), we will be focusing our efforts in the coming year on joint health for individuals and families in the bleeding disorder community. As a result of this collaboration, we will be encouraging our community members to take a look at their own health and behaviors and see how and where improvement can be made. One of the tools that we will be utilizing is the Body Mass Index (BMI). While we understand that it is not a perfect way to measure a healthy weight, it is a fast, straightforward screening tool that can generally indicate if a person is underweight or overweight. An individual with a high or low BMI should always be further evaluated by a trained healthcare provider who should perform appropriate health assessments in order to evaluate an individual’s health status and risks. Learn about all about BMI and how it can help you decide what healthy changes you can start making in your life.

WHAT IS BMI?

BMI stands for Body Mass Index and is a quick and easy method to determine if an individual is at a healthy weight. It is calculated by dividing weight in kilograms by height in meters squared, or weight (kg) / [height (m)]². It can also be calculated by dividing weight in pounds by height in inches squared multiplied by 703, or weight (lbs) / [height (in)]² * 703. A BMI calculator can be found on the CDC’s website at http://goo.gl/rBQrrY.

The standard weight status categories associated with BMI ranges for adults are shown below.

<table>
<thead>
<tr>
<th>BMI</th>
<th>WEIGHT STATUS</th>
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<tbody>
<tr>
<td>Below 18.5</td>
<td>Underweight</td>
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<tr>
<td>18.5 – 24.9</td>
<td>Normal or Healthy Weight</td>
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<tr>
<td>25.0 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30.0 and Above</td>
<td>Obese</td>
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</tbody>
</table>

For example, someone who weighs 95 kg (210 lbs) and is 1.778 m (70 in) tall has a BMI of 30.1 and a weight status of “obese.”

WHAT BMI IS NOT

A common misconception is that BMI is a measurement of body fat. Because BMI does not consider body composition (proportion of fat and lean body mass), the BMI ranges shown above can falsely classify a body builder as obese. For example, when Arnold Schwarzenegger won the Mr. Olympia title, his BMI was 30.6. On the other end of the spectrum, a petite, sedentary woman who has a BMI of 23 can appear to be healthy because she is not overweight. However, her body fat could in reality be 35% and her risk for disease high.

By itself, BMI is not a complete measurement of health or fitness. To get a more comprehensive assessment, other measurements to consider are waist circumference and body fat percent. Body fat percent can be measured by an experienced health and fitness professional using skinfold calipers. If you do not have access to a fitness facility that offers body fat analysis, BMI along with waist circumference is a useful place to start to determine your risk for obesity-related health problems. Waist circumference is measured at the smallest part of your torso below your rib cage and above your hip bones. A measurement of less than 35 inches for women and less than 40 inches for men is ideal.
**I HAVE CALCULATED MY BMI, NOW WHAT?**

Regardless of your BMI number, evaluating your eating habits and exercise routine can always be beneficial. Even if your BMI is in the healthy weight range, assessing the quality of your nutrition and physical activity and then making healthy changes accordingly can make a tremendous difference in your health and how you feel.

If your BMI is 25.0 or higher, you could be at a higher risk for health-related problems/diseases, fatigue, and joint pain. Being overweight can cause stress on the joints, contribute to a joint bleed and lead to osteoarthritis. In fact, being only 10 pounds overweight increases the force on the knee by 30-60 pounds with each step. Losing weight through sound nutrition and exercise is a great way to keep your health and joint pain in check.

To improve eating habits, a great question to ask is “how can I eat to reduce inflammation?” One key place to start is by reducing and working toward eliminating added sugar. The obvious sources of sugar are candy, pastries, juice and sodas. Some less obvious foods include breakfast cereals, nutrition bars, flavored yogurt, condiments, most packaged snacks for kids, and many foods labeled as non-fat or low fat.

Reading the nutrition facts and ingredients list on the foods you buy will be the best way to know if you are getting too much sugar. In the ingredients list, look for the different names for sugar such as corn syrup, high-fructose corn syrup, molasses, and maltodextrin. On the nutrition facts, look for the number of grams of sugar which should be 5 grams or less per serving. In addition, limit daily sugar intake to 25 grams for women and 37.5 grams for men.

The benefits of weight loss include lower blood pressure; improved sleep apnea; reduced risk of chronic diseases such as heart disease, stroke, cancer and diabetes; reduced inflammation and pain; increased energy; improved mood; and more visible veins. This last benefit is especially pertinent to members of the bleeding disorder community, because with easier-to-find veins, it is possible for the infusion process to go more smoothly.

Strength training can aid in weight loss as well as provide other benefits, including stronger bones, reduced risk of osteoporosis, a boost in stamina, and healthier joints. Strength training helps to make the muscles around the joints stronger thus making the joints more stable and less painful. Having strong muscles can also lower your risk of injury and therefore help to prevent joint bleeds.

*Before beginning any new activity or, or if you are having joint or bleeding problems, make sure you check with your physician or physical therapist.*

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**TAKE HOME MESSAGE**

Calculate your BMI and start making healthy changes accordingly. Before you know it, you’ll be healthier, moving easier, have more energy and feel better overall.

Check out HFA’s Get in Gear app! Enter your height and weight and the app automatically calculates your BMI. Track all of your physical activity too!!

Michelle Morath is the owner of JourneyFit, LLC, www.journey-fit.com, in Albuquerque, New Mexico. She is currently enrolled in the Doctor of Naprapathy program at the Southwest University of Naprapathic Medicine. She was awarded a Bachelors of University Studies degree with emphasis in Exercise Science and Business, summa cum laude, at the University of New Mexico in May 2010. Michelle has been a nationally Certified Personal Trainer since 2003 through National Strength & Conditioning Association and since 2004 through National Academy of Sports Medicine. She is certified as a Corrective Exercise Specialist through National Academy of Sports Medicine. Michelle strongly believes that, through appropriate exercise and nutrition, anyone can improve their quality of life and rejuvenate.

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John and Carol Reed

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Congratulations to the 2015 HFA Scholarship Winners!

Each year, HFA awards scholarships to promising students in the bleeding disorders community. In order to better serve the students in our community, in 2015 we awarded 4 scholarships (instead of 10) for an increased amount of $2,000-$4,000 (instead of 1,000 each) in three categories:

- Educational Scholarship
- Parent/Sibling/Child Educational Scholarship
- Medical/Healthcare Services Educational Scholarship

We are thrilled to announce the 2015 HFA scholarship winners! Learn more about these rising students and their dedication to make a difference in the bleeding disorders community!

Haylee
HFA Educational Scholarship | $2,000 | Anderson University

Art has always played a huge role in my life. With this scholarship I will be able to continue my education and study ceramics. I work at a summer camp for kids with bleeding disorders and I would love to be the arts and crafts director one day and be able to share my love of art with the kids there.

Amber
HFA Parent/Sibling/Child Educational Scholarship
$2,000 | LSU Health Sciences Center Shreveport (LSUHSC)

The hope and resilience of the bleeding disorders community inspired me to go into medicine. I’m looking forward to serving my community and providing empathetic care for my patients throughout my training in medical school, residency, and for the rest of my life, so that I might instill that same hope in all of my patients.

Trevor
HFA Educational Scholarship | $2,000 | Belmont University

Knowing that the hemophilia community is backing up my decision to pursue my music career in college is very reassuring. I am very excited to improve my musical skills, and share my talents with others.

Malia
HFA Medical/Healthcare Services Educational Scholarship | $4,000
University of Colorado, Colorado Springs (UCCS)

My goal of becoming a physician’s assistant began when I became involved with the hemophilia community because of my diagnosis of a bleeding disorder. I want to share my passion for helping others who suffer from similar disorders and help educate society about the help that is available.

Learn more about educational scholarships for the bleeding disorders community: www.hemophiliafed.org
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**Thank You!** Your support makes it possible to serve our community nationwide!

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**Living with Hemophilia: A Young Adult Perspective**

An interview with Dakota Rosenfelt

The transition to adulthood is an exciting time for any young adult, and can include living on their own for the first time, beginning a job, or starting a college/higher education experience. However, this also means young adults must learn quickly how to juggle the inevitable increase of personal responsibility.

Dakota, age 20, is a PharmD student at the University of Missouri—Kansas City’s School of Pharmacy. Dakota shares in the below Q&A:

- How he balances all these new responsibilities as a young adult living with severe hemophilia.
- Why he chooses to stay involved in the bleeding disorder community.
- How having a bleeding disorder has helped direct his career path in college.
- Offers important advice for other young adults living with a chronic condition.

**Q.** What kind of a bleeding disorder do you have? When were you diagnosed?

**A.** I have severe hemophilia A. Suspicion that something wasn’t right began when I was 4 months old due to the heavy amount of bruising which started showing up all over my legs. After many visits to the pediatrician and an interesting encounter between my parents and DFS (Department of Family Services; they actually thought my parents were beating me profusely) my final diagnosis came at 13 months old!

**Q.** What was it like to live with a bleeding disorder growing up?

**A.** Growing up with a bleeding disorder wasn’t terrible at all. From a young age, I knew there were certain activities, such as wrestling or football; I would never be able to participate in. I learned to compensate by doing other things, which essentially meant that I spent a ton of time outside (I was never good at video games so we will leave that area uncharted) either lifting weights, running, or swimming with friends and my family.

**Q.** How has a bleeding disorder influenced your career?

**A.** My bleeding disorder practically steered me in the direction I am currently going in with my career. This fall I will start classes at the University of Missouri—Kansas City School of Pharmacy and am eagerly pursuing a Doctor of Pharmacy (PharmD)! I considered myself amongst the lucky ones who knew what they wanted to pursue as a career in my high school years. A majority is thanks to my involvement with the bleeding disorder community from when I was diagnosed.

**Q.** Studies have shown that “healthier bodies bleed less.” What do you do to stay healthy?

**A.** I like to think I live a relatively healthy lifestyle. I work with weights as well as doing some form of cardio 5 days a week, and I am pretty well disciplined eating healthy most of the time (unless it’s around the holidays, but again, we won’t get into things I’m bad at). Many of these activities tend to put a lot of heavy strain on my joints, to compensate I infuse on a “prophy” schedule three times a week to prevent any unwanted (but really, when are they wanted?) bleeds.

**Q.** Recently you created an app, called HemoTool. What was the idea and purpose behind it?

**A.** Initially, HemoTool started as a project I intended to use for myself and only myself. However, the more functionality I put into it, the more I decided it could be used to help many other people who live with bleeding disorders (including their caregivers). Yes, I knew there were already apps out there, but none of them seemed to work for me. In an industry where choice is being progressively lessened to patients dealing with a bleeding disor-
der, offering up HemoTool to people as a free download and more choice would mean I was doing my part to give back to the community and help people (and their caregivers) better manage their condition. For those that aren’t aware, HemoTool is a simple, “click and go” solution to logging bleeds and keeping track of their infusions. Not only does it allow users to log any treatment, but it also enables them to order new medication from their pharmacy, submit logs to insurance companies/physicians, and locate an HTC when on the go anywhere within the US! It’s been a project of mine for quite some time, and I’m thankful to watch it start to really take off.

Q. Why do you choose to stay involved in the bleeding disorders community?

A. Staying involved in the bleeding disorder community isn’t always easy with regards to strenuous schoolwork and obligations in my personal life. However I always find time to give back to a community, which has given me so much over the years. I wouldn’t be the person I am today, if it hadn’t been for the way some of the great role models in this community have molded and shaped me.

Q. If you could give advice to a new parent of a recently diagnosed child, what would it be?

A. The first thing I want them to know is this: you are in great hands and I promise we don’t bite. Everyone involved in the bleeding disorder community, be it the caregivers, the physicians, or even other people living with the condition, is there for you at any time. Get involved in a local chapter and reach out to other families for support; it’s comforting and shows how little you are actually alone. Yes, I will admit, it is a bit overwhelming at first, but with all of the resources available it will be easy to recognize this community is much more of a family than meets the eye. Now, the family might have some crazy aunts or an unruly cousin twice removed, but what family doesn’t?

Q. If you could give advice to a teenager with a bleeding disorder not involved in the community, what would it be?

A. GET INVOLVED! With all of the opportunities around, getting involved whether it be through volunteering at a local camp, volunteering at a fundraiser, or writing for one of the many newsletters, there are tons of ways to get involved and be heard. Any form of leadership you can acquire makes you stand out as a leader and mentor to the younger kids in the community, which is a feeling that can’t be mimicked. The worst thing anyone can do is live with regrets, and not being involved as the ever-growing success of our community becomes more and more evident is something anyone will truly regret.

Q. What does our community’s history mean to you?

A. The bleeding disorder community is as a great example of getting back up after being kicked down. The HIV/AIDS epidemic in the 1980s affected everyone with a bleeding disorder and their loved ones in so many ways. As the years went on, those who survived discovered the true meaning of life and moved on to advocate for the future generations of “Bleeders.” They now show the world “We are still here, and we won’t be giving up that easy.” Stories like that make me appreciate this community in a whole new light, and it’s one I’m proud to say I’m a part of.

Q. If a magic wand could take away your bleeding disorder, would you do it. Why or why not?

A. Absolutely not. Having hemophilia has shaped me, it has given me direction in life and most importantly it has given me a great group of life-long friends. Taking away my hemophilia would be like taking away a part of me. Not just any part either, but one of the most important ones which makes me who I am.
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