PEN

inside

Problems in Paradise?

Hemophilia in Our "51st State"

Laurie Kelley

Mention Puerto Rico–a tiny island jewel in the Caribbean Sea–and wait for the sighs and dreamy looks. Sunny weather, white beaches, friendly people, delicious food, world-class rum–what's not to like? Puerto Rico was voted best place in the Caribbean to visit by more than 250,000 readers in *Caribbean Travel + Life's* "Best of the Caribbean" Readers' Choice Awards.[1] A small tropical paradise about the size of Connecticut, Puerto Rico is a short flight from the US–where English is spoken, the US dollar is currency, and you don't need a passport. Take that, Canada!

Puerto Rico is often called our 51st state, and indeed Puerto Ricans are Americans.[2] As a US territory, Puerto Rico enjoys many benefits provided by the American government: we handle its foreign relations, defense, postal service, and customs. Residents do not have to pay US federal income tax–but they don't get to vote, either. The US is the island's largest trading partner, importing apparel, electronics, rum, and pharmaceuticals. In fact, because of lucrative tax incentives, over half of the world's leading pharmaceutical companies have manufacturing operations on the island.

And compared to the other Latin American countries, Puerto Rico stands tall: it has a long life expectancy, an educated workforce, and only Argentina is slightly higher in gross domestic product (GDP) per capita–a measure of a country's wealth.[3]

But not all is perfect in paradise. Puerto Ricans are Americans, but do they enjoy the same standards of hemophilia care that we do in the States? What's life like if you have hemophilia on *La Isla del Encanto*? Maybe not so enchanted.

Return Voyage

I first visited Puerto Rico in 1998, after receiving a call for advice from Yolanda Vega, a young mother of a child with hemophilia who was paying $300 a month out-of-pocket for

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1. Kitty Bean Yancey, "What's the Best Overall Caribbean Destination?" *USA Today*, Feb. 10, 2011. 2. Puerto Rico became a US territory following the Spanish-American War in 1898; its residents became US citizens in 1917. It has been a US commonwealth since 1952. 3. https://www.cia.gov/library.

Photos: LA Kelley Communications

welcome

Laurie Kelley

Laurie with Johnny Márquez of APH and a local hemophilia family

I've traveled to more than 25 developing countries in the past 16 years, trying to help find ways to improve hemophilia care. Often this means working directly with the national hemophilia nonprofit organization, or even helping to found a nonprofit if one doesn't exist. I enjoy doing this charitable work overseas, but sometimes charity begins at home.

Puerto Rico is "home," one of our national treasures: a small, sparkling island in the Caribbean, a frequent destination of honeymooners and corporate sales meetings. But I learned in 1998 that Puerto Rico is not a honeymoon location for hemophilia. After my first visit in 1998, I did see progress–home therapy was introduced, and new products–under the leadership of several young parents of children with hemophilia. But since about 2005, progress has slowed. Patients are leaving the island to come to the States for treatment–a difficult move, and not always the best one.

It's time we looked at healthcare for *all* Americans, even those in US "possessions" such as Puerto Rico, Guam, and Saipan. We have an obligation to see that these Americans do not suffer needlessly. My feature article paints a portrait of hemophilia in Puerto Rico: How much factor do the residents get? Who pays for it? What happens when a child with hemophilia transitions to adulthood? How are inhibitors handled? What's the single biggest challenge facing hemophilia healthcare in Puerto Rico today?

I'm pleased to say that as a result of my recent investigative visit to Puerto Rico in April, I've been invited back by the patient hemophilia association on August 18 to start working on a national strategy to improve care. It's an honor for me, and a way to serve our own country and people. And as always, I know I'll find that I receive much more than I give. Puerto Ricans are warm, friendly, hard-working people who are proud of their heritage. It's a pleasure to work with them, and for them. I hope our feature article in this issue of PEN is a new start for Puerto Rico. *Bienvenido a un futuro brillante con muchas opportunidades*–welcome to a brilliant future with many opportunities.

inbox: see page 15

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as i see it

Osvaldo Ocasio Rodriguez

Yo Soy Americano: Living in Puerto Rico with Hemophilia

LA Kelley Communications

"I am an American": Osvaldo Ocasio struggles with hemophilia in Puerto Rico

As Puerto Ricans, are we truly American citizens, and do we have rights? For a person living with hemophilia in Puerto Rico, like me, these are questions that make you wonder. Unfortunately, suffering from severe hemophilia A with inhibitors, the message I receive from my health-care providers and health insurance representatives is that the level of healthcare that can be provided depends on the cost of the factor. This means using a less effective factor for me because it costs less, although it will be costlier in the long run because more doses will be needed. Every time a nurse or doctor comes to see me, they remind me of how expensive my medication is.

I'm writing this article while admitted at the only hemophilia treatment center (HTC) in Puerto Rico, the Hospital Universitario Centro Médico de Puerto Rico. I have compartment syndrome–a bleed in a muscle in my forearm that has swelled, and is putting pressure on the blood vessels and nerves in my arm. It's June 9, 2012. My forearm has been cut open from wrist to elbow to relieve the pressure. I've been here for 29 days, and I haven't received any kind of factor for the past five days. When I ask why, there is always some excuse: the pharmacy hasn't bought it, or the doctor hasn't posted the order to the chart. I may not be the only patient under the staff's care, but I expect to be treated responsibly. How many times have I requested to speak to a doctor, and they send some young intern who has no clue how to treat the situation and tells me, "Let me consult and I'll get back to you." Meanwhile, my treatment is not progressing, and it may take 24 hours to have an answer to my questions. Waiting to administer the factor has put my life in jeopardy.

Does the price of factor determine my health and well-being, or am I entitled to the same rights as other Americans? Although we are Americans, it's like we are the ugly duckling or the black sheep of the family. I know they have factor in the hospital pharmacy, but they want to save it only for my upcoming surgery because of the cost.

Compare that to the experience I had in New York City in 2008. I left Puerto Rico to seek a knee replacement, following a doctor's recommendation, because there was no hematologist specializing in inhibitors on the island. In New York, I started the long process of having my two knees replaced, after a battery of studies and tests. I had the first knee replaced in January 2010, receiving NovoSeven®RT every two hours for several months of rehabilitation.

That same year I had the second knee replacement in May, and I was very surprised by the personal care, pain management program, facilities, and equipment available for me. It was like checking into a hotel–better yet, because I was getting the best treatment available in the States, like the rest of the hemophilia population living in the US. After the second knee replacement, I learned that my bilateral knee replacement cost a little over $6.2 million. But that's nothing compared to the chance of walking normally again and a much-improved quality of life. In the States, no one badgered me about the cost of treatment. No one constantly reminded me how expensive my treatment was. The treatment was supplied, without making me feel that I was not worthy of it. That's the big difference between being a Puerto Rican with hemophilia, living in Puerto Rico, and being an American with hemophilia, living in the States.

Osvaldo Ocasio Rodriguez is 27 and lives in San Juan, Puerto Rico.

Jo Schaffel

ITI: Will Budget Constraints Prevent Access?

An inhibitor diagnosis is stressful and scary. We're fortunate to be living at a time when bleeds with inhibitors can be treated successfully, and sometimes inhibitors can even be eradicated. But will all of our options remain available, as healthcare costs continue to rise, and as the US healthcare industry undergoes reform?

People with inhibitors often suffer more complications related to bleeds than those without inhibitors. Bypassing agents, though they can control bleeds, are not as effective as treating bleeds with specific factor VIII or IX concentrates in the absence of inhibitors. For this reason, the best option is to eradicate the inhibitor so factor VIII or IX can be used to treat bleeds. Once the inhibitor is eliminated, patients can use normal doses of factor prophylactically, so the body "remembers" factor and doesn't target it for destruction.

Inhibitors can be reduced or eliminated through various treatment protocols collectively known as immune tolerance induction (ITI).[1] ITI involves frequent, regular infusions (typically daily) of the missing clotting factor, to try to *tolerize*, or train, the patient's immune system to accept the factor instead of destroying or deactivating it. ITI is expensive because it requires extraordinarily high doses of factor, and it may take several months or a year or more to induce tolerance. ITI also involves many blood tests and doctor or hospital visits. But when ITI is successful, it produces a significant lifetime cost savings, as well as a longer life span and greatly improved quality of life.

But what if ITI weren't an option? What if your insurance company or a government agency decided that ITI was too expensive, and refused to offer it as a treatment? Sadly, as you can read in our feature article, this is the case in Puerto Rico, a US territory. That's right–believe it or not, some American citizens can't obtain ITI as a treatment.

A proven track record

The concept of ITI to eliminate inhibitors has been around for almost 40 years. ITI was first used successfully in 1977 in Germany. A patient with a high-titer inhibitor was treated with high doses of factor VIII and aPCC.[2] His bleeding was brought under control, and his inhibitor was reduced. Additional patients then received this treatment protocol with a good success rate. aPCCs are no longer used for ITI. Between the late 1970s and 1990, patients received plasma-derived factor concentrates for ITI. Today, in the US, recombinant concentrates are most commonly used for ITI.

Studies are ongoing to determine the most successful protocols for ITI: how much factor to give, which type of factor to use, how often to dose, and for how long. It is known that ITI is more successful when implemented soon after the inhibitor is diagnosed and when the inhibiter titer is less than 10 Bethesda Units (BU).

> "We would be devastated if we were told we could not engage in a treatment regimen that might get rid of our inhibitor, due to insurance issues."
>
> —A. D., Arizona

Money matters

Unfortunately, ITI is not successful in 20% to 40% of patients. If ITI does not eradicate the inhibitor, or if ITI is unavailable, then the patient must continue to treat bleeds using expensive and less-effective bypassing agents.

Budgetary concerns about ITI are real. ITI can use $3,000 worth of factor per day, for months. A course of ITI for a five-year-old may exceed $1 million. Some governments or insurance agencies may consider ITI too expensive; they may prefer short-term cost containment over longer-term medical strategies. So patients who live where budgets are tight may not be given a chance to see if their inhibitor can be eradicated.

> "I am concerned that with the continued changes with insurance–this may become a real issue in our lives and in the inhibitor community."
>
> —C. N., Maryland

How will treatment decisions be made?

With all the turmoil in the US healthcare industry today, many people fear that profits, rather than medicine, will have an increasing influence on treatment decisions. This is already

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1. Immune tolerance induction is sometimes called immune tolerance therapy, or ITT. 2. Activated prothrombin complex concentrate (aPCC) is a type of bypassing agent that contains several clotting factors.

richard's review

Ann Woodruff

Richard J. Atwood with Zoraida Rosado

Vampiros y Hemofilia

hemophilia & vampir

Jóvenes Vampiros: El códice secreto / Young Vampires: The secret codex
Texto e ilustraciones de José Aguilar (2007)

¿En qué creemos? Como individuos, nuestras creencias son muy variables. Por ejemplo, ¿Creemos que habrá una cura para la hemofilia un día? ¿Creemos en el romance eterno? O tal vez incluso en los vampiros? Nada parece imposible cuando creemos.

Autor español e ilustrador José Aguilar pide que creamos en todas estas cosas, mediante el uso de nuestra imaginación. Aguilar escribió su novela para adultos jóvenes, Jóvenes Vampiros, y luego dibujó las ilustraciones vívidas. Para despertar el interés del lector, Aguilar incluye una joven protagonista femenina que tiene hemofilia, además un diabólico vampiro, que frustra la relación de la pareja romántica.

La historia es narrada por el monje Fray Filippo de Ansua, que de alguna manera ha adquirido un cuaderno y dibujos de Leonardo da Vinci. El romance comienza cuando el joven Marco Tulio, de la noble casa de Padutti de Verona, jura un compromiso secreto de amor con su hermosa prima lejana, Isabel. Sellan su ceremonia romántica pinchando sus dedos en un tallo de la rosa y luego la mezcla de su sangre.

Trágicamente, Isabel es hemofílica, con hemorragia imparable. Pero, afortunadamente, su familia conoce a Leonardo da Vinci, que es capaz de detener la hemorragia. Sin embargo, el malvado vampiro Tristán de Padua, señor del castillo de Monenero, convence a Marcos que Isabel se puede curar para siempre de la hemofilia si es mordida en el cuello. Esto da lugar a engaño en la muerte de Isabel–y los medios que ella no es santa, no puede ser enterrada en el cementerio.

Marco se aflige por cinco años por su amor fallecida antes de planear su venganza. Él se enfrenta al malvado vampiro Tristán en el carnaval de Venecia, acusándolo de asesinato. Cuando Tristán hunde sus colmillos en el cuello de Marco, el vampiro muere repentinamente––porque Marco ha envenenado a su propia sangre. Añadir a la tragedia, Marco luego se quita la vida. En su honor, Leonardo da Vinci esculpe un monumento de los dos jóvenes enamorados cogidos de la mano sobre sus tumbas rodeadas de rosas rojas.

Cuando se lee la lectura de ficción, no tenemos que creer todo lo que escribe el autor. Podemos disfrutar de la historia al mismo tiempo de ser crítico. Esta trágica historia, el amor de ficción, que incluye a un personaje con hemofilia, vale la pena leer. Por supuesto, sabemos que Leonardo da Vinci no tenía un tratamiento para la hemofilia, aunque la historia era más interesante con esa sugerencia. Pero todavía hay una lección: para nuestro propio cuidado de la hemofilia, hay que tomar decisiones sólidas basadas en la evidencia científica, porque cuando estamos bien informados, podemos tomar mejores decisiones.

We've printed Richard's Review in Spanish, the original language of this young adult novel. Download an English copy of this review on the LA Kelley website: www.kelleycom.com under Publications Archives.

PROJECT SHARE
It's time to give back

Zoraida Rosado

No Place Too Far: Saving a Life on a Remote Island

Little Toakau Teraira, who has just turned four, can't stray far from his small home on Christmas Island in the Central Pacific without one of his parents ushering him back to relative safety. You might call Toakau's parents overly protective, but you can't blame them. Both of Toakau's brothers died of uncontrollable bleeding, and Toakau is the last remaining son.

Because Toakau has severe hemophilia A, he needs to avoid the crashing surf and watch out for sharp coral sticking out of the atoll sand. Prompt treatment is difficult on a remote island. But although Toakau must be cautious when playing, he is blessed in one respect: his father, Bangao Teraira, is the medical doctor on Christmas Island.

Faraway Care for Chronic Disorders

The Terairas' home is in one of the most remote places on earth: 1,200 miles south of the Hawaiian Islands and 1,000 miles north of Tahiti.

Christmas Island and its two neighboring islands, Tabaurean and Teraina, are home to more than 10,000 islanders, isolated from the rest of the world in every sense. Their country is called the Republic of Kiribati (pronounced *Ki-ri-bass*), and consists of 31 atolls strewn across the equator for more than 2,000 miles. The capital of Kiribati is Tarawa, more than 2,000 miles from Christmas Island.

Dr. Desiree Medeiros (left), with Toakau and his mom, Taan

Most islanders live a subsistence life, catching fish and harvesting coconuts. Supply ships don't visit Christmas Island often, but an Air Pacific flight touches down weekly. A monthly air cargo flight from Honolulu brings basic supplies, and a small cargo sailing vessel calls at the island about four times a year.

No factor, or even cryoprecipitate, is available on Christmas Island. Late last year, Toakau's uncontrollable internal bleeding was stopped only by massive infusions of whole blood, administered by his father. But Dr. Teraira knew that life couldn't continue this way for Toakau, who had already lost his two brothers: one to a large hematoma and the other to an intracranial hemorrhage. A male cousin and an uncle also died from uncontrolled bleeding.

There was no educational material about hemophilia anywhere in Kiribati, and no factor concentrate to keep Toakau alive. But thanks to the efforts of dedicated people and several organizations that rallied to help, this story has a happy ending.

Developing a Network of Aid

Dr. Teraira, a modest and compassionate physician, was initially reluctant to ask for help for his son because–as he told us later–"There are so many in our small country who are suffering and need help,

Toakau with his parents

and I didn't want to ask for myself." But his wife insisted he reach out to his colleagues, and that's what he did.

First, Dr. George Buchanan, a renowned hemophilia specialist, offered to help Toakau at the University of Texas Southwestern Medical Center; but he recommended that Toakau be taken instead to Kapi'olani Medical Center in Honolulu because it's closer to Christmas Island, and Toakau could be treated by one of Buchanan's former students, Dr. Desiree Medeiros.

So on February 16, Toakau arrived at Kapi'olani Medical Center with an ear bleed. After testing, he was diagnosed with severe hemophilia A and treated with factor. The next day, social worker Chanel Galario began searching for life-saving medicine for Toakau to bring home with him. Taokau had already had several bleeds in his ankle, elbows, and knees, and now his family was looking for a way to treat at home and save on the cost of travel to Honolulu.

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Yolanda Vega, first president of APH, and husband René, co-founder

factor. This didn't sound right, and I knew we could find a solution; sure enough, a few phone calls later, we had removed her monthly copay. But this experience led us both to question what else was amiss in Puerto Rico. By coincidence, I was headed for the nearby Dominican Republic at the time, and decided to take a side trip to Puerto Rico. I wanted to meet Yoli and also satisfy my own curiosity: for months, bulk shipments of my newsletter PEN had been returned from the Puerto Rican Hemophilia Association (Asociación Puertorriqueña de Hemofilia [APH]), and no one was answering my emails or calls. It seemed that no one knew what was happening in Puerto Rico, not even parents like Yoli.

Yoli and I met with the medical team at Hospital Universitario Centro Médico, the main public hospital in San Juan, the capital. I was surprised to learn that hemophilia patients had access to only a plasma-derived product, while State-side Americans had been using both plasma-derived and recombinant products for five years. I was told by Dr. Pedro Santiago-Borrero, chief hematologist, that recombinant products were too expensive for their tight healthcare budgets. Within months, Yoli resurrected the defunct APH, became president, and lobbied for access to all products. Within a year, she had secured program funds, started a camp, and initiated scholarships. The first Puerto Rican patients began using recombinant products within two years after Yoli became president. Puerto Rican citizens with hemophilia also began attending National Hemophilia Foundation (NHF) meetings in the States. Problems solved. Life was good again.

When Yoli and her husband René left Puerto Rico in 2007 to enroll their children in high school in the US, I checked in periodically with new APH president Johnny Márquez, and all seemed well. But as a consultant–even volunteer–it's best to be at ground zero to assess what's happening. And I felt emotionally and professionally vested in Puerto Rico, which by then had fallen off the US hemophilia community's radar. So I made a return trip in April 2012, and brought with me

Johnny Márquez, current president of APH, and father of a son with hemophilia

Zoraida Rosado, my assistant of nine years, because–conveniently–she's Puerto Rican and speaks fluent Spanish. We stayed a few days, meeting with APH, the Centro Médico team, and some pharmaceutical representatives, and also traveling to patients' homes. As we delved deeper into hemophilia in Puerto Rico, what we discovered both pleased us and perplexed us.

Snapshot of Puerto Rico

Puerto Rico is 110 miles long and 35 miles wide, with almost 300 miles of coastline and beaches. With a population of 3.8 million, it's considered one of the most densely populated regions in the world. First discovered by Europeans when Columbus annexed it to the Spanish Empire, Puerto Rico is populated by a beautiful blend of Span-

Hospital Universitario Centro Médico, the only HTC on the island

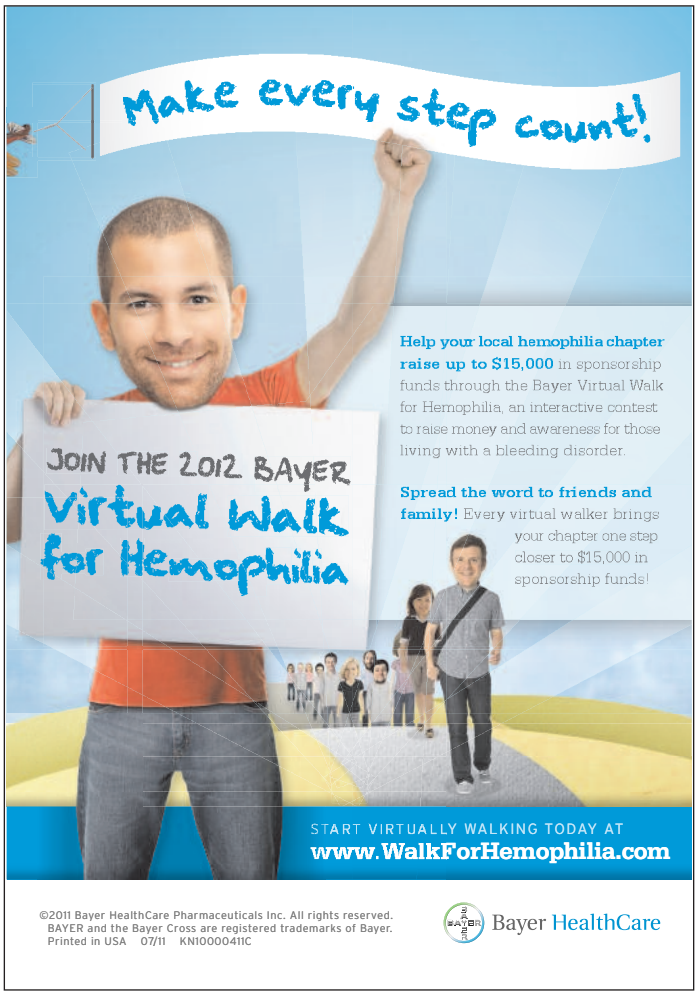
LA Kelley Communications president Laurie Kelley (far left) and assistant Zoraida Rosado (second from right) meet with HTC staff

ish, native Taíno Indian, and African. The island that's produced Latin superstars like Ricky Martin, Jennifer Lopez, and Marc Anthony also produces more Miss Universe pageant winners per capita than any other country.

Literacy is high: over 94% can read and write, and most Puerto Ricans are bilingual, with Spanish the primary language. About 97% are Christian, owing to the island's Spanish heritage. Despite the dense population, the birth rate is dropping.

In a population of 3.8 million, 3 to 4 babies are born every year with hemophilia in Puerto Rico, compared to 300 to 400 in the States. Currently, an estimated 250 Puerto Ricans have hemophilia. But unlike in the States, an astonishing 95% of these patients are registered. Dr. Santiago-Borrero proudly states, "The Centro Médico knows 94% of all who have been born with hemophilia [in Puerto Rico] in the past twenty-five years."

Dr. Santiago is most proud of the Centro's pediatric program, which has about 26 registered teens and 74 registered pediatric patients. Only about 30 inhibitor patients have been known during the past 30 years; currently there are about 8. Independence seems encouraged: parents get a hemophilia ID card to enable safe travel overseas, are offered classes for home infusion, and often infuse at home. Home infusion was an important legacy of Yoli's tenure as APH president.



If you lived in Puerto Rico instead of the United States, you would...

- Make 63% less money
- Have a 34% higher chance of having a baby die in infancy
- Have a 29% higher chance of being unemployed

Source: www.ifitweremyhome.com

The Centro Médico is the main treatment center for the island, and most hemophilia patients go there for treatment with plasma-derived products, recombinant products, von Willebrand disease (VWD) products, and both kinds of bypassing agents (FEIBA and NovoSeven® RT). As I scanned the product registration sheet at the treatment center, it seemed to me that only one or two factor manufacturers dominate the factor concentrate market on the island. This isn't surprising. For such a small population, Puerto Rican government health agencies do what many countries do: they issue a *tender*. The government requests private bids from manufacturers for various classes of products, and then typically chooses the provider with the lowest-cost product in each class. It's not unusual to see first-generation recombinants dominate, or even third-generation products with lower market shares in the States. What doesn't sell well in the US may sell well in Puerto Rico.

But that's irrelevant to Puerto Ricans: most hemophilia patients do not pay for their products or their insurance. Unlike in the States, where about 27% of hemophilia patients are on Medicaid, a staggering 98% of Puerto Rican hemophilia patients are on Medicaid. And this is US Medicaid, administered in Puerto Rico by Puerto Rico Health Reform (often just called *Reforma* in Spanish), the government agency that provides medical and healthcare services to indigent and impoverished Puerto Ricans. But Medicaid funding in Puerto Rico operates differently than in the States. Medicaid funding in US territories is capped: territories receive a set amount and no more. If Puerto Rico's costs exceed the amount it receives for Medicaid, the government is responsible for 100% of the difference. Medicaid assistance for US territories

is severely underfunded, and has been for decades.[4]

Our sources in Puerto Rico estimate that only about three patients with hemophilia are using private insurance. That may sound enticing and even unfair–think of not having to pay the coinsurance and deductibles of private insurance. But dig a little deeper, and you'll find that providing products at no cost causes its own problems.

A Problem of Complacency

Ask the average Puerto Rican if she considers herself Puerto Rican first or American first, and chances are she'll say Puerto Rican. Puerto Ricans are proud of their rich heritage and culture. But they have a dual identity, for they are also Americans; Americans who do not vote, who are on the fringe. As healthy as the island looks when compared to the rest of Latin America, it's a different story when these Americans are compared to those in the States. Fully 45% of Puerto Ricans live below the poverty line, compared to 15.1% in the US.[5]

"We are a welfare state," explains Johnny Márquez, a lawyer who is also the father of a young son with hemophilia. "Hemophilia is a big problem here. The island pays a lot of money for healthcare. As long as factor is coming in and there are no complications, people don't ask questions about their healthcare." He says candidly, "We come from a mentality that we've been given so much through welfare, that if we raise questions, we may upset the authorities. They may take back what they have given to us for free. This is in the back of our heads all the time."

This belief was confirmed by many–business people, medical staff, patients–during our three-day visit in April. Rather than believe that healthcare is a right that they have earned, most Puerto Ricans live with complacency: they are grateful for what they have, but their mindset is not to rock the boat, not to complain, not to cause trouble. Contrast this with life in the US, where we tend to see healthcare as a right, and where patients are willing to fight the system to defend against what we consider inequitable or unfair healthcare laws or practices.

"Patients don't demand their rights here," agreed one pharma rep we spoke with. "Sometimes the payer does not approve the entire dose [prescribed by the doctor]. Patients think: 'It's free. They're giving me what they can.' They are afraid then to push, to question the medical decision."

I'm as Puerto Rican as...

The coqui is a tiny frog found only in Puerto Rico. Its image abounds in Puerto Rican culture and heritage, although it is not an official national symbol. When Puerto Ricans want to express their nationality, they say, *Soy de aquí como el coquí* (I'm as Puerto Rican as a coquí).

Milagros Rodriquez with son José (left), who needs an operation on his knees

We saw this when we visited Milagros Torres Rodriquez, mother of José, 12, who has severe factor IX deficiency. Milagros lives in a government-subsidized house in a quiet but densely settled neighborhood in the south of the island. Her entire family lives either with her or a few steps away. They all turned out to greet us, and offered a delicious lunch of home-cooked rice and beans. José travels to Centro Médico about every two months, a journey of two hours each way. He's one of the very few Puerto Rican patients on prophylaxis.

"I'm satisfied with the [hemophilia] treatment here," Milagros told us. But when her doctors recommended that José have knee surgery to reduce swelling from apparent synovitis, Reforma wanted her to pay $30,000. Why so much? She didn't know, and didn't question the amount. Instead, Milagros turned to a relative in Michigan and is trying to arrange surgery there, where she believes that it will be free.

One Island, One HTC, One Long Commute

Zoraida and I toured the island on Saturday, April 23, with Johnny and his wife Tammy. The long distances gave us a taste of how patients fare

4. According to the Center on Budget and Policy Priorities (CBPP), "in 2005, the federal government picked up only 20 percent of Puerto Rico's Medicaid costs. Even in 2010, which incorporated both a permanent but modest increase in the federal Medicaid funding cap for the territories, enacted in 2005, and a temporary increase in the funding cap under the 2009 Recovery Act, federal funding accounted for only 35 percent—or $364 million—of Puerto Rico's Medicaid costs of nearly $1.1 billion." CBPP says, "To help address this problem, the ACA [Affordable Care Act] raised the federal funding caps for Puerto Rico and the other territories—American Samoa, the Northern Mariana Islands, Guam, and the U.S. Virgin Islands—by $6.3 billion between July 1, 2011 and the end of fiscal year 2019. Puerto Rico is scheduled to receive the large majority of this funding increase—about $5.5 billion." See http://www.cbpp.org.
5. Sabrina Tavernise, "Soaring Poverty Casts Spotlight on 'Lost Decade.'" *New York Times*, Sep. 13, 2011.

with only one hemophilia treatment center (HTC).

"There are other pediatric hospitals on the island, but they don't treat hemophilia patients," explained a medical team member. One doctor, Nelson Robles, keeps factor in his hospital in the center of the country, at the Mennonite General Hospital in Aibonito, and some patients feel comfortable going there. But for most who need expert care, they must travel long distances to get to the Centro Médico in San Juan. Road conditions in Puerto Rico are variable; the main highways are generally in excellent condition, but many secondary roads are deteriorated.

Team Asociación Puertorriqueña de Hemofilia faces challenges but is determined to succeed

Not everyone owns cars, or multiple cars, and sometimes families must rely on relatives or friends to drive them. The families we met would love an HTC on the opposite side of the island, to cater to patients living far from the capital.

Inhibitor Patients without ITI

Perhaps the biggest surprise for us was learning how inhibitors are managed. The approximately eight patients with inhibitors can obtain bypassing agents, but inventory is limited. Worse, immune tolerance induction (ITI) is not an option. Indeed, it has never been implemented in Puerto Rico. And there is a prevailing mindset in the Puerto Rican medical community that this is not a problem.

"Only 5% of our patients have inhibitors," explained Dr. Santiago-Borrero. "Only two or three have a high titer. Most have a low titer, and we just give bypassing agents. By being conservative, we can avoid immune tolerance therapy. And if we just leave the inhibitor alone, [often] the inhibitor goes away."

ITI is the infusion of massive quantities of regular factor over a period of months to overwhelm and eliminate or weaken the inhibitor. If ITI is successful, patients can use regular factor VIII or IX instead of bypassing agents to treat bleeds. They also must remain on prophylaxis to keep the inhibitor from returning. ITI is often more successful when implemented soon after the inhibitor is detected–in most cases, when the patient is a child. But for people in developing countries, ITI is often prohibitively expensive. Nor does ITI guarantee elimination of the inhibitor (ITI is unsuccessful in 20% to 40% of attempts). When ITI is successful, lifetime costs are significantly reduced and quality of life is greatly improved. Yet Dr. Santiago-Borrero maintained, "Our survival rate is as good as any state and we have good results with our inhibitor patients."

And here is where Puerto Rican hemophilia care differs dramatically: ITI is accessible to almost everyone in the States. Dr. Leonard Valentino, a leading global expert on inhibitors, can't recall ever hearing of anyone denied ITI in the US–except for one adult–on the basis that it was too expensive, given the patient's weight. Typically, when a hematologist orders ITI as a treatment for inhibitors, both Medicaid and private insurance reimburse.

Not all patients would agree with Dr. Santiago-Borrero's statement about good results for inhibitor patients. Bypassing agents in Puerto Rico are often in short supply. The lack of bypassing agent inventory can be frightening. Osvaldo Ocasio Rodriguez, age 27, entered a Puerto Rican hospital just after our April visit, with compartment syndrome[6] in his left wrist. He texted us from his hospital bed: he had been admitted for 30 days so far. He claimed to have gone five days without factor, despite having inhibitors, with his forearm sliced open from wrist to elbow to relieve the pressure (see *As I See It*, p. 3). He sent us an extremely graphic photo of his splayed arm. "They are dosing me with 5 micrograms [of NovoSeven] every four hours," Osvaldo texted. "In New York City, where I was treated once, I received 11 micrograms every two hours. Here in Puerto Rico, when I ask for the proper dosage, the doctors tell me they don't have the money. They tell me they are the doctors, not me. But I tell them, you think I don't know about my condition but I do. I'm suffering."

Adults with Hemophilia? Good Luck with That

Osvaldo's situation highlights arguably the biggest problem facing hemophilia care in Puerto Rico: the lack of an adult HTC. The Young Adult Clinic at Centro Médico tries to cover patients aged 18 to 25, but eventually they must transition out. Technically, by age 21 patients must report to the hematology/

6. Compartment syndrome is caused by excessive bleeding within a muscle. The blood is retained in the muscle sheath, causing increased pressure, which can cut off the blood flow to an extremity and result in permanent nerve damage.

oncology department across the street, in a basement office.

One young adult complained to us, "You go from a private setting in pediatrics where everyone knows you, to an open setting combined with cancer and oncology patients. We're not a priority. People don't know you. They don't understand hemophilia. You don't see any experts on hemophilia because they don't see a critical mass of patients."

"It's depressing," said another. "It's very shocking. You see your friends across the street getting care, but you can't join them anymore."

One hematologist at Centro Médico told us, "I don't feel that they receive comprehensive care at the adult center. Patients prefer the pediatric ward here and not the adult ward there."

"You don't transition," noted one mother. "You go from a familiar group where people know your name to a place where no one knows you. Many of the adult patients don't keep going."

"It's true," agreed the Centro Médico social worker, Nora. "It's sad that after all these years, no one is adequately trained in adult [hemophilia] care [in Puerto Rico]. One doctor is, but he's far away and not everyone can get there. A lot of adults were lost because of lack of care."

Osvaldo said of the adult hematology/oncology ward, "They act like I am a stranger." He is now contemplating a move to the States for better adult inhibitor care.

Problem of Emigration

Osvaldo isn't alone. Economic woes, such as a 15% unemployment rate, have contributed to the ongoing problem of emigration. Today there are almost as many Puerto Ricans in the States as on the island.

Emigration to the States began after World War II, because of poverty, proximity, cheap airfares, US citizenship, and a campaign by the island government. Emigration continues as young people, often the most educated, set off to find jobs during depressed economic times. And if the birth rate continues to fall, the island will have a higher proportion of elderly, with the entire population naturally declining in the next couple of decades.

Puerto Ricans with hemophilia attend the APH annual meeting

Worse still for hemophilia is the brain drain: doctors and nurses emigrate to higher-paying jobs in the States. Puerto Rican hemophilia patients might one day be without staff not only for an adult HTC, but also for the pediatric center.

"Luchar por ella": Do you really want it?

Most of the challenges facing Puerto Ricans with hemophilia point to one major culprit: lack of money. Because payment for healthcare expenses depends heavily on Medicaid (through a restricted budget handed down by the US government), medical teams must constantly weigh decisions based solely on cost: which product to buy, how much to buy, and how to make so many dollars spread out to so many patients.

ITI is too expensive, and doesn't make it as a budget line item. Very few patients are on prophylaxis, says Johnny Márquez, due to cost. Bypassing agents are used sparingly. Johnny notes that once the prescribed number of vials of regular factor ordered for his son Sebastian was cut. When

Yadira Rosario de Barranjitas, a lawyer and mother of a son with hemophilia, tells patients to speak up for their rights

Sebastian was on prophylaxis, using 15 vials each month, insurance limited him to 12 vials to save money.

But another, less concrete culprit exists–Puerto Rican patients' lack of confidence, and their complacency. To succeed in bringing hemophilia care up to acceptable American standards, patients must first realize that they should organize and aim for higher standards of treatment. Citizens must try to lobby their government, or, in the words of Ricky Martin's pop song "La Copa de Vida," *luchar por ella*–fight for it.[7] One pharma rep advised, "Patients need to educate the payers about hemophilia, because right now, patients don't have enough of a voice with them." Even so, the desire for change smolders just beneath the surface.

At the APH annual meeting, held during our visit, a roundtable discussion of parents got animated, then

7. "The Cup of Life" was recorded by Puerto Rican singer Ricky Martin, and included on his fifth album, *Ricky Martin* (1999). It was the theme song of the 1998 Soccer World Cup, held in France. Composers: Desmond Child & Jerry Ray. Arranger: Luis Gomez Escolar. Lyricist: Robi Rosa.

heated, when the talk turned to changes the patients want, and what can be done to improve hemophilia care. Patients pointed fingers at healthcare providers, seated in the back of the room, and providers in turn pointed at patients.

Yadira Rosario de Barranjitas, a lawyer and mother of a son with hemophilia, stepped in to clarify. Using a microphone to ensure that all heard her at the friendly gathering, she stressed, "You *have* to advocate, *have* to be educated about hemophilia, and ask the right questions to get a good doctor and treatment." If you are waiting in the emergency department, she told the audience of families, "Tell staff, 'I must see a hematologist!'" She urged parents to stand up for their rights, but first, to know what those rights are.

Lobbying helped Puerto Rico back in 1998, after my visit, when Yoli Vega and her new team were able to secure recombinant products, even after initially being told there wasn't money in the budget. "No money in the budget" should be the red flag waved in front of APH that motivates it to stand up, organize its people, stamp the ground, and point its horns at the government.

Unfortunately, APH is not a registered nonprofit. This leaves it somewhat crippled–unable to take advantage of NHF's expertise and resources on advocacy for people with bleeding disorders; unable to be an effective patient-advocacy leadership organization.

Manufacturers want to help APH get organized and implement strategies to catapult Puerto Rico to a new level of care. But pharma's position on Puerto Rico needs to change, too. Most factor manufacturers view Puerto Rico as "Latin America" and not "US." This affects how pharma spends its marketing money. The US has the largest hemophilia market, at about $2 billion. Few of those dollars flow into Puerto Rico, because pharma doesn't consider the island part of its market. The Latin American divisions of factor manufacturers have much smaller budgets than their US counterparts. And without nonprofit status, APH can't accept charitable donations anyway.

But patients don't think in terms of markets or corporate cost centers. They simply want equitable, available care. Puerto Ricans don't want to be secondhand Americans–left behind, isolated, dependent.

Keishla, a girl with hemophilia and inhibitors, is the face of Puerto Rico's future

Keishla is one of the lucky ones. Rare already as a Puerto Rican with hemophilia, Keishla is the rarest of the rare–a girl with factor VIII deficiency and inhibitors. When we visited her home, Keishla was preparing for her high school prom that evening. Although her left ankle is a problem, she infuses with bypassing agent to treat any bleed. She normally stores about 9,000 IU at home. Her father still infuses her–a statement that unleashed a torrent of motivational comments from Zoraida and me about self-infusing–yet Keishla bravely traveled to Boston last summer to attend NHF's Inhibitor Educational Summit, with a grant from Novo Nordisk. Did she feel out of place? Not at all.

Although she lives on this small island–where soon she will not be eligible for the personalized care she receives at Centro Médico's pediatric hemophilia center, and where an inadequate budget can't always accommodate her inhibitor needs–Keishla told us that she does not feel isolated or hopeless, though she would like to meet other girls with hemophilia.

"There are more people interested about and active with hemophilia in the States," Keishla reflected. "But there's a lot of people with hemophilia who need help here too." And although she knows she is American, true to her heritage, she admits, "I feel like I am Puerto Rican first." Keishla is the face of a future that wants to bring the two hemophilia populations–both American–closer together, for understanding, support, and improved medical care.

headlines

SCIENTIFIC

Zinc Fingers

Shire and Sangamo BioSciences (Richmond, California) have entered into a collaboration and license agreement to develop a type of gene therapy for hemophilia, using Sangamo's zinc finger DNA-binding protein (ZFP) technology. ZFP technology uses a "cut-and-paste" operation to modify DNA in human cells. The zinc finger proteins, with a good copy of the gene attached, are designed to locate the defective gene in the cell, cut it from the DNA, and insert the correct gene. Production of stable levels of corrected human clotting factor IX has been demonstrated in mice, with restoration of clotting times to the normal range after a single, systemic administration of ZFPs specific for the factor IX gene. Why this matters: Gene therapy still holds the ultimate hope for curing hemophilia.

For info: www.sangamo.com

NONPROFIT

Walk On

The second annual Bayer Virtual Walk for Hemophilia helps support people living with bleeding disorders. Bayer HealthCare is offering sponsorship funds to National Hemophilia Foundation (NHF), its local participating chapters, and the international nonprofit Save One Life (www.saveonelife.net). Prizes for the top five participating local NHF chapters with the most virtual walkers: 1st place $15,000; 2nd place $10,000; 3rd place $5,000; 4th place $2,500; 5th place $1,000. Bayer will also award up to $30,000 to NHF's national office in New York City, and up to $7,000 to Save One Life. Why this matters: As donations become scarce, this is a great way for patients, parents, and pharma to come together to support bleeding disorder nonprofits.

For info: www.walkforhemophilia.com

NHF 64th Annual Meeting!

Orlando, Florida

November 8–10, 2012

Start planning now for NHF's annual meeting, "Mapping Our Future." Florida is one of the most popular destinations for NHF meetings, with many attendees extending their visits to vacation. NHF expects a huge attendance at this largest national gathering of consumers in the bleeding disorder community. Why this matters: NHF conferences are ideal places to learn about the latest treatments while connecting with many others in the community.

For info: www.hemophilia.org

GLOBAL

More Factor for Latin America

The therapeutic plasma protein market in Latin America expanded 56% between 2007 and 2010, reaching $987.7 million, driven by strong growth in the demand for factor VIII and IX, and IVIG therapies. Among 16 countries surveyed, Brazil accounted for the largest single market in Latin American, with 44% of the region's dollar sales, followed by Mexico (19%) and Argentina (10%). Baxter International was the Latin America sales leader in 2010 with 35% market share, followed by Octapharma (18%) and Grifols (10%). Why this matters: Increased availability of factor VIII and IX is good news for Latin Americans living with hemophilia.

Source: *IBPN*, March 2012

Team Sky's Dream Guy

Alex Dowsett, 23, of Essex, England, is trying out for the British Olympic team in both the time trial and the road race. He believes he could be the only person with hemophilia competing in this year's Olympics. Why this matters: Alex wants to spread the message to parents of children with hemophilia that with proper medical treatment, their kids can stay active.

For info: gatorade.co.uk/greenbottle

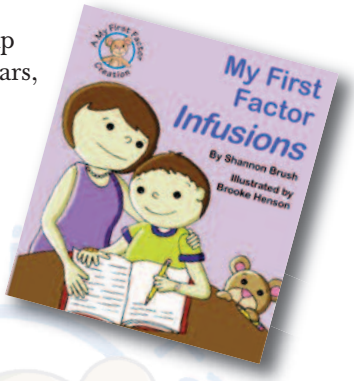
featured by LA Kelley Communications, Inc.

My First Factor series is designed to help young children, ages 18 months to 4 years, understand their bleeding disorder.

My First Factor: *Infusions*

What are the steps in an infusion? A first look for toddlers. Help your child with a bleeding disorder better understand the infusion process. By Shannon Brush, mother of a son with hemophilia. Illustrated by Brooke Henson. Published October 2011 by LA Kelley Communications, Inc. Sponsored by Factor Support Network.

To order: www.kelleycom.com



Inhibitor Insights... from p. 4

> "We have not had the experience of being refused ITI treatment. I can't imagine the addition of that stress on an already stressful situation!"
>
> —K. C., New York

happening in Puerto Rico. Will the rest of the US follow?

Almost all Puerto Rican hemophilia patients are on Medicaid and, unlike in the rest of the US, their Medicaid funds are capped. So physicians in Puerto Rico have a difficult choice to make: do they help one person with inhibitors by initiating ITI, possibly using up their entire budget? Or do they do what's best for the largest number of people, by supplying everyone with factor and helping the person with inhibitors as much as possible? Of course, these physicians know that eliminating the inhibitor through ITI is best for patients (and for long-term cost savings), but given their funding limitations, do they really have any other option?

"At what point does an insurance company have the right to step in and say, 'We're not funding this any longer,' or 'You can continue this treatment but we will no longer cover it'?" wonders C. N., who has two sons with inhibitors.

Help and advocacy

Even if your state or insurance company covers ITI, you may be concerned about cuts in insurance coverage: could this affect the decision to place a patient on ITI? You may also be confused about what will happen as healthcare policies change. Your local hemophilia organization can help inhibitor families like yours sort out insurance and treatment issues. You can keep up-to-date on the latest research on ITI and future possible treatments for inhibitors through meetings or Internet research. You can join others to help lobby to keep all treatment options available for everyone.

"We were never refused ITI," says Rachel G., "but I know that I would be in a panic and totally overwhelmed. It is stressful enough to deal with hemophilia itself and all that comes with it. I think we as a country need to start looking at what is best for people's health." Most families would agree with her.

Project SHARE... from p. 6

A few days later, after the Terairas had returned home, Project SHARE received a call from Carlton Smith, president of Pacific Islands Medical Aid, Inc., a small humanitarian charity that brings doctors, medicines, medical supplies, communications equipment, and other aid to Kiribati. He works closely with Toakau's father, he told us, and would be traveling to Christmas Island in a week. Could he act as courier to bring medicine to the family?

So on March 13, the Teraira family received a donation of factor from Project SHARE. And since then, we have been able to donate factor to Toakau twice, with the help of Carlton Smith and the many others who worked together to help a small boy on a remote island. Today, Toakau is doing well.

in memoriam

Carlos Fuentes

Latin American author whose son had hemophilia

Influential author Carlos Fuentes died May 15, 2012, at age 83. Born in Panama, Fuentes wrote fiction and nonfiction, plays, short stories, essays, and newspaper and journal articles. He was politically active in the causes of justice and human rights, and also served briefly as Mexico's ambassador to France. In its recent obituary, the *New York Times* called Fuentes "Mexico's elegant public intellectual and grand man of letters."

Like many writers, Fuentes was influenced by personal and family tragedy. His collection of essays, *This I Believe: An A to Z of a Life* (2005), is dedicated to the memory of his son Carlos Fuentes Lemus, born in 1973. Young Carlos, who had hemophilia, was a promising writer, photographer, painter, and director. He died May 5, 1999, from a blood clot in the lung during a transfusion.

–Richard Atwood

If you're already a fan of ours...thank you!

If you're not a fan yet, then come join us today to read publications, quarterly newsletters, HemaBlog posts, and other important updates concerning the bleeding disorder community!

Like us on Facebook

inbox

PEN May 2012

You do such a great job. We love PEN, and loved the update on gene therapy. Keep up the good work!

Ken Olson
Hong Kong

Thank you so much for giving us lots of information about new generations of medicine and gene therapy. I'm always interested in such subjects. I hope the gene therapy trials in hemophilia A will soon be undertaken.

Le Huu Hung
Vietnam

I was very impressed with the May issue. Fantastic content!

Aaron M. Flatt
Communications Coordinator
Bleeding Disorders Alliance Illinois

Project SHARE

I am so pleased that the 13 vials of BeneFIX have arrived in Mauritius. The little boy has started his treatment, and his parents are very thankful. He had missed over two months of school due to this bleed, and we are thrilled to have him under treatment and hope to have him back in school soon. Thank you for this considerate gesture.

Tatiana Bathfield
Hemophilia Association of Mauritius
Republic of Mauritius

We have received the factor IX for Antido Gabriel. Thank you for helping us.

Raymond Nanos
Blood Brothers Aid
Philippines

My brother Jimmy has used all of the factor that you sent. He is very well now. Thank you so much for your help to save him. God bless you all.

Chandra Galih Permana
Indonesia

I've finished with all academic work for my bachelor's degree! I'm now awaiting my graduation in June. Thanks for your faithful assistance [with factor donations], without which I would not have been able to make it this far. God richly bless you.

Emmanuel Agyekum Fofie
Ghana

On behalf of Haemophilia Society of Tanzania and Muhimbili National Hospital as a treatment center, we thank Project SHARE and LA Kelley Communications for the donation [of factor].

Dr. James E. Rwehabura
Hematologist
Muhimbili National Hospital
Tanzania

Parenting Moment

Familia is the very center of Latino culture. I don't feel the media has really seen that. It is the strongest thing about us and the most universal.
–Gregory Nava, filmmaker

I implore you to see with a child's eyes, to hear with a child's ears, and to feel with a child's heart.
–Dr. Antonio Novello

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