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Parent Empowerment Newsletter

Another Option for Venous Access in Children with Hemophilia:

THE ARTERIO-VENOUS FISTULA

Parents of young children with hemophilia face a challenging decision—how to best access small veins? With the rise of prophylaxis, many parents consider implanted devices like ports. Now there's a new option: the arterio-venous fistula, or AV Fistula. It's not a port or other implanted device—it's a surgical procedure that creates an enlarged, natural vessel that parents can access more easily. It's new to the hemophilia community, and it's worth exploring if your child has difficult-to-access veins, and you are not comfortable with the current options for venous access.

by
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CARING FOR A NEW BABY WITH HEMOPHILIA IS A DAUNTING TASK. BUT WHAT HAPPENS when the arrival of your baby is accompanied by the news that he has hemophilia? You must learn about this disorder, and the complex therapies needed to keep your child healthy and happy. You may feel anxious and fearful about hemophilia's many unknowns, while facing the practical medical challenges of caring for your baby. Most of all, you want to feel a sense of control over this disorder.

You can establish a real sense of control once you learn how to administer antihemophilic factor concentrate, or "factor." As parents, you will need to determine a plan for therapy with your doctor and nurse, and decide how best to administer factor to your child. You may choose to give episode-based factor infusions in response to each bleed–what we call "on-demand." Or you may choose prophylaxis–regular preventative injections when your child isn't bleeding. Learning to start an IV and give factor at home can be stressful. Yet once this skill is mastered, families soon feel a sense of freedom, independence and empowerment. Today, with prophylaxis treatment on the rise, parents must learn to do regular needlesticks. And parents of children with severe hemophilia may need to infuse their children daily.

Traditionally, parents of children who need regular factor infusions–whether for prophylaxis or immune tolerance therapy–have two options to deliver factor to the blood. First, they can use a simple needlestick with a butterfly needle (a process also called "peripheral venous access"). Increasingly, parents have opted for the second choice: the placement of a central venous access device (CVAD), such as Broviac®, Hickman® or Port-A-Cath®.

But for many parents, these two traditional choices present problems. Enter the AV Fistula, a third option for accessing your child's veins.

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inside PEN

LA Kelley Communications, Inc.

welcome

Although Tommy, my son with hemophilia, is now 15, I recall well our infusion experiences when he was a baby. Whenever he had a bleed, the successful relief of his pain, and of my emotional anguish, seemed to depend on one thing–accessing a vein. As the moment approached, our anxiety level rose. With my baby crying, we wanted desperately to get a vein on the first try.

We sometimes stuck him numerous times to find his tiny veins. Luckily, Tommy had good veins, but other children were not so fortunate. Back then, ports weren't an available option. Even today, many children must undergo repeated attempts to access small veins. Just recently, a friend called to say that she couldn't access veins in her 12-year-old son! Although every child with hemophilia has a unique situation, venous access to administer factor is a consistent need for us all.

Fortunately, today we have more options–ports, venous scopes, and more experienced staff. We also have a new procedure, the AV Fistula. It's so new to our community that few HTCs implement it. Read our feature article carefully, and see how the treatment staff at RUSH are using this procedure to make life easier for families with hemophilia. Improved quality of life for our children often starts with easy venous access.

Quality of life is also Dr. Prasad Mathew's focus. He discusses how using super concentrate factor can offer benefits, particularly during infusion time. And as the school year winds down and summer camp season gears up, Debra Honig, M.S.W., L.C.S.W., offers great ideas to consider for September. She compares and contrasts the structured and regulated hemophilia camp experience with the possibly not-so-structured school (especially school playground) experience.

You'll find lots of intriguing topics in this issue of *PEN*. Empower yourself by reading, and share this information to improve the quality of life of another hemophilia family you know.

letters

I am the current President of Hemophilia of Iowa, Inc. I found your recent article about the NHF and HFA very informative ["Two Organizations, Two Visions: How the NHF and HFA Meet the Needs of the American Hemophilia Community," *PEN*, Feb. 2003]. We were mentioned in the article as a chapter not belonging to either organization, and I felt the need to express our reasoning for not joining.

I am a recent member of Hemophilia of Iowa, Inc., and while I don't know the past reasoning, I know we currently have two reasons for not joining. The first is that according to our mission statement, we provide education and support for people. I view our organization as a large support group. Our second reason is the same as that of the Puerto Rican Association of Hemophilia. The membership fee is just too high for our organization's budget. I feel our money is better spent locally. However, I know that some of our individuals are members of one organization or the other.

Our organization is funded by the following sources: home health care companies, pharmaceutical companies, our memberships, and generous donations from people outside the bleeding disorders community.

It is necessary to keep all our options open, but for now we will remain independent.

Lisa Wolterman, President, HEMOPHILIA OF IOWA, INC.
www.hemophiliaofiowa.org

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by Prasad Mathew, M.D.

IMPROVING *Quality of Life* THROUGH *Advancements in Care*

Advancements in care during the past 15 years have dramatically improved the lives of hemophilia patients. Our community has seen two major exciting changes taking place: first, changes in "ambience of care," reflected in the emergence of hemophilia treatment centers (HTCs) and the trend from in-patient care to a home care setting. Second, the research and development of new technologies in factor production and gene therapy.

Under the guidance of the National Hemophilia Foundation (NHF), hemophilia treatment centers have personalized the management of hemophilia. HTCs provide an ambience, or atmosphere, of care that enhances quality of life. To provide comprehensive care, HTCs approach disease management from a multidisciplinary perspective, integrating psychosocial and medical therapies. Essential to comprehensive care is the annual visit, designed to reduce or prevent bleeding complications. Also key is patient and family or caregiver education.

Home therapy is now considered the standard of care for those with moderate to severe hemophilia. HTC physicians, nurses and social workers create partnerships with patients and families to formulate strategies, identify problems, and manage hemophilia at home. All aspects of the patient's life are integrated into ongoing management strategies.

Managing hemophilia also depends on technological advances. Recombinant factor VIII was a significant breakthrough, creating a safer product with reduced risk of transmission of undesirable proteins and contaminants. Since its development, researchers have discovered new ways to formulate and purify products to eliminate the addition of human albumin. No viral transmission through these products has been documented in hemophilia patients in the past 15 years.

Early recombinant factor VIII products were followed by the development of second-generation products, like ReFacto® and Kogenate® FS/ Helixate® FS. These products lack human albumin in their final formulations, and are considered theoretically safer than first-generation products. They also undergo an additional purification process (solvent-detergent virus inactivation). All assay sizes of Kogenate FS are reconstituted in 2.5 ml sterile water per vial (approximately one-fourth of the volume needed to reconstitute first-generation recombinant factor VIII products). All assays of ReFacto are reconstituted in 4.0 ml sterile water per vial. These "low volume" diluent products represent the latest revolution in clinical care and enhanced patient convenience, with increased clinical benefit in certain patients. Because less pressure is needed to inject the lower diluent volume, these products are easier to administer to babies and young children, children learning to self-infuse, and those with limited dexterity–pushing a 30 to 40 cc syringe can be challenging, even for an experienced self-infuser. Since one syringe can contain a high dosage, these low volume products are convenient and timesaving for patients with busy lifestyles, and those who must infuse regularly. Third-generation factor VIII products are currently in clinical trials in patients with hemophilia, and should soon be available to the community.

But the question remains: is efficacy compromised, and product wasted, with these lower diluent volume formulations? Findings from a recent clinical study[1] show that lower and higher diluent volume products have comparable efficacy, in both previously treated and untreated patients.

Hemophilia trials have been initiated in patients, and the hemophilia community eagerly awaits the results of these trials. Preliminary results show some promise regarding factor levels; yet safety issues are a concern, and the patients in these trials are monitored very closely.

Over the past 15 years, we have witnessed dramatic developments in the treatment of hemophilia, although we admittedly have much more to accomplish. While safety remains a key component in treating hemophilia, we must remember to keep the quality of our patients' lives an important goal of our endeavors–without compromising efficacy.

Prasad Mathew, M.D. is Director of the Ted R. Montoya Hemophilia Center, and Associate Professor of Pediatrics at the University of New Mexico, Albuquerque.

[1] Tobias M. Suiter, M.D., Ph.D. "First and next generation native rFVIII in the treatment of hemophilia A. What has been achieved? Can patients be switched safely?" *Seminars in Thrombosis and Hemostasis.* 2002;28(3):277-283.

by Paul Clement

Closing the Window:

Virus Detection Technology

COMES OF AGE

Prior to 1985, the hemophilia community was often described as the proverbial "canary in a coal mine" when it came to blood safety. Fortunately, viral inactivation processes for factor concentrates were introduced in 1985. But before that, an emerging virus or blood supply problem often showed up first in the hemophilia community, because of our heavy use of blood products. This was dramatically demonstrated when viral contamination of the US blood supply resulted in nearly 8,000 HIV infections from contaminated factor concentrates between 1978 and 1985. Since then, our community has been an ardent watchdog of the nation's blood supply–for our own children and patients, and for the nation as a whole. Now, a new test may help ease our fears.

What's the real risk of viral contamination in the blood products we use? For clotting factor concentrates, our risk is exceedingly small. Factor concentrates undergo stringent viral inactivation and purification procedures to destroy and/or remove most viruses from the final product, and hundreds of quality control tests. But this is not true for whole blood, which does not undergo viral inactivation or purification. For whole blood, our risk of contracting a virus is related to our ability to *detect* the virus. Unfortunately, our current viral blood tests are unable to detect viral infections *for several days to several months after a person is infected*, thus allowing their donated blood–which tests negative for viral infection but is actually infectious–to be transfused.

Since 1997, the US Food and Drug Administration (FDA) has encouraged large-scale study of a sensitive new test for the presence of viruses in blood and plasma. The new test is called NAT[1], short for "Nucleic Acid Test." NAT is able to detect viral infections earlier than current tests can, thus making our blood supply safer.

What Is NAT?

NAT detects very small amounts of genetic material (DNA or RNA, which are types of nucleic acids). NAT is an extremely powerful and sensitive test that is capable of amplifying a small part of viral or other genetic material over a billion times. This amplification of genetic material makes it possible for us to pick a "needle out of a haystack." By looking for the presence of the amplified gene, we can now detect minute amounts of viruses much earlier than we can with other tests–viruses like Hepatitis C (HCV) and HIV (AIDS), which may hide in blood or plasma.

NAT's Advantages Over Current Viral Tests

When a virus infects a person, it enters certain cells and begins to replicate, or make copies of itself. As the virus replicates, virus particles called *antigens* start to appear in the blood. In response to these viral antigens produced by the viral infection, the body's immune system gears up to make *antibodies* that are specific to the virus. The job of antibodies is to circulate in the blood and seek out the particular virus; then inactivate it, or mark it for destruction by other elements of the immune system. This is how we combat the infection. Current viral blood tests check for the presence of either antibodies or antigens in the blood or plasma, indicating that the person has been exposed to the virus. However, these tests do *not* look for viral genetic material.

Antibody and antigen tests also suffer from a problem of timing: there is a lag time between the point where a person becomes infected, and when antigens or antibodies are detectable in the blood. During this lag time, known as the *window period*, a person's blood or plasma will be infective, but will show up negative on antibody/antigen blood tests for the virus. The window period differs for different viruses: for HCV, the window period is approximately 82 days with antibody tests; for HIV-1, it's 22 days with antibody tests. Antigen tests have a shorter window period, and when testing for HIV, both antibody and antigen tests are used.

NAT dramatically cuts the window period. When NAT tests are used to detect HCV in blood or plasma, the window period drops from an average of 82 days to about 25 days. For HIV-1, the average window period with antibody tests is 22 days, and approximately 16 days with antigen testing. NAT further reduces the window period to 12 days.

The American Red Cross (ARC) estimates that only a very small percentage of infected donors–about one per 4 million

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[1] Sometimes called Polymerase Chain Reaction (PCR) tests, after the most common type of NAT.

ONE STEP AT A TIME

A Project SHARE Story

by Pamela Mosesian
Director of Project SHARE℠

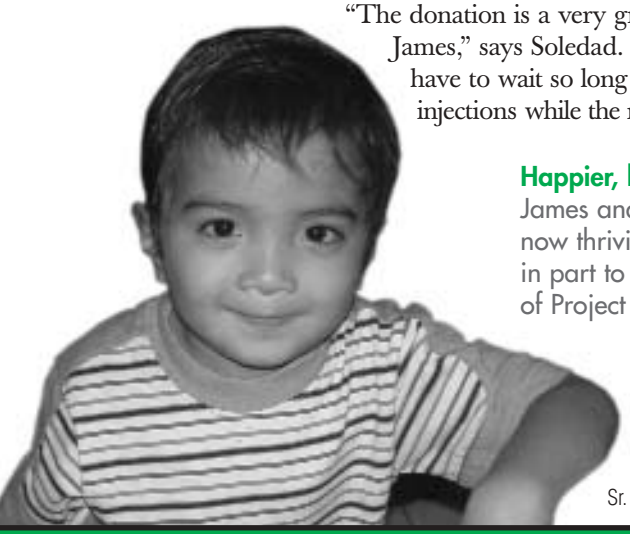
James Raphael Ordonez

James Raphael Ordonez loves cartoons, painting, and playing with matchbox cars. He is like any other three-year-old, except that he has severe hemophilia A with inhibitors, and struggles to survive in an impoverished country.

James lives in Manila, Philippines, with his parents and nine-year-old sister, Emilie-Marie. His mother, Soledad, is a fish vendor in a wet market and his father, Rommel, is temporarily unable to work.

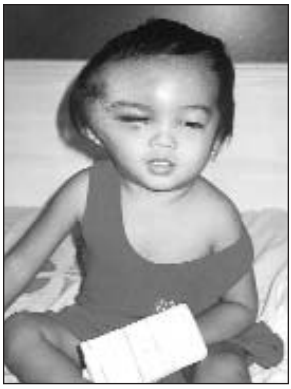
The Ordonez family is very poor, and factor is extremely expensive and difficult to obtain in the Philippines. Soledad says, "When James has a bleed, he is totally incapable of doing anything. Since he is so active, he gets very frustrated when he must rest. We feel helpless, and must be at the mercy of others." The ordeal has taken a terrible physical toll on James, who suffered a massive head bleed at age two, and was hospitalized for nearly a month. The graphic photo from that incident reveals an injury aftermath not usually seen in the US. Hemophilia has taken an enormous emotional and financial toll on the entire family, often leaving them in despair.

Fortunately, James recently received a donation of NovoSeven® from Project SHARE. He is now thriving. "The donation is a very great help for James," says Soledad. "He doesn't have to wait so long to get his injections while the medicine from Project SHARE lasts. The donation also relieved our worries, even though this may be temporary. Once the medicine is finished, our worries begin again."



Sr. Emilia Marcelo, MIC

Happier, healthier: James and others are now thriving, thanks in part to the efforts of Project SHARE.



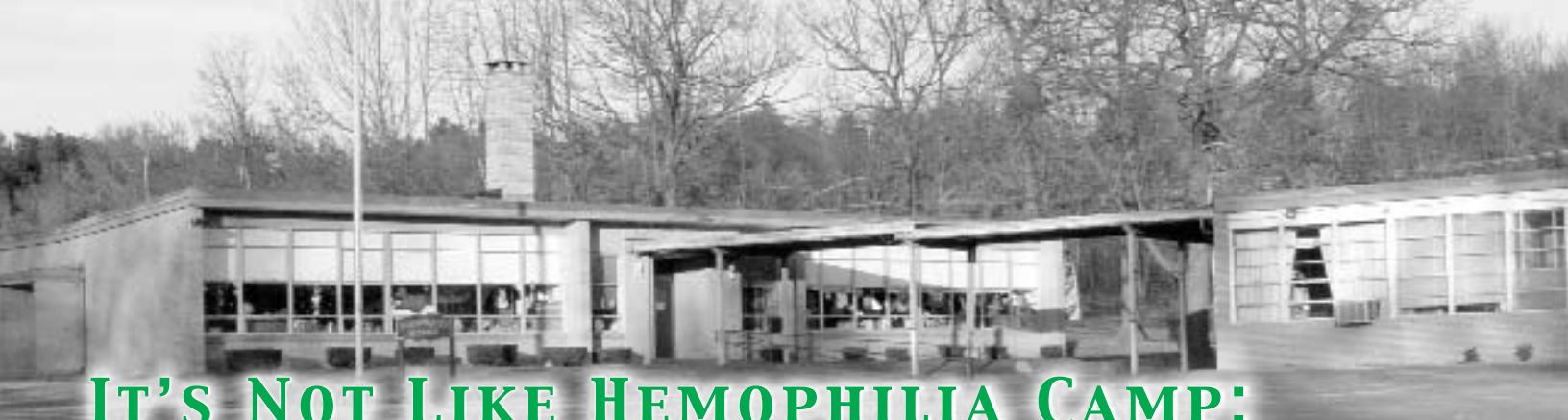
Unnecessary suffering: In developing countries, an injury aftermath like James's can be horrific, but is treatable with factor.

James is only one of an estimated 4,300 people with hemophilia in the Philippines. According to Dr. Flerida Hernandez, President of HAPLOS, the country's national hemophilia organization, "Only about 650 of these patients are registered with the National Treatment Center and HAPLOS, and 90% of them live below the poverty level." Dr. Maria Dioko, of the University of Santo Tomas Hospital, explains, "Our dilemma is that we know what to do, but we don't have the medicines available because of financial constraints. Generally, almost all people with hemophilia in our country do not receive adequate treatment, and they just receive blood products when they have bleeding."

The Ordonez family has one wish: for James to lead a normal life. How can you help patients like James? Project SHARE accepts donations of in-date factor and ancillary medical supplies, and needs volunteers.

To learn more about helping children with hemophilia in developing countries, please visit www.kelleycom.com/iha/projshare.html or contact Pam Mosesian at (978) 352-7657 or pam@kelleycom.com.

Project SHARE℠ is an international humanitarian program administered by LA Kelley Communications, Inc. in partnership with Baxter BioScience, Bayer HealthCare, Hemophilia Health Services and Novo Nordisk Pharmaceuticals, Inc. Factor donations are primarily from private sources.



It's Not Like Hemophilia Camp: *Creating Partnerships With Schools*

by Debra Honig, M.S.W., L.C.S.W., RUSH HTC

As summer approaches, many children with bleeding disorders anticipate the adventure, security and joy of hemophilia camp. Camp offers school-aged children a unique opportunity to develop a peer group, be independent from parents, learn that they're not alone, and enjoy physical activity while surrounded by knowledgeable staff. It's reassuring for patients and parents to know that campers can take reasonable risks, have fun, and deal with injuries responsibly. New campers often feel uneasy, and must gear up physically and mentally for this independent adventure. When they return from camp, children have a new vigor for life, and are active and confident in their abilities. But once camp ends, the challenges of the school year begin.

Most students are advancing to the next grade, while some may be going to a new school or preschool. Some may have the same teacher, but most will meet new teachers. Getting ready for school, like getting ready for camp, means practical considerations like clothing and books, as well as mental preparation: with every change comes a challenge. The student and family must adapt, readjust and aim for a new equilibrium. For many families of children with hemophilia, school represents the first time that a child is free of the direct control of his parents. He's left to face the "big world" on his own, where most people have never heard of hemophilia, can't even spell it, and rarely have an accurate understanding of the disorder.

The big world of school is *not* like hemophilia camp. In many cases, school personnel are unfamiliar with hemophilia. Misconceptions are common regarding medication, limits to activity, and safety risks. Making the transition from familiar surroundings, like home or camp, can present a challenge to patients and families. Children with hemophilia and their parents have addressed and mastered challenges before, but school may be difficult–in the school environment, control is outside the family boundaries, often for the first time.

Like other HTC social workers, I communicate frequently with school staff when advocating for patients. It often strikes me that staff is not well informed about hemophilia and bleeding disorders. School personnel mean well, but harbor misconceptions and fears, and frequently recommend excluding the child from outdoor play or physical activities. Most school staff members welcome HTC specialists into the school, ask many questions, and are invested in learning about hemophilia and its management. For those who are extremely fearful of injury, liability and "the unknown," our efforts as HTC representatives must be intensified. The questions posed by school staff help me appreciate the struggle to understand hemophilia through the eyes of those on the "other side." With this understanding, I am more sympathetic and, I hope, more effective in allaying fears and communicating information. Once issues are

When clear and concise standards are presented to the school, staff gain a better understanding. A *policy* helps pave the way.

clarified for the school, children can enjoy a school atmosphere that is more sensitive to and supportive of their needs. Armed with knowledge, schools are less likely to inadvertently ostracize children with bleeding disorders.

Here are some examples of the challenges faced by students, and the fears voiced by school personnel:

Andre is a 12-year-old with severe hemophilia A, receiving regular prophylaxis. We recommended full participation in physical education, but no contact sports. An NHF brochure was given to the principal. The physical education teacher determined that basketball was a contact sport, and wouldn't let Andre participate.

Ben is a 15-year-old high school student with severe hemophilia A who wanted to join the tennis team. A doctor's note granted him medical clearance to participate. His parents gave written permission. He infused prior to practice. Despite these interventions, the coach feared injury, and prevented Ben from participating. Ben, who wants to be an athlete, finally became disgusted and quit.

Carlos is an eight-year-old with moderate hemophilia who rarely bleeds. The school insisted that he sit at the front of the school bus at all times, and wear a soft protective helmet. Carlos had to sit next to a teacher at all assemblies, and had to be accompanied on field trips by his mother. He was excluded from recess unless aides were present. The school suggested that Carlos not play on playground equipment because it was elevated above six feet.

Darlene is a nine-year-old girl with moderately severe type 1 von Willebrand disease. She bruises easily, and frequently develops soft tissue hematomas. A school in-service by our care team included a slide presentation, discussion, fill-in-the-blank teaching tool, pain scale, and NHF brochures. A treatment plan was given to the school nurse, and reviewed with the principal and Darlene's teachers. Despite these interventions, the school remained resistant to administering DDAVP following injuries involving swelling, bruising and pain, or nosebleeds. School staff believed that Darlene's mother was overestimating the significance of VWD.

Ethan is a six-year-old with severe hemophilia, on prophylaxis. During first grade recess, Ethan was typically pushed to the ground. He fractured his left humerus. The school asked if the injury could have been prevented.

Every objection, fear and concern posed by school personnel and parents teaches me something new. I bring each issue to our staff for discussion, and we search for guidelines: for example, should a child with hemophilia wear a helmet on the school bus? What's the rule? What factors, if any, determine the best practice? Should a child with hemophilia play on elevated playground equipment? Do severity and factor level affect the decision? Finally, the question of restricting physical education: it seemed obvious for our team to conclude, "No contact sports." Variables that influence our recommendations include factor level and severity of the disorder, history of major injuries and target bleeds, high-risk behaviors, age, and use of factor for prophylaxis. Certain activities are acceptable; others acceptable only with protective gear.

Due to the lack of guidelines and standards in the bleeding disorders community, we began forming our own standards. When clear and concise standards are presented to the school, staff gain a better understanding. A *policy* helps pave the way.

What else should be done? Consider our examples. For both Andre and Ben, our task was to listen carefully to concerns, pinpoint fears and misconceptions, and provide facts–like NHF recommendations for different risk levels for certain activities. Schools should understand that benefits may outweigh risks. They need to hear from medical staff, and the patient and family, that any risks are *chosen* by the family. Schools need to know that the medical team is providing clearance, which decreases the school's fear of liability for these risks.

The social and emotional costs of significantly restricting a child, for no valid medical reason, must be spelled out. In Carlos's case, the boy with moderate hemophilia, we addressed the need for *each* safety precaution

New England Hemophilia Association

Exploring new heights: Even high-risk sports can be enjoyed safely with proper instruction and supervision.

suggested by the school. As we tackled issues one by one, we were challenged to consider the medical rationale for every precaution–was each one appropriate? For example, our policy that a child should wear a helmet on equipment higher than his head seemed medically appropriate and allayed some fears. With support and education, the school staff's anxiety about the "crystal" boy eventually decreased.

In Darlene's case, the school needed to be challenged–in a supportive way–to review its general policy on administering medications. We did this to help clarify whether the school was discriminating based on the diagnosis of VWD, or if this was the general pattern. Education followed. In Ethan's situation, the school needed to hear that injuries from bullying could not be prevented. Ethan's injury had nothing do with the hemophilia specifically, but school staff needed to understand the implications of such an injury–serious and potentially fatal bleeding–for a second grader who happens to have hemophilia. We focused on preventing acts of bullying of *all* children.

It's helpful to educate school staff about current data on playground injuries. According to the US National Safety Council, 40% of all playground injuries are associated with playground climbing equipment, so the safety of monkey bars for *all* children is in question. Of playground-related injuries, 70% occur as a result of falls to the ground. It is often useful to raise the issue of injury risks for all children on the playground, while identifying special considerations for the student with a bleeding disorder.

We find that school staff's opinions regarding risks and the need for safety precautions are colored to some extent by parental perceptions. If, as hemophilia treaters, we lack clear standards, then families certainly struggle as well. Since parents are experts in day-to-day living with hemophilia, we should consider their opinions about the need for safety precautions at school. To determine which precautions are deemed necessary by parents, RUSH HTC sent questionnaires to parents of children with bleeding disorders. The preliminary results are fascinating, and represent a wide range of views. We wonder how medical professionals would answer the same questions.

Attending school is exciting and challenging, but requires preparation. It's always beneficial for children to learn to get along with differences, small and large, physical and social. Presenting schools and child care providers with safety precaution standards can help families prepare for learning environments that limit unnecessary exclusions, and encourage full inclusion. There is little doubt that safety standards should be established for children with bleeding disorders at play. Ideally, development of such standards would include input from specialists at HTCs nationwide, and from parents. Standards should serve as a *flexible* guide to meet the needs of individual children. The goal of a system of standards would be to provide a starting place. The final destination must be determined on an individual basis.

For more information, visit the National Safety Council website at www.nsc.org or the National Hemophilia Foundation at (800) 42-HANDI.

Debra Honig is a clinical social worker for the RUSH University Hemophilia & Thrombophilia Center in Chicago, Illinois. She earned her M.S.W. from the University of Illinois, and has been working with pediatric hematology patients since 1990. She is the proud mother of a seven-year-old son.

RUSH–Presbyterian–St. Luke's Medical Center

Communication is key: Educate school staff about hemophilia, and develop safety standards for playground enjoyment.

Another Option... continued from cover

Problems With Traditional Options

When considering options for venous access, parents and physicians must carefully evaluate the risks and benefits together. The health care team must estimate how often infusions may be needed, based on the child's severity level. Prophylaxis may be recommended. Unfortunately, even with the best of care, complications may still arise. [The advantages and disadvantages of each option are shown in the table below.]

Let's consider needlesticks. In newborns, young babies and even toddlers, veins are often difficult to see, and even more difficult to enter with a needle. Many experienced pediatric nurses have trouble placing a needle into the vein of a young boy with hemophilia. Magdalena Torres, mother of Brandon, age three, has often visited the emergency room. "Brandon had a lot of bleeding episodes, and it was hard to find a vein," she says. "Sometimes at the ER they tried ten, twelve times to find his vein–for only a ten-minute infusion!" Naturally, this was stressful for Magdalena and Brandon.

Placement of a CVAD can also be stressful, and result in complications like infection and clotting. Kelly Millette's son, Chris Gulledge, had two external Broviac catheters by the time he was three. The first one was placed when he was a year old, and had to be removed because of infection. "It pretty much came out on its own," recalls Kelly. "The cuff exposed itself. I don't know if that was because of the infection, or because Chris was very young and got 'curious' with it a couple of times." Chris had a second Broviac placed two months later. "We were told that he would have a double cuff," explains Kelly, "so if the first cuff was exposed, it would still hold itself in, and we'd be able to use it. But it exposed itself the same way, and we had to remove it."

Donna Smiley's son, Sean, had a similar CVAD experience. The first line developed infections; and while the second line had fewer infections, it had to be repaired when the line weakened. "When Sean was smaller," says Donna, "I would catch him scratching his chest. I think that's what caused the staph infection."

Recently, a group of experts convened in Washington, D.C. to discuss the uses and problems of CVADs. They concluded that injections in the veins of the arms or hands (peripheral veins) is highly desirable, and should be the first choice for venous access in a boy with hemophilia. This conclusion was based mainly on the high rate of infection that occurs with CVADs. The

Comparison of venous access options

Method	Advantages	Disadvantages
Peripheral veins: external needlesticks	Low cost, fast and safe.	Small veins may be difficult to access; may require multiple attempts. May be stressful for child and parents, or require frequent HTC visits for babies and toddlers.
CVAD: implanted port device	Easy to access, low visibility and reliable.	Infections, blood clots. Requires time and effort for training. Time-consuming when used properly (20 minutes or more). Expensive to place. Requires skilled surgeon and anesthesia.
CVAD: external central venous catheter	Easy to access, painless and reliable.	Infections, blood clots, altered body image, restricted activities. Requires surgical placement with anesthesia.
AV Fistula: arterio-venous fistula	Easy to access, quick, reliable, low visibility, low risk of infection.	Requires time and effort for training. Expensive to place. Requires skilled surgeon and anesthesia.

complications of CVADs were chronicled in a report[1] concerning 2,704 patients, who had a total of 2,970 CVADs placed. Forty percent of the CVADs became infected, on average within 295 days after placement. Further raising concerns, deep-vein blood clots related to CVADs are reported with increasing frequency. When peripheral venous access is difficult, and limits the ability to provide optimal care, parents may want to consider an alternative to CVADs. At RUSH Children's Hospital in Chicago, we have chosen to offer the AV Fistula as an option for families with hemophilia.

The Arterio-Venous Fistula

The AV Fistula is *not* an implanted port, catheter, or other synthetic device. It's not a device at all, but a procedure. The surgical procedure results in the enlargement of a vein, usually in a child's upper arm, so that parents can gain easy venous access by a regular needlestick. To create an AV Fistula, the surgeon establishes a connection between a selected artery and a vein. As the AV Fistula "matures" after surgery, this connection promotes the growth and enlargement of the selected vein.

These AV Fistulae are "natural," and do not involve synthetic implants (often used in hemodialysis[2]). Because no device or foreign body is used, the risk of infection is very low. On the other hand, the vein and artery used are quite small, and occlusion or fistula thrombosis is a possibility. This risk is estimated at not more than 5%, or one in 20 cases.

USING THE AV Fistula

USING THE AV FISTULA IS SIMPLE BECAUSE the vein is large, and can be seen and felt through the skin. First, the skin is cleansed with alcohol and Betadine®. Analgesic cream (such as EMLA® Cream) may be used, but after a short time is usually not necessary. Next, the fingers of one hand are used to feel the vein and the "thrill," or surge, of blood flowing through the AV Fistula — no tourniquet is needed. A 25-gauge butterfly needle, held in the other hand, is used to pierce the skin and enter the vein. A flash of blood appears immediately when the vein is entered. Factor is then infused, just as parents would do with a peripheral vein or CVAD. Finally, the needle set is flushed with saline, the needle withdrawn from the vein, and pressure applied to the puncture site for about ten minutes.

Less conspicuous: AV Fistulae may be barely noticeable...

... or obvious, with an enlarged vein visible as a lump under the skin.

[1]Personal communication

[2]Possible complications of AV Fistulae when used in patients receiving hemodialysis include aneurysm formation, and high-output left ventricular failure; but these concerns are minimized with AV Fistulae in hemophilia patients, because smaller arteries and veins are used.

RUSH–Presbyterian–St. Luke's Medical Center

Once the AV Fistula is created, there is a six to eight week waiting period, during which the vein matures and becomes ready for use. Until then, factor is given through a PICC line (a tube, or catheter, inserted into an arm vein, that stays in place while the AV Fistula matures) that is placed at the time of the surgery. The AV Fistula surgery can be "reversed" if there are complications or cosmetic concerns. But if the vein fails to mature, no intervention is required.

Keep in mind that this procedure requires a skilled surgeon with experience in AV Fistula placement. Your surgeon should carefully explain all the risks, benefits and alternatives. The entire process takes about three hours, in the operating room with anesthesia. First, an ultrasound is performed, to identify possible veins and arteries to use. Next, while the patient is anesthetized, two incisions are made in the arm, either above or below the elbow. Then the surgeon isolates the selected vein and artery, and connects them–creating a "short-circuit" path for blood to flow. To make this end-to-side (vein-to-artery) connection, the surgeon first opens the artery and vein; then joins them, so that arterial blood flows into the vein, and to the hand below the AV Fistula. This results in enlargement and thickening of the vein wall, so that it can be seen, felt, and accessed repeatedly. So far, when used in kidney dialysis patients, there is no apparent problem related to the "mixing" of venous and arterial blood.

The AV Fistula is not new to hemophilia. The first one was placed in a hemophilia patient in the early 1970s. Still, we do not yet know the long-term effects, and whether a patient will experience circulation problems later in life. Currently, this procedure should be reserved for patients who have failed traditional forms of venous access, or are participants in clinical research to collect data on the effectiveness of the AV Fistula procedure.

Hemophilia is an expensive disorder. Families don't need the additional financial burden of unnecessary surgical procedures. Therefore, the need for "artificial" venous access–placement of a CVAD or AV Fistula–must be clear. Third party payers have traditionally covered the costs of placing a CVAD or AV Fistula. "We had no problems covering the procedure with insurance," comments Kelly Millette. At RUSH, the average cost, including factor, in 2002 for the placement of an AV Fistula in a boy with hemophilia was $29,000 compared to $40,000 for the placement of a Port-A-Cath.

Peace of mind: Chris's AV Fistula builds his self-confidence, and gives his mother more peace.

Kelly Millette

Testimonials From Parents

Because of the early success of the AV Fistula, RUSH Hospital has offered this option to eight patients in Chicago. So far, five have had the procedure performed. The first was placed in October 2000, in three-year-old Chris Gulledge, who has severe hemophilia A and a high titer inhibitor. After Chris's two CVADs were removed because of infection, Kelly was faced with the need to administer factor daily for immune tolerance therapy. She chose the AV Fistula.

"They wouldn't place ports in patients with inhibitors," explains Kelly. "I read about the AV Fistula, and decided to go that route, because at that time Chris was receiving factor every day, and I didn't want to just stop cold."

Chris turned five in April. So far, he and his mother have had success with the AV Fistula. "It's worked out great," says Kelly. "In the beginning, we used a PICC line until it matured. Now, we use it every day. It's matured to where I can use the actual vein, and there are tons of tiny veins all over his arm and hand that I can access as well." Kelly reports no arm bleeds, no swelling, and no infections. "It's kind of impossible to blow a vein, because it's huge."

George Corpeno, a four-year-old with severe hemophilia on prophylaxis, had his AV Fistula placed at age three. His earlier CVAD was continually infected, and had to be removed. "I decided to go with the AV Fistula," explains George's mother Juliana, "because there's no metal, there's nothing inside–just a vein."

George's AV Fistula matured in about two and a half months, during which time the Corpenos used a PICC line. Now, says Juliana, "It's very, very simple. I like it a lot. It's easy because there's no poking of different parts of his body. And George helps me."

Donna Smiley and her son Sean recently opted for an AV Fistula. Sean, who has severe hemophilia, turned seven in April. Already in his young life, he has had two central lines. "I was contemplating getting the AV Fistula," says Donna, "because I thought it would be better for Sean. The central line made him 'different,' and he didn't like to be different. He couldn't shower normally, he couldn't swim; and with certain shirts, it could be seen. That was a big problem for him." Sometimes, Donna dressed Sean's

THE AV Fistula IN EUROPE

Recently in Italy, interest in the AV Fistula has grown. Dr. Santagostino from Milan reported on her experience with 27 patients with hemophilia who had 31 AV Fistulae placed.[3]

The complication rate was low. Mild hematomas formed at the surgical site in five patients, including three with inhibitors. A clot in the AV Fistula occurred in one child with an inhibitor, but resolved spontaneously and the AV Fistula remained functional. Of the 31 Fistulae placed by Dr. Santagostino's group, four (13%) failed to mature, or develop fully to allow adequate blood flow. Despite these failures, patient and parent satisfaction was high, and compliance with the prescribed treatments was excellent. The complication rate was acceptable enough that Dr. Santagostino's group now offers the AV Fistula as a first option for venous access in children with hemophilia when peripheral access is not feasible.

[3]Personal communication

line so it would be close to his body to prevent his rolling over in his sleep and pulling the line, causing it to bleed slightly. "He'd wake up crying," recalls Donna. "It was just little things like that."

But the last straw came in February of this year. When Sean was at school, an older child kicked him and grabbed his collar, pulling his line out of place. After that, says Donna, "I just didn't want to go back to the central line."

Sean's AV Fistula was placed on February 24, 2003, and has been in use since April. "If I had known about the Fistula earlier," comments Donna, "I probably would have wanted it sooner, because Sean had a 'thing' with needles. Even though this is just a small stick, he'll still have to get used to it."

What does Sean think so far? "He's just very happy," laughs Donna. "You can't tell that he has a line. He had a PICC line temporarily, and he was just waiting for that to come out. He wants *nothing* hanging out of him."

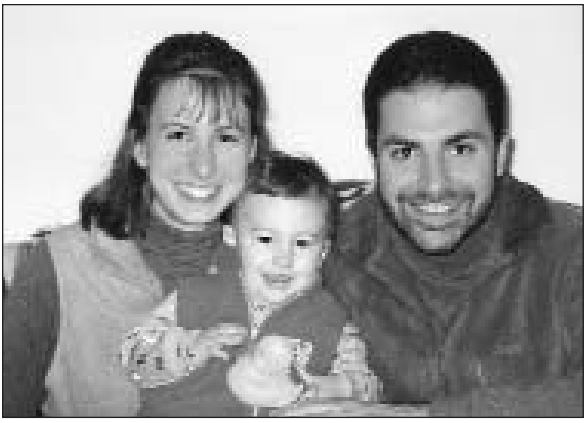
Brandon Acevedo-Torres, age three, has severe hemophilia. He had no CVAD before having his AV Fistula placed last August, when he was two. "I'm a single parent," explains his mother Magdalena, "and I have a daughter, too. It was very difficult for me to take Brandon to the ER almost every month, sometimes twice a month."

At first, Magdalena was hesitant about trying an AV Fistula. "I thought it would be very difficult for me to infuse Brandon at home; but on the contrary, it was very easy. He knows when it's time to receive his infusion, and he sits down, gives me his arm and cooperates." She continues, "Now it's easier for me to control his bleeding. I don't have to run with him to the ER."

Cautions for Parents

Tavon Mitchell is three, with severe hemophilia and an inhibitor. By the time he was two, he had a Port-A-Cath; then a Broviac line that was continually infected and had to be removed. When Tavon's parents, Latrice and Timothy, heard about the possibility of fewer infections, they decided to try the AV Fistula. But things didn't turn out as planned. "After he got the AV Fistula placed," says Latrice, "we found out that it didn't work." What happened? "They were looking for the 'thrill,'" she explains. "He got the pulse, but he never got the thrill." Tavon's AV Fistula had clotted off, a complication of aggressively treating his inhibitor.

Tavon has now had a Broviac line for six months, with no infections so far. What about his AV Fistula? "It's still there," says Latrice. "We asked the surgeon if we had to take it out, and he said no, just leave it in because it's nothing



Cautious curiosity: The Castaldos prefer the AV Fistula, but will delay surgery as son Luke is doing well.

The Castaldo family

foreign. He said that once it doesn't work, it'll never work." If Latrice and Timothy decided to try the AV Fistula again, the surgeon would have to find a new site.

"We really didn't know much about it at the time," admits Latrice, "but since other patients with hemophilia had it, we thought it would be a good thing for Tavon because he needs infusions every day." But she wouldn't risk another AV Fistula procedure. "He's had the Port-A-Cath, the Broviac line, the Fistula, and now back to the Broviac line. He had a surgery that he didn't really have to go through. I don't think I want to put him through that again."

Still, Latrice remains philosophical. "Things didn't work out. It was just something we tried, but it didn't work for us. Everyone's different."

Parents should remember that the AV Fistula procedure is still being tested, and should thoroughly discuss the known risks with their hematologist and surgeon. This procedure is new to the hemophilia community, and holds promise, but has not yet been completely evaluated.

The Decision Process

For some families, beginning with peripheral venous access–regular needlesticks with butterfly needles–is a good option. Medical training and experience, a prior child or sibling with hemophilia, or a combination of these factors may influence the decision. Most parents don't immediately have the ability to start an IV, and are fearful of "hurting" their son with needlesticks. But with positive training by HTC staff, these parents usually gain skill and confidence.

Some parents opt for a CVAD. Subcutaneous (below the skin), totally implanted devices like the Port-A-Cath are most frequently used. They have the advantage of low visibility, and are easy to access. However, they may become infected and need to be removed. External central venous catheters like the Broviac or Hickman are typically reserved for children with hemophilia complicated by inhibitors, or for short-term venous access–for example, to treat a troublesome target joint. They carry an increased risk of infection, and may be accidentally extracted. Both external and subcutaneous devices carry a risk of blood clots.

Fortunately, creating an AV Fistula may combine the advantages of using peripheral veins with the benefits of a CVAD. However, all three options require surgery, and are expensive. Parents need to do their homework when it comes to selecting an option for venous access.

Angela Castaldo is the mother of 15-month-old Luke, who has severe hemophilia. She and her husband Chris researched the AV Fistula because they were searching for better options for Luke. "We were going to just go ahead and do peripheral access," says Angela. "We were never quite comfortable with [the idea of] the port. We also weren't comfortable with the possibility of infection, but we were willing to go for it if necessary."

Easier venous access: Brandon's AV Fistula allows better control of bleeding, and helps him lead a more normal life.

Magdalena Torres

Instead, the Castaldos began exploring the AV Fistula–not as a result of infected lines or failed venous access; they simply worried about accessing Luke's tiny veins, and wanted him to be able to infuse himself easily. "First we started looking online," says Angela. "We looked at it with kidney dialysis patients, and saw that it wasn't a new procedure–it was just new within the hemophilia community." So although it's currently recommended for people who've had problems with venous access or failed CVADs, the AV Fistula may become viable as a first choice in the future. "We've researched it, we've heard the horror stories–but there's no risk of infection," says Angela. "There are a lot of advantages. The downside, people say: it *is* permanent. Yes, it is, but in an emergency situation, we'll always be able to get access."

The Castaldos are considering getting an AV Fistula within the next two years. "We were hotly pursuing it," says Angela, "because of the venous access. But Luke isn't bleeding as regularly as other children with severe hemophilia do, so we decided to wait. Luke's doing so well that we can put off the surgery." Still, she concludes, "If we were to go with an access device, comparing the port and the AV Fistula, we decided the Fistula would be better for a couple of reasons. One, it's permanent. And two, hopefully later on Luke would be able to access it just fine."

Option For The Future?

The choice of venous access is difficult, but must be approached with enthusiasm, information and empowerment. Parent involvement is essential in the decision process. If your child has a CVAD that has become infected, or if venous access is a problem, talk to your doctor about the AV Fistula. It might be the right option for your family.

What's the future of the procedure? Judging from the Acevedo-Torres family, the AV Fistula may soon be the first option of families with no venous access problems behind them. A step further toward the future, the Castaldos have decided on the AV Fistula even before their son has needed regular venous access. But be prepared: many hematologists haven't yet seen the AV Fistula in use in hemophilia patients. Magdalena Torres says, "I've moved to Florida, and because the AV Fistula is a new thing, the doctors here don't know much about it. Brandon's hematologist knows about the Fistula through the information I've given to her, but we're her first case."

As more families undergo the AV Fistula procedure, and more data is collected, the future looks promising. Currently, this procedure is used most often in cases where traditional needlesticks or CVADs have failed. But while the success and use of the AV Fistula is being debated, parents should at least be aware that it is an option. When you have more options for treating your child, your sense of empowerment and control increases–and you can make better decisions for the life of your child.

AVF advocate: Dr. Leonard A. Valentino has performed the AV Fistula procedure on several US hemophilia patients.

LA Kelley Communications, Inc.

Dr. Leonard Valentino earned his B.S. and M.D. degrees from Creighton University in Omaha, Nebraska. He completed his pediatric residency at the University of Illinois and his fellowship in pediatric hematology-oncology at the University of California, Los Angeles. In 1994, Dr. Valentino joined the section of Pediatric Hematology-Oncology at RUSH Children's Hospital, as the Director of the newly formed RUSH Hemophilia and Thrombophilia Center. In 1998, he became Director of Section. He is also an Associate Professor of Pediatrics at RUSH Medical College.

This article's joint authors are the team from the Departments of Pediatrics and Vascular Surgery, RUSH–Presbyterian–St. Luke's Medical Center and the RUSH Hemophilia and Thrombophilia Center, RUSH Children's Hospital. The RUSH team currently treats 150 hemophilia patients and 200 VWD patients.

For more information on the AV Fistula, contact the RUSH team at lvalentino@rush.edu or (312) 942-5983.

For more information on CVADs, visit www.kelleycom.com/articles/pen_cvad.htm

Prince Leopold: The Untold Story of Queen Victoria's Youngest Son

by Charlotte Zeepvat

Review by Chris Hodgson

Alexis, son of the last Tsar of Russia, was not the only prince with hemophilia. Charlotte Zeepvat's fascinating story of Prince Leopold (1853–84), youngest child of Queen Victoria and Prince Albert, represents only the beginning of hemophilia's effect on European history during the early part of the twentieth century. Zeepvat also uncovers Queen Victoria's deep feelings toward her son, and shows how our approach to a child with a disability has changed since Leopold's time.

This book is appealing and easy to read, thanks to Zeepvat's ability to portray, time and again, the frustrations Leopold endured in his short life. Leopold's experiences with his own disorder contributed to the compassion, patience and understanding he showed most people.

Queen Victoria decided to wrap Leopold in cotton wool[1] to protect him from the dangers of the outside world. Leopold was the closest to Albert, in character and ability, of all Victoria's children; losing him would bring an almost intolerable sense of guilt at not being able to protect him after Albert's death. It is strange that in her attempt, she subjected Leopold to the humiliating behavior of Archie Brown (brother of her servant and confidante John Brown), dismissed supportive tutors, and forbade the company of his siblings. Determined that Leopold's future should be at her side, Victoria succeeded in making his life intolerable, and eventually drove him from her.

We can only admire Leopold's determination, like that of many children with hemophilia, to lead a life as normal as possible. This desire for independence intensified when Leopold left home to attend Oxford University. For the first time, he was able to taste freedom, choose his own friends, have his own house, and study subjects that interested him.

Little did Leopold realize, when he opened a new wing of the Radcliffe Infirmary at Oxford, that he was so close to the place where the breakthrough in hemophilia treatment would occur. The means by which clotting factors work was discovered in the early 1960s at Churchill Hospital, Oxford, changing forever the lives of people with hemophilia.

Zeepvat convinces us that if Victoria had allowed him more freedom, Leopold would have contributed greatly to his country. The Queen interfered with his ambition to become Governor of Canada and, later, Governor of Victoria, Australia. Leopold must have felt intense anger at life with hemophilia, and at his mother's attitude. Yet Leopold had at least one consolation: a short period of happiness with his wife Helena, his small daughter, and the knowledge of another child to be born, although he never knew his son.

In many ways, this is a sad book. But the example of Leopold's mastery of his disability, despite overwhelming obstacles, moves us to share his enjoyment of life. I was reminded of my own childhood with hemophilia: when I was born in 1941, there was no treatment and little understanding of the condition. Like Leopold, I experienced the terrible pain of swollen joints, months away from school, and the frustration of being unable to participate in sports I knew I could play well–like tennis, which Leopold also attempted to play.

Zeepvat's book brings us a sense of history. Through Queen Victoria's descendants, hemophilia had a devastating effect on the royal families of Germany, Russia and Spain, and contributed to the causes of the Russian Revolution and Spanish Civil War. This is obviously a book of painstaking research, right down to the memorable photographs.

Charlotte Zeepvat, *Prince Leopold: The Untold Story of Queen Victoria's Youngest Son.* Sutton Publishing, 1998. Available at www.amazon.com.

Adapted with permission from *Haemophilia Quarterly* (formerly *The Bulletin*), the newsletter of the UK Haemophilia Society, 1998, Issue 3.

Chris Hodgson is Chairman of the Haemophilia Society, England, and a person with hemophilia.

[1] bandages

Online correspondence reprinted with permission of contributors, through the International Hemophilia Club (IHC) hemophilia mailing list at http://groups.yahoo.com/group/hemophilia, the Bleeding Disorders mailing list at http://groups.yahoo.com/group/Bleeding-Disorders, and the Hemophilia Support mailing list at www.boygenius.com/lists.html. *For this issue, the names of the authors have been changed.*

Sterile Technique

used by hospital staff when accessing a port

Infection is a common complication of ports. Roughly one-third of the ports in children with hemophilia become infected. The cornerstone to preventing port infections is good sterile technique, yet many hospital staff do not follow proper sterile technique when accessing ports. How would you deal with this problem?

Q: After witnessing the way hospital staff accesses our port, I always do it myself now. But I'm still not sure how to handle the blood draws. What is the sterile technique protocol used by a good HTC for drawing blood or giving medicine through an already accessed port?

We're very strict at home, which I feel has helped us remain infection-free. How far do I ask hospital staff to go? To draw blood, should they put on sterile gloves, and drop sterile syringes on a sterile field? I don't think staff is careful enough when changing the injection cap at the hospital. When my son had a PICC line (a tube or catheter inserted into the arm vein), the home health nurse put on a mask and sterile gloves, and picked up the injection cap with sterile 2x2s. I like our HTC nurse, but she doesn't always have everything ready before starting, and seems to work by the "seat of her pants." No gloves to draw blood from the port, or even change the cap. Air is sometimes pushed in while flushing. I don't wish to alienate her, but we go every three months for labs and I don't want my boys needlessly risking danger. Should I be the only one touching the port from now on? I hate being difficult, but my sons' health is important to me.

Melissa

A: Any time we're in the hospital, I cringe when I see the "pros" handle my son's port. If he needs to be accessed while we're there, I do it myself. I'm more careful, and have a better sterile technique, than any hospital staff I've ever seen. I may go overboard with precautions, but I'd rather be safe. My sterile technique involves the following steps. But remember, your HTC may not supply you with precisely the same materials; and the materials we receive have been changed several times, requiring changes in our technique. Also, there are several types of ports. My son has a Port-A-Cath®, with a target about the size of a dime.

1) Wash hands thoroughly, and clean surface for preparation of materials with Lysol antibacterial cleaner or a mixture of bleach and water.
2) Gather necessary materials: dressing kit, syringes, needles, access device and end cap. (Currently, our HTC supplies us with prefilled saline syringes. The fluid path is sterile, but the syringes themselves are not. This makes a difference: the syringes cannot be dropped on the sterile field without risking contamination. We'll assume that you are using sterile empty syringes, and filling them from standard saline vials.)
3) Wash hands again.
4) Open the sterile dressing kit. My kits come with a package of three sterile alcohol swabs, three Betadine® swabs, gauze, mask and sterile gloves. When unwrapped, the mask and gloves are on top, and can be removed from the field–taking care not to touch anything else in the field.
5) Put on the mask. Carefully open each of these items and drop them on the sterile field: syringe, needle, access device and "end."
6) Open the saline vial and wipe the top with alcohol wipes.
7) Put on the sterile gloves. Do this without touching any part of the outside of the gloves. **If you accidentally touch the outside of the gloves, or anything else, trash it all and start again**. Once the gloves are on, you can touch the items in your sterile field.
8) Attach the needle to the syringe, insert into saline, and draw a quantity of saline into the syringe. We use 10 ml. Do **not** touch the saline vial, as the outside of the vial is not sterile. Have someone pull the vial from the needle.
9) Remove the needle, and attach the "end" to the syringe and the access device. Prime the access device by pushing saline through until it squirts from the needle, and clamp it closed. Return the assembly to the sterile field.
10) Open the alcohol swabs and, using a circular motion, begin cleaning at the point of entry and moving outward about four inches. Repeat for all three alcohol swabs, ensuring good coverage. Allow to dry 15–30 seconds; then repeat with Betadine. Do not touch any part of the swabs

that might come into contact with the patient. (I drop the used swabs in the empty packaging from the dressing kit.) Allow 30 seconds for the Betadine to dry. If you are leaving the patient accessed, the sterile covering (Tegaderm™) won't stick well to wet skin. I've been told that it is the drying action of the alcohol and Betadine that kills the bacteria.

11) Assuming that nothing has so far contaminated the kit or your hands, pick up the access device, carefully remove the protective covering from the needle, and insert into the port. Since we don't leave my son accessed, I like to use longer access needles so I can feel them hit the back of the port.

12) Draw the plunger of the syringe back and ensure a good blood return. Then flush the saline through the port followed with any medications you are infusing. Flush again with saline, then heparin.

This is a lot to remember, but much of it is common sense that will be easier to understand when you are actually doing it. If I wonder whether I've made a mistake or contaminated something, I trash it all and start again. We follow these steps every other morning before my son goes to school. If he sits still, the whole procedure takes about 20 minutes, including mixing his factor.

GREG

A: At our HTC, all they did was wipe the rubber end of the cap before accessing the line. Gloves are always worn and sterile syringes always used. If you're concerned, don't hesitate to say something. If they brush you off, be firm. We parents realize how vital these lines are for our children, but others may not understand or be as careful as necessary.

For a while, we did the boys' blood draws through their ports, especially when they were having pre- and one-hour post-infusion factor levels drawn. Eventually, I preferred to have the lab and nursing staff try for a peripheral vein, because accessing and technique were problematic. Lab staff wouldn't draw off a port, even an already accessed port; and the only nursing staff who would do this were part of the central line team. This meant paging them, and waiting because they're so busy. So we decided to let the lab do draws the regular way. I always made them clean the peripheral sites with Betadine as long at the port was still in.

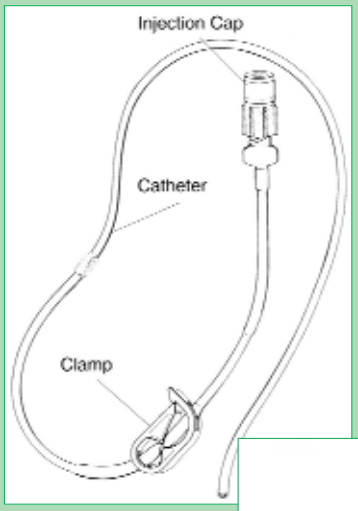
I know that we (and you) are using the port because of poor peripheral access–but might it be an option to give a peripheral stick just for lab work? I know that peripheral access can be difficult, but perhaps this would ease your mind. I was nervous when we decided to try it, but it cut down our lab work time by at least 90 minutes. It also helped the boys understand that eventually, all things will be done peripherally.

JULIE

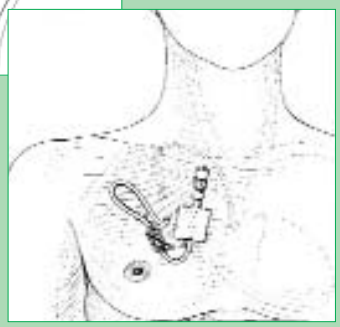
Melissa's Reply

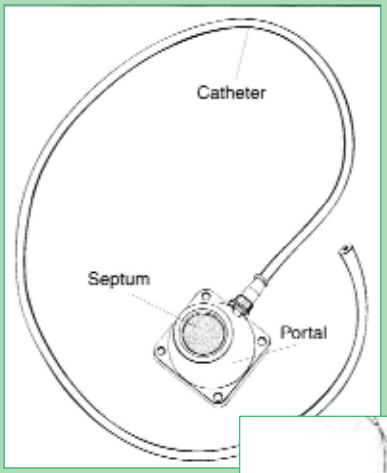
I look forward to the day when we transition to peripheral sticks for everything. But because of our current situation, I'm not ready yet. For the study the HTC is doing, our sons have labs done every three months, immediately followed by an infusion of factor. I believe it's possible to draw blood from the port with good sterile technique–they're just not very good at it at our HTC. Right now, peripheral sticks would be tough because my sons are two, and very active. I need to first make sure that anything done with the port is done with strict sterile technique, even if this means that I am the only person touching it. This isn't easy, since I am not very confrontational, but I can be assertive–and I will be, for my sons' health.

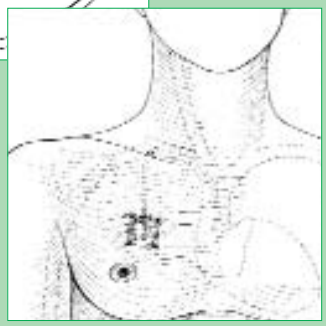
Central Venous Access Devices (CVADs)



Central venous catheter before (left) and after (below) surgical implantation. One end is threaded into a vein. The other exits the chest wall, extending several inches on the outside.







Implantable venous port before (above) and after (right) surgical implantation. One end of tubing is inserted into a vein. The other end is capped with an injection chamber that is also placed under the skin of the chest wall.

Drawing courtesy of SIMS Deltec, Inc., St. Paul, MN

The information provided in Parent-to-Parent should **not** be construed as medical advice. It is advice from one parent to another. Please consult your HTC for information on any medically related questions.

Avigen to Resume Gene Therapy Trials for Hemophilia B?

Avigen, Inc. will receive **$2.5 million** from **Bayer HealthCare** to continue the development program of Coagulin-B(r)®, currently under clinical investigation for gene therapy treatment of hemophilia B. The trial uses an adeno-associated viral vector to transfer the factor IX gene to the liver. Factor IX levels of 10% were achieved in one recent patient, who unfortunately developed high levels of a liver transaminase that temporarily halted the trial. The trial is a developmental cooperation between Avigen, Inc. and Bayer HealthCare, and may resume in the near future.

For more information, visit www.Avigen.com or www.bayerbiologicals.com
Source: Bayer Corporation

Gene Therapy for Hemophilia A Halted

Transkaryotic Therapies, Inc. (TKT) of Cambridge recently announced a series of management and business changes that include a **suspension of all gene therapy work**. TKT initiated the world's first hemophilia gene trials in December 1998. TKT has completed a Phase I gene therapy trial to treat hemophilia A patients at Beth Israel-Deaconess Hospital in Boston, but new CEO Michael Astrue said that TKT will not initiate additional trials unless a corporate sponsor can be found to help fund the research.

For more information, visit www.tktx.com
Source: www.tktx.com

CSL Acquiring Aventis Behring?

Picking up where Bayer Biological Products left off, the Australian biopharmaceutical firm **CSL** has entered into preliminary negotiations with Aventis, concerning the **potential acquisition of Aventis Behring**'s plasma products division. This deal would put CSL's plasma products business on par with that of Baxter Healthcare, currently the world's largest manufacturer.

Source: IBPN, March 2003

"Advate" New Recombinant Factor VIII Product?

Advate is the proposed proprietary name for **Baxter**'s newest recombinant factor VIII therapy, which could be approved for consumer use as early as this summer. "Adv" stands for "advanced" and "ate" for factor VIII. Advate will be the **first factor VIII recombinant therapy to be prepared without adding any human- or animal-derived raw materials to the cell culture process, purification or final formula**.

For more information, visit www.hemophiliagalaxy.com
Source: Baxter International, Inc.

$250,000 Grant Fund for Bleeding Disorders Community

The **Factor Foundation of America** has released **$250,000 in grant funds** available to hemophilia treatment centers, NHF and HFA chapters, and other organizations that provide education, research, clinical services, and special assistance to people affected by hemophilia and inherited bleeding disorders. The Foundation will fund specific projects that measurably improve the quality of life and self-sufficiency of people with bleeding disorders.

Source: www.factorfoundation.com

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Your February 2003 issue of *PEN* tackled several controversial topics in a clear, non-biased manner. The article comparing the NHF and the HFA was particularly well done. Kudos!

Mary Anne Schall
Great Lakes Hemophilia Foundation

Thank you for the copies of *PEN*, which are in our patient information rack in the clinic. It's wonderful to have a batch for that purpose.

Carol Kasper, M.D.
Orthopedic Hospital, Los Angeles

I am interested to know about hemophilia because there are four children in our home with it. Unfortunately, we don't know much about hemophilia–where it comes from, what the symptoms are. We have many questions. You are our only source for information and answers. I hope you can help by sending some reading material.

Abraham Alemayehu
Ethiopia

Editor's Note: LA Kelley Communications will send educational material and resources to this family.

Insights... continued from page 4

for HIV-1, and one per 275,000 for HCV–donate during the window period and test negative for these viruses on current screening tests. These donors would be detected by the currently licensed NAT. Prior to the use of NAT, the overall risk of contracting HIV through a single unit of blood was one in 675,000 donors. With NAT, the risk decreased to the range of one in 1,000,000–2,000,000 donors. For hepatitis C, the risk was one in 100,000 donors. With NAT, it is now just one in 1,000,000 donors. Data extrapolated from ARC clinical trials of NAT indicates that each year in the US, NAT could possibly identify about 100 additional HCV-infected units of donated blood, and two to six additional HIV-infected units during the window period.

Window To The Future

NAT requires sophisticated laboratories, specialized equipment and highly trained staff–it can't be done economically at your local hospital or blood/plasma collection center. To reduce costs, under the FDA protocol, NAT has been performed on pools of blood or plasma. Whole blood has been pooled in lots of 16 to 24 different donations per pool, and tested using NAT. Source plasma (used by fractionators for making blood products like clotting factor concentrates) has been pooled in lots of 96 to 1,200 units of plasma, and tested using NAT. After NAT testing, those pools that test positive for HIV or HCV are then traced backward, to determine which donor was infective.

The trend in the blood industry is to move away from pool testing to individual donation testing of whole blood with NAT. Although individual donation testing is more expensive than pool testing, it is more sensitive–pooling donations dilutes the gene concentration, and decreases NAT's sensitivity. However, fractionators will likely continue to use relatively large pools of plasma for NAT testing. This is because most fractionated blood products (derived from source plasma) undergo viral inactivation and purification procedures to destroy and/or remove viruses from the final product.

One of the blood industry's stated goals is to have a zero-risk blood supply. Although creating a zero-risk blood supply is impossible, implementing NAT for whole blood donations will be a significant step toward reducing the risk of viral infection by HCV and HIV through blood transfusions. Most blood centers do not presently use NAT for single donor testing.[2] However, over the next few years blood centers across the nation will implement single-donor NAT. And as new, fully-automated NAT tests are approved by the FDA, NAT will move from regional blood centers with sophisticated labs to your local hospital, thus inching us closer to a "zero-risk" blood supply.[3] With the implementation of single-donor NAT, the blood industry will be one step closer to closing the window on blood-borne infections, and opening the window on a new era of blood safety.

Glossary

Antibody	Proteins produced by the body to fight viral infections. Antibodies are produced by the immune system after stimulation by an antigen, and act specifically against the antigen in an immune response.
Antigen	A molecule (from a virus, for example) that is capable of stimulating an immune response, as in the formation of antibodies.
DNA	Deoxyribonucleic acid, the basic building block of a gene. DNA is a small unit of genetic material.

[2] Pooled NAT has been in use by fractionators and blood centers since 1999 under an FDA Investigational New Drug (IND) application. In July 2002, the Oklahoma Blood Institute became the first US blood center to use NAT for HIV and HCV testing of individual units of blood.

[3] In February 2002, the FDA licensed the first semi-automated NAT for whole blood donations.

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