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A publication of the North American Thrombosis Forum

Patient Perspective: Sam R's Story

Sam, an athletic 21 year-old, experienced her blood clots while studying at Colby College in Maine. Inspired by her experience, she is interning this summer at the Thrombosis Research Group at Brigham and Women's Hospital. Sam hopes to go to medical school after she graduates.

Q: When did your experience with blot clots begin?

I'm a rising senior at Colby. During my first two years of college, I was on the soccer team. I played goalie. I had been super involved in athletics since I was a little kid.

Last summer, I was training for soccer. We had a pretty intense training

Continued on page 2



How long should I be on an anticoagulant?

People take anticoagulants (commonly known as "blood thinners") for many different reasons. Some use anticoagulants to help prevent a stroke when they have a heart arrhythmia called atrial fibrillation (aka "AFib"). Others use it to treat a deep vein thrombosis (DVT; blood clot in the leg) or pulmonary embolism (PE; blood clot in the lung). Still others use it to help prevent a mechanical heart valve from building up a clot and becoming dysfunctional.

When people begin taking anticoagulants for conditions like these, there are several important questions that must be answered. An important first question is, which anticoagulant to use? Currently there are a number of oral anticoagulants available in the United States (e.g. warfarin, apixaban, dabigatran,



edoxaban, rivaroxaban). Another important question, once you've chosen the right medicine, is what dose of anticoagulant is appropriate? Finally, many people want to know how long they should be on the anticoagulant.



Making these decisions can be very challenging and involves the consideration of several factors unique to an individual person. Two of the most important considerations are

Inside

Patient Perspective	1
How long should I be on an anticoagulant?	1
Upcoming Events	2
Bring Support to your Community!	3
DOAC Reversal Deep Dive: Andexanet Alfa	4
Board of Directors and Staff . . .	6

the risk of bleeding and the risk of clotting. Your care team can estimate your risk of bleeding and clotting by taking into account your reason(s) for anticoagulation, such as age, sex, weight, medical history, family history, alcohol use, other medical conditions,

imaging studies and/or blood work. These factors are often used in conjunction with studies on thousands of patients that help to outline the risks and benefits of short vs. long courses of anticoagulation.

Finally, you (the patient) are a critical piece of the puzzle. Your input about your goals of medical therapy,

your understanding of your medical condition, any side effects that you are experiencing, the cost of the medication, and many other factors

Continued on page 3



Upcoming Events

In-Person Blood Clot Support Group at BWH

There will be no in-person support group for August. We look forward to seeing you all in the fall!

September 17, 2018

October 15, 2018

November 15, 2018

December 5, 2018

All support groups start at 7:00 p.m. and are held at Brigham and Women's Hospital. To register, email Kathryn Mikkelsen at KMikkelsen@NATFonline.org or call 617-730-4120.

Online Blood Clot Support Group

August – Summer Vacation

September 18 with Dr. Umberto Campia – Peripheral Artery Disease: What your legs can tell you about the health of your heart

October 11 with Gary Raskob, PhD – World Thrombosis Day and How You Can Help

November 5 with Dr. Christian Ruff – Genetics and Blood Clots: What's in the genes?

December 11 with Dr. Samuel Berkman – What's New? An Update on Bleeding While on Anticoagulants

NATF's Online Blood Clot Support Group offers patients the opportunity to share common concerns, offer support to one-another, and learn up-to-date and accurate information, including new research on blood clot prevention and treatments. Dates and speakers for our upcoming meetings can be found at www.natfonline.org/patients/support-groups. To register for this online support group, please email info@natfonline.org.

European Society of Cardiology Meeting

August 27, 2018

Munich, Germany

"Preventing PE & DVT in Heart Failure and Other Medically Ill Patients: An Innovative Action Plan"

2018 NATF Summit

September 26, 2018, 5:30 p.m. – 9:00 p.m.

The Fairmont Copley Plaza, Boston, MA

This special dinner program will provide a comprehensive review of the most important changes and advances impacting the care of patients who have, or are at risk for, diabetes and cardiovascular disease. Updates in treatment, diagnosis, and prevention will be given by leading experts in the fields of endocrinology, cardiology, and nephrology. This CME accredited program is for any healthcare provider involved in the care of patients with, or at risk for developing, diabetes and cardiovascular disease, and chronic kidney disease.

New Strategies for Preventing Pulmonary Embolism, DVT, and Stroke

September 28, 2018

Loyola University of Chicago, Stritch School of Medicine

This course is designed to define best-practice usage of direct oral anticoagulants (DOACs) for long-term prevention of stroke and venous thromboembolism. Participants will gain insights into updated implementation guidelines and recommendations to treat thrombosis.

Celebration of Gratitude

October 25, 2018

The Museum of Science Boston

NATF would like to invite you to join us for the 2018 Celebration of Gratitude, NATF's premier fundraising event. It will be an exciting night of inspiration, fun, and discovery. Guests will get exclusive access to the Museum of Science's Blue Wing and will get to spend the night exploring the wing's variety of eye-opening exhibits.

For more information on any of these events, please visit www.natfonline.org/events. We look forward to hearing from you!



PATIENT PERSPECTIVE

Continued from page 1

workout. The first week of August, in the middle of a workout, I had sudden groin pain and I thought to myself, "Oh, that's really weird."

It didn't make a lot of sense. I took it easy for a couple of days and applied ice. A few days later, it was gone. There was no leg pain.

Then, I slowly felt my stamina deteriorating. I was getting tired during simple exercises. As I got closer to my tryouts, I was having heart palpitations without really knowing what they were. My chest was very tight and I was incredibly fatigued. I had all of these symptoms that I couldn't explain.



Q: When did you realize how serious the problem was?

On the day of my soccer team's fitness test, August 30th, I had to drop out of the test because I couldn't breathe, and I had this horrible burning pain in my lungs. I had no idea what it was, because I should have been really fit given all of the training I had done.

That's when I knew something was wrong. I went to the health center at Colby and, luckily, met with a nurse practitioner who had seen pulmonary embolism (PE) in young people before. She knew to order me a D-Dimer test. I went to the hospital right down the street from school and got a CT scan, which later revealed that I had multiple bilateral PEs.

Q: What was your experience in the hospital like?

On August 31st, I was admitted to Maine General in Augusta, and I stayed there until September fifth, which was my twenty-first birthday. I was the only patient on the

Continued on page 5



HOW LONG SHOULD I BE ON AN ANTICOAGULANT?

Continued from page 1

should be considered. When determining how long you should be on an anticoagulant, it is important that you consult with a provider who specializes in such decisions and come up with an informed care plan with which you are comfortable. If you are unsure that the advice you received for how long to continue an anticoagulant is right for you, it is appropriate to get a second opinion.

In general, most people who have atrial fibrillation will require long-term courses of anticoagulation. This is because atrial fibrillation puts people at risk of developing a stroke. Even people who are not in atrial fibrillation regularly, those who take medicines to keep them out of atrial fibrillation, and those who have undergone ablation procedures are still at risk. Some people may choose to undergo a surgical procedure that can reduce the risk of stroke without the need for long-term anticoagulation. However, the majority of people with atrial fibrillation are recommended to take an anticoagulant for many years (often life-long).

People who have undergone surgery to have a mechanical heart valve placed are usually treated with anticoagulants. As long as the mechanical valve remains in your heart, you should remain on a blood thinner. Currently, warfarin is the only oral blood thinner used for people with mechanical heart valves.

How long to take a blood thinner is a more complicated question for people with a DVT or PE. Sometimes a DVT or PE has developed because of a temporary (and reversible) risk factor. Examples include a recent surgery or immobilization, or the use of hormone contraceptive pills. For these people, the risk of developing another DVT or PE in the future is lower. So shorter courses of blood thinners (e.g. 3-6 months) are usually recommended for their first blood clot. Other people develop a DVT or PE without a good reason (called "unprovoked"). These people have a higher risk of developing another blood clot, so longer courses of anticoagulation are often recommended. Anyone who has developed recurrent unprovoked DVT's or PE's is usually recommended to be on long-term (or life-long) anticoagulation.

Of course, every person is unique, and it is important for you, your family, and your provider to discuss the risks and benefits of short- vs. long-term anticoagulation. The newer anticoagulants are often easier to take and associated with lower risks of bleeding (including the most dangerous forms of bleeding). Many more people are being recommended to take long courses of anticoagulation because the treatment is relatively safer than a decade ago.

Similarly, long-term anticoagulation does not necessarily mean life-long. Factors may change, and new therapies are always in development. This is why it is important to check in with your provider at least once a year to make sure that staying on an anticoagulant is still the best choice for you!



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Bring Support to your Community!

NATF is looking for patients or healthcare providers that would like to start a blood clot support group in their area.

With short appointment times, it can be difficult for patients to get the answers and support they need to understand and process their blood clot diagnosis. Starting a blood clot support group with the North American Thrombosis Forum can help!

Don't take our word for it! One Boston support group member described their experience as, "Very encouraging. It became very clear that life after a blood clot is certainly a possibility and a real positive possibility."

If you, or someone you know, may benefit from starting a blood clot support group, email kmeredith@natfonline.org to learn more.



DOAC Reversal Deep

Dive: Andexanet Alfa

For the past several decades, warfarin has been the only FDA-approved oral anticoagulant for stroke prevention in atrial fibrillation as well as the treatment and prevention of venous thromboembolism, but new treatments have recently emerged in the form of direct oral anticoagulants (DOACs). These newer anticoagulants are at least as effective as warfarin and have a similar or decreased risk of bleeding; especially major bleeding.

Despite the lower risk of major bleeding with these agents, some risk remains and may increase due to trauma or major surgery. Until recently, there has not been a specific reversal agent available for these agents in the event of significant bleeding or an unexpected urgent procedure. A few years ago, the reversal agent, idaraziumab (Praxbind), became available to reverse the effects of dabigatran (an oral direct thrombin inhibitor) and now andexanet alfa (Andexxa) is available to reverse the factor Xa inhibitors (such as apixaban and rivaroxaban).

NATF is dedicated to offering readers a closer look at each DOAC and their reversal agents in order to empower patients to make informed healthcare decisions. In this issue of *The Beat*, NATF takes a closer look at andexanet alfa:

WHAT IS ANDEXANET?

Andexanet alfa, also known as Andexxa or coagulation factor Xa (recombinant), inactivated-zhzo, is an antidote that reverses the anticoagulant effects of the factor Xa inhibitors (e.g. apixaban



and rivaroxaban). It was approved by the FDA in May 2018 and made available to hospitals under an early supply program – a wider supply of commercial product is expected in 2019. Prior to the approval of andexanet, healthcare providers would manage bleeding and reversal of anticoagulation with supportive measures and blood factors which would replace the proteins in the body that were being blocked by the anticoagulant.

This new reversal agent is currently approved to reverse the effects of rivaroxaban and apixaban in the event of serious bleeding that cannot be controlled with supportive measures. It currently is not approved to reverse the effects of the other factor Xa inhibitors, betrixaban and edoxaban or the indirect Xa-inhibitors, such as enoxaparin. It is also not approved to reverse anticoagulation prior to procedures. Further studies are needed to confirm the safety and efficacy of andexanet to reverse the anticoagulant effects of the remaining

direct and indirect acting factor Xa inhibitors and to determine if it is a safe and effective strategy to reverse anticoagulation prior to emergent procedures.

The ANNEXA-A and ANNEXA-R trials showed that andexanet alfa quickly reversed the anticoagulant effect of rivaroxaban and apixaban in healthy patients and the ANNEXA-4 trial provided safety and efficacy data for patients on factor Xa inhibitors who were actively bleeding and required reversal. The trials showed that andexanet alfa, when given to patients actively bleeding, results in improved clotting factor levels and stops bleeding in the majority of patients.

HOW DOES IT WORK?

To understand how andexanet works, it is helpful to understand how the factor Xa inhibitors work. The factor Xa inhibitors block factor Xa, which is part of a system known as the “clotting cascade.” The clotting cascade is the system that allows blood to clot. By blocking factor Xa, apixaban and rivaroxaban reduce the risk of the body developing a blood clot in a place where it shouldn’t, but also decrease the body’s ability to form a clot when there is active bleeding. Andexanet alfa was designed to mimic factor Xa as a decoy. It binds to the anticoagulant, making it inactive and unable to block factor Xa. This allows the clotting cascade to act as it normally would in the event of bleeding - using factor Xa to form a clot and stop the bleeding.

Andexanet alfa is given as an infusion and requires administration in a hospital by a healthcare provider. It is given as a quick infusion at a higher dose, followed by a slower infusion over 2 hours. The dose of the infusion depends on the specific anticoagulant that the patient was taking, as well as the dose and the time since the last dose was ingested. The duration of effect of andexanet alfa is relatively short; just long enough to allow the body to initiate its normal clotting process. The healthcare team will monitor laboratory markers, as well as signs and symptoms of bleeding, to ensure that the medication was effective and to determine if other treatments are required.

WHAT ARE THE RISKS?

Patients who require anticoagulation either have already had a blood clot or are at risk of having a blood clot. By reversing anticoagulation, the risk of developing a blood clot increases back to where it was prior to treatment with the anticoagulant. To minimize the risk of developing a blood clot after administration of andexanet alfa, the healthcare team will evaluate the patient to determine if and when it is safe to re-start anticoagulation.

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PATIENT PERSPECTIVE

Continued from page 2

floor under seventy when I was admitted. My mom said they treated me like a rare unicorn, because they weren't used to seeing young people like me.

I got discharged on my birthday and I started classes the next day. The doctors wanted to keep me one extra day because my INR wasn't therapeutic yet. My levels were low, but I refused to miss the first day of classes. So, I had to give myself lovenox shots, which were really not fun. But, I went right into classes.

Q: Do you have any family history of blood clots or do the doctors know why you got them?

Yes, my clots were provoked. My grandfather had a history of deep vein thrombosis and pulmonary embolism when he was much older, and he had a lot of comorbidities. I was also taking birth control pills, which I'd been on since I was seventeen. I definitely think that the relationship between birth control pills and thrombotic events is one that isn't really discussed as much as it should be. On top of that, the doctors found that I'm heterozygous for the prothrombin gene mutation. So, with family history, genetics, and the triggering estrogen pills, it was the perfect storm.

Q: How are you feeling now?

It's been eleven months since the episode. I feel much better, physically and mentally. I was on warfarin for seven months. I know there are a lot of newer treatment options, but my parents were familiar with warfarin and felt comfortable having me go for weekly INR check-ins when I was away at school. I came off warfarin and have been feeling pretty good. I do cardio every day, taking an off day here and there, and I make healthy choices.

Q: How has this experience impacted your life?

The most immediate change in my life is that I'm not going to play soccer next year. Mentally, I'm just not ready yet. When you're on warfarin, you have to avoid trauma. You have to live life so cautiously. I'm trying to minimize my risk of having another episode. But, other than that, I did well in school and was able to do most of the things that I've always done.

Being a year out, I still have anxiety, but this experience has given me a whole new perspective on life. I stopped stressing the little things so much. My mindset switched from a "have to" to a "get to" attitude. I view everything that used to stress me out as a privilege. In classes I thought, "Wow. Everyone's worried about taking this exam, but two weeks ago I didn't know if I'd ever be taking another exam." I was lucky to be at school and sit for any exam, because I could have easily died from this.

Q: What would you want other blood clot patients your age to know about your experience?

This year my motto is, "it's not what you have, but what you do with it."

At first, when I was in the hospital it was awful, because I went from being a perfectly healthy athlete to a sick person. I felt horrible physically. Then, upon discharge I returned to my tiny liberal arts school and it seemed like everybody had their own perfect life while mine was going up in flames.

Initially I thought, "Why me?" I didn't smoke, I worked out, I wasn't supposed to be sick. My advice to anyone going through any health problem is to try to find the silver lining. I worked really hard to find the good in a very bad situation. I connected with the Thrombosis Research Group, and through studying what I have and reading other patients' stories, I've realized that I'm not alone in this. It's important to know that you are never alone in your struggles, and you can't look at yourself and say that you're defined by your medical condition.

The way everyone was reacting when I was first diagnosed, I thought, "Wow. I am such a medical anomaly." But the more people I talked to, the more I researched, and then coming to Boston, I've learned it's really not the case because PE and DVT can affect just about anyone at any point. This can really happen across all ages and genders.

Q: Did this impact your decision to become a doctor?

I've wanted to be a doctor since I was ten years old. But, when I became the patient myself, I gained a new appreciation for life that furthered my desire to practice medicine.

At the first soccer practice that I was able to watch after being in the hospital, I was on the field, and I just thought, "Wow, I'm really here. I'm living."

I was given this second chance at life that a lot of people that have blood clots don't get. I was really overcome by this realization and I thought, "What better way to spend my life than to be a doctor and grant that second chance to other people?"

Q: What advice do you have for other people?

Know your body. I had undiagnosed PE for three weeks. Being an athlete, we're conditioned to tough everything out. I knew something was wrong with me, but I had a fitness test to run. I thought, "Well, I'm not going to just not run my test. I'm an athlete, I'll do it."

It's important to listen to your body. If something is wrong and you have a gut feeling about it, get yourself seen by a nurse or a doctor, instead of trying to tough it out and risk a bad outcome. Nobody is invincible, and when you're an athlete you tend to think you are. I definitely thought I was. Anything can happen on any day, which is why you have to live in the moment and make the most of the time you have with the people you love.

Are you looking for support? Attend NATF's in-person support group in Boston or visit www.natfonline.org for information about NATF's online support groups.

Thank you, Sam, for sharing your story!

Are you inspired by stories like Sam's? You can help patients similar to Sam by starting a support group in your community. Join us in the fight against blood clots and email: info@natfonline.org.



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