GLOBAL HEMOPHILIA REPORT

SEASON ONE SUMMARY

Led by science, curiosity, and storytelling, the Global Hemophilia Report from BloodStream Media is an entertaining monthly journey through the investigations and science driving hemophilia research around the world.

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EPISODE 01

Inhibitors: Prevention, Eradication, and Lived Experiences

Contributors:

- Dr. Glaivy Batsuli
- Dr. Shannon Carpenter
- Dr. Michael Recht
- Dr. Shannon Meeks
- Kevin Finkle (patient)
- Ashley Druckenmiller (caregiver)
- Michelle Johanssen (caregiver)
- Natalie Boehm
- Dr. Guy Young

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The issue with inhibitors is they make what the patient needs not effective.

- Dr. Glaivy Batsuli

The Backdrop

Inhibitors have been considered the most significant complication of severe hemophilia for the past 20 years. While many have benefited from continued development of replacement factor products, those with inhibitors have been unable to effectively prevent bleeding. In 2017, the approval of the first non-factor therapy, emicizumab, revolutionized treatment and dramatically improved the lives of those with severe hemophilia A and inhibitors, but has led to additional questions about ideal strategies, particularly in pediatric patients.

The Breakdown

This episode covers what an inhibitor is, risk factors, consequences for people with inhibitors, why inhibitors are so difficult to manage, how immune tolerance therapy is helping some people, how emicizumab's introduction altered the landscape and considerations, and where the current research focus is.

We still want to get rid of inhibitors if we can.

- Dr. Mike Recht

The Bottom Line

We still need to know more about inhibitors so we can figure out how to prevent and eliminate them entirely. We don't know why inhibitors develop in some people and not in others. While emicizumab was a breakthrough, it doesn't solve the problem of inhibitors. It doesn't prevent all bleeds and it doesn't work for everyone, including those with hemophilia B, making continued research on inhibitors important.

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EPISODE 02

Novel Therapies: Entering Uncharted Territory

Contributors:

- Dr. Maria Elisa Mancuso
- Dr. Glenn Pierce
- Dr. Steven Pipe
- Dr. Lindsey George
- Dr. Margareth Ozelo
- Dr. Guy Young
- Dr. Michael Recht
- Dr. Rich Gorman (patient POV)
- Mark Skinner (patient POV)
- Luke Pembroke (patient POV)

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The Backdrop

People with hemophilia have benefited from advanced therapies over the past three decades. However, more recently, there has been unprecedented therapeutic innovation aimed at the prevention and treatment of bleeding and the potential cure of clotting factor deficiency. Gene therapy. Hemostatic rebalancing therapies. Factor memetic therapies. New factor replacement therapy. All of these novel therapies are being explored in clinical trials.

The Breakdown

This episode covers the current state of novel therapy investigation in hemophilia, their safety and effectiveness, and the challenges they might create, such as insurance coverage, global availability, and navigating the many treatment options.

If we really want to go for a super extended half-life factor VIII, we're going to have to divorce it from binding to Von Willebrand factor.

- Dr. Steve Pipe on innovation to recombinant factor VIII

The Bottom Line

While these potential therapies might pave the way to better and easier treatment — perhaps even a cure — they are also sweeping the hemophilia community into uncharted territory. There are still a lot of questions left to be answered, including how any approved novel therapies will be paid for and integrated into current care in both the U.S. and globally.

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EPISODE 03

Prophylaxis: Protection, Achievements, and Shortcomings

Contributors:

- Dr. Marilyn Manco-Johnson (also topic advisor)
- Dr. Kathelijn Fischer (also topic advisor)
- Dr. Robert Sidonio
- Dr. Manuel Carcao
- Dr. Maria Elisa Mancuso
- Susan Lynch (caregiver)

Episode Advisors:

- Dr. Marilyn Manco Johnson
- Dr. Kathelijn Fischer

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In Italy primary prophylaxis arrived rather late in comparison with other countries. This was pretty much related to the tragedy of the bloodborne viral infections, which had a very bad impact, psychologically.

- Dr. Maria Elisa Mancuso

The Backdrop

Prophylaxis in hemophilia has led to extraordinary progress. But while the overall musculoskeletal health of people with hemophilia has significantly improved, the goal of having musculoskeletal health comparable to those without hemophilia has still not been achieved. Furthermore, the impact of prophylaxis has been uneven across hemophilia populations, and the promise of greater physical activity free of bleeding has not been entirely fulfilled.

The Breakdown

This episode covers the history, evolution, and current state of prophylaxis — including its use in females as well as in patients with moderate and mild hemophilia — and highlights current and future areas of research.

This is a whole new world.

- Dr. Marilyn Manco-Johnson

The Bottom Line

While revolutionary and life-changing for so many, prophylaxis is not a cure. We are still learning about how and why it works better in some people and its impact, including the effects of undetected “microbleeding” in joints. Even if gene therapy becomes a reality, prophylaxis will continue to play an important role, including in those not eligible or able to access gene therapy.

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EPISODE 04

Bone and Joint Health: Monitoring and Detection Strategies

Contributors:

- Dr. Marilyn Manco-Johnson (also topic advisor)
- Dr. Kathelijn Fischer (also topic advisor)
- Dr. Annette Von Drygalski
- Dr. Tyler W. Buckner
- Dr. Amy Dunn
- Dr. Suchitra S. Acharya
- Dr. Andrea Doria
- Dr. Beth Warren
- Tom Russomano (patient)

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I think that MRI right now is the most sensitive imaging.

- Dr. Marilyn Manco-Johnson

The Backdrop

Even with the significant advancement of prophylaxis, the goal of achieving perfect bone and joint health for people with hemophilia through normalizing homeostasis remains elusive. Furthermore, prophylaxis has not been available equally across hemophilia populations, meaning not everyone with hemophilia has access to the promise of few or no bleeds.

The Breakdown

This episode covers the current monitoring and detection strategies for bleeds and the investigational work aimed at enhancing existing tools, validating suspected tools, and discovering entirely new ones with the goal of positively impacting lifelong bone and joint health.

Ultrasound, I find it very useful. It’s my favorite toy.

- Dr. Kathelijn Fischer

The Bottom Line

Ongoing goals in the treatment and research arenas are to eliminate chronic pain and improve joint and bone function. Having perfect joints and bones is not a realistic goal for most people — with or without hemophilia. However, it is worth striving to help people with hemophilia get to a place where their joint and musculoskeletal health matches that of a healthy person their age without hemophilia.

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EPISODE 05

Mental Health and Hemophilia in Adolescence and Young Adulthood

Contributors:

- Dr. Michelle Witkop (also topic advisor)
- Samantha Carlson, LMSW (also topic advisor)
- Randall G. Curtis, MBA (patient)
- Dr. Gráinne O’Brien
- Dr. Duc “Bobby” Tran
- Amanda Stahl, LCSW

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To my knowledge, there are no good mental health tools or interventions to help successfully transition patients from adolescence to adulthood.

- Dr. Bobby Tran

The Backdrop

In March 2022, a Washington Post article highlighted a mental health crisis among children and adolescents in the U.S., pointing out that society has turned a blind eye. The crisis predates the COVID-19 pandemic, which has only increased feelings of anxiety and major depressive disorders in young people across the globe. How does a hemophilia diagnosis further complicate a young person's mental wellbeing? And what data exists to support interventions?

The Breakdown

This episode covers the understanding of hemophilia's impact on a young person's mental health, the role of transition to independence, and the state of research.

The Bottom Line

People of all ages with hemophilia experience stressors and challenges, including acute and chronic pain, fear of bleeds, strain on relationships, school and work functioning, and exclusion from activities. However, there is little research specific to the effect of hemophilia on the mental wellbeing of children and young people. There does appear to be a connection between physical symptoms and mental health in adolescents, but more research is needed.

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EPISODE 06

Women with Hemophilia: Research Priorities

Contributors:

- Dr. Angela Weyand (also topic advisor)
- Dr. Robert Sidonio (also topic advisor)
- Dr. Andra James
- Dr. Tyler Buckner
- Dr. Maureen Baldwin
- Connie Miller, PhD (patient)
- Kristin Paulyson Nunez, MS, CGC
- Dawn Rotellini (patient)
- Yannick Colle (patient)

Episode Advisors:

- Angela Weyand, MD
- Robert Sidonio, MD

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All of our definitions of hemophilia are based on males. We don’t know what factor level is required to have normal menstrual periods or to have normal delivery.

- Dr. Connie Miller

The Backdrop

Women, girls, and people with the potential to menstruate (WGPPM) who live with hemophilia have more difficulty getting a diagnosis and accessing adequate care than their biological male counterparts. But why? What research is underway to support the needs of these individuals?

The Breakdown

This episode takes a wide-lens approach to exploring the sociocultural barriers and challenges that WGPPM in the global hemophilia community face.

The Bottom Line

Historically, hemophilia was thought to only affect males, with females thought of as only “carriers” and assumed to be free from bleeding problems. We know this is not true today, but it has likely contributed to WGPPM facing delayed and often inaccurate diagnosis, underestimation of their bleeding symptoms, and lack of treatment. There is also a societal gender bias and discrimination against WGPPM, including lack of research focused on this population.

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EPISODE 07

Mid-Point Conversations: A Summary

Contributors:

- Patrick James Lynch
- Laurence Woollard
- Donna DiMichele, MD

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The Backdrop

In this episode, Global Hemophilia Report Executive Producer Patrick James Lynch is joined by Senior Advisor Dr. Donna DiMichele and Writer/Host Laurence Woollard.

The Breakdown

The trio gathered in-person at the National Hemophilia Foundation Bleeding Disorders Conference in August 2022 to reflect on Season 1 so far, as well as to debate existing and emerging research priorities from each previous episode.

The Bottom Line

The previous episodes have been enlightening and educational — even for some of the contributors to the podcast — but there is much more to cover. There are so many nuances to hemophilia management, treatment, and research, and some of those issues will be explored in future episodes.

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EPISODE 08

Hemophilia B & the story of Tsarevich Alexei — Part 1

Contributors:

- Dr. Amy Shapiro (also topic advisor)
- Professor Jan Astermark (also topic advisor)
- Dr. Bethany Samuelson Bannow
- Kathaleen M. Schnur, MSW, LCSW
- Brian O’Mahony

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“Alexei had a surgeon, Dr. Derevenko, and his assistant Nagorny, assigned to him full time as his personal attendants and bodyguard in the event of a bleeding episode. According to Pierre Gilliard, who was appointed as Alexei’s tutor in 1913, Dr. Derevenko explained that the Heir was a, quote-on-quote, “prey to haemophilia” and that the “slightest wound might cause the boy’s death”. As such, “all that could be done was to watch over him closely day and night, especially in his early years, and by extreme vigilance try to prevent accidents.

- Tsarevich Alexei

A lot of individuals who have hemophilia B actually have some circulating protein. That protein may not work as well as normal protein, but it can still go to places outside the circulation, which factor IX does, and ultimately interfere- potentially- with factor IX treatment.

- Dr. Jan Astermark

The Backdrop

Hemophilia B is a rare inherited X-linked disorder characterized by a congenital anomaly in the factor IX gene that leads to a variable deficiency in clotting factor IX. Tsarevich Alexei Nikolaevich Romanov is one of the more famous people in history to have hemophilia. He was born in 1904 with hemophilia B. He was the heir apparent of Russia, but he was murdered with his family when he was only a young teenager.

The Breakdown

In this episode, we cover the known differences between hemophilia B and hemophilia A, inhibitor development in hemophilia B, and the priority areas for further research into hemophilia B. The episode also guides listeners on an entertaining journey through 19th and 20th century European monarchy and the unlikely role that hemophilia played in forever shaping Europe’s governance.

If we really want to go for a super extended half-life factor VIII, we're going to have to divorce it from binding to Von Willebrand factor.

- Dr. Jan Astermark

The Bottom Line

Hemophilia B has clear genetic differences from hemophilia A — it's not simply a difference in which clotting factor is deficient. This leads to a unique pattern of mutations and distinctly different risks and manifestations of inhibitor development in Hemophilia B. Tune in to episode 9 for the continuation of the story about Tsarevich Alexei.

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EPISODE 09

Hemophilia B & the story of Tsarevich Alexei — Part 2

Contributors:

- Dr. Amy Shapiro (also topic advisor)
- Professor Jan Astermark (also topic advisor)
- Dr. Bethany Samuelson Bannow
- Kathaleen M. Schnur, MSW, LCSW
- Brian O’Mahony

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Factor VIII goes up in pregnancy. Factor IX does not. So most of my patients who are ‘carriers’ of hemophilia A, their factor VIII level normalizes around the time of delivery. That’s not true with factor IX, and we don’t know what the goal is.

- Dr. Bethany Samuelson Bannow

The Backdrop

Hemophilia B is a rare inherited X-linked disorder characterized by a congenital anomaly in the factor IX gene that leads to a variable deficiency in clotting factor IX. Like with hemophilia A, women, girls, and people with the potential to menstruate (WGPPM) who have hemophilia B face barriers of diagnosis, treatment, and research.

The Breakdown

In this episode, we spotlight research priorities in WGPPM with hemophilia B and novel therapies to treat people with hemophilia B. We also conclude the story of Tsarevich Alexei.

The Bottom Line

Hemophilia B has clear genetic differences from hemophilia A — it's not simply a difference in which clotting factor is deficient. This means hemophilia B can clinically manifest differently from hemophilia A. In pregnancy, for example, factor IX does not increase in pregnancy like factor VIII does with hemophilia A. Differences also apply to how treatment advances have impacted individuals with hemophilia B and how research into novel therapies for hemophilia B has been driven. The episode concludes the story about Tsarevich Alexei.

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EPISODE 10

Pain in Hemophilia — Part 1 — Prevalence, Mechanisms, and Assessment

Contributors:

- Nathalie Anne Roussel, PhD, MSc, PT
- Paul Mc Laughlin, BSc, MSc, MMACP
- Michelle Rice
- Michelle Witkop, DNP, FNP-BC (also topic advisor)
- Dr. Tyler Buckner (also topic advisor)

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Pain is a personal experience and we often refer to that as being subjective. However, that doesn't mean that we can't ask about pain and measure pain in a way that is helpful.

- Dr. Tyler Buckner

The Backdrop

According to the Centers for Disease Control and Prevention, pain is one of the most common reasons people seek medical care. However, for those with hemophilia A and B, the experience of pain provides the subtext for so many issues related to health and wellbeing across the lifespan — irrespective of gender, age, and hemophilia severity levels.

The Breakdown

This episode explores pain's prevalence, mechanisms, and more. Pain is embedded in the life experience of a person with hemophilia. It is a substantial contributor to poor health-related quality of life in adolescence and young adulthood — although it is not characterized as much in children. The negative impact of pain often increases throughout adulthood

The Bottom Line

One of the challenges with pain is that it's hard for a person to describe their personal "subjective" pain and pain levels. The types of pain treatment vary — from medication to meditation, surgery to exercise — and not all treatments work for every individual. On a typical hemophilia treatment center care team no one person takes ownership of pain when addressing an individual's pain. We need to create a system that takes responsibility for comprehensively addressing an individual's pain.

EPISODE 11

Pain in Hemophilia — Part 2 — Exercise, Medication, and Investigations

Contributors:

- Nathalie Anne Roussel, PhD, MSc, PT
- Paul Mc Laughlin, BSc, MSc, MMACP
- Michelle Witkop, DNP, FNP-BC (also topic advisor)
- Dr. Tyler Buckner (also topic advisor)

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We did a literature study a couple of years ago to better understand chronic pelvic pain in the general population. So not in the bleeding disorder community. Two conclusions were very clear from this research: he mental health was not taken into account, so there was a lack of research exploring psychological distress and psychological factors related to chronic pelvic pain. It is a sensitive issue. It is a delicate region.

- Nathalie Roussel, PhD

The Backdrop

Pain can affect a person's life in many profound ways. Beyond the actual horrible feeling of pain, pain creates endless consequences and disruptions to an individual's life.

The Breakdown

This episode continues the discussion of chronic pain in hemophilia including the socioeconomic drivers of pain, clinical assessment of an individual's experience of pain, and the multimodal approaches to pain management including PT, exercise and medication. The need for more and better research is highlighted.

The Bottom Line

We lack research data on pain itself, as well as many different areas of pain in people with hemophilia. A multi-year opioid crisis has led to restrictions on pain medication, while research on and access to cannabis continues to be restricted. We also need more research on pain's effect based on many socioeconomic factors, such as race, employment status, economic status, and access to care.

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EPISODE 12

Where Does Research Go From Here?

Contributors:

- Patrick James Lynch
- Donna DiMichele, MD

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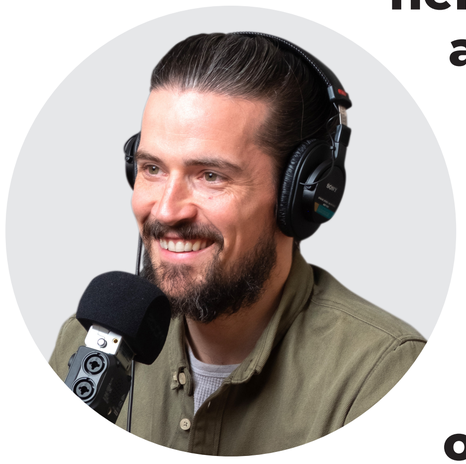
After just one season of the Global Hemophilia Report, I have a much greater appreciation of the role of research. Today I am proud and honored to know that my former doc went on to become one of the most influential leaders in not just hemophilia research but all kinds of research through her role at the National Institutes of Health. And I'm proud yet again that I now call her a colleague on this podcast.



- Patrick James Lynch

The Backdrop

Host Patrick James Lynch sits down with the Global Hemophilia Report's Senior Advisor Dr. Donna DiMichele.

The Breakdown

Renowned hematologist, researcher, and senior advisor to the Global Hemophilia Report Dr. Donna DiMichele shares some of her Season 1 takeaways and thoughts about the future of hemophilia research.

The Bottom Line

We delve a little deeper into research in hemophilia which will set up our first episode of Season 2. We also hear some of Dr. DiMichele's thoughts on the first season of the podcast

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