



Synovitis in Haemophilia: A Factor Think Tank Podcast Series

Episode 3. Impact on joint health
Slide summary

Disclaimer

- The Factor Think Tank is an educational activity funded by Sobi. Synovitis in Haemophilia: A Factor Think Tank Podcast Series was developed by the Factor Think Tank working group and the accompanying slide deck is only intended for healthcare professionals
- Slides 6–8 summarise content from the e-Delphi consensus article by Mancuso et al.;¹ wording closely resembles that of the article to reflect the e-Delphi consensus discussions
- All views and opinions expressed in the podcast are those of the participants only
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Synovitis in Haemophilia: A Factor Think Tank Podcast Series (1)

- Findings from the e-Delphi consensus study on synovitis and joint health in haemophilia have been published in [Haemophilia](#) and provide the basis for the podcast series

HAEMOPHILIA

Synovitis and joint health in patients with haemophilia:
Statements from a European e-Delphi consensus study

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Synovitis in Haemophilia: A Factor Think Tank Podcast Series (2)

- The e-Delphi consensus examined five key domains relevant to synovitis in haemophilia:
 - Definition and pathophysiology
 - Diagnosis
 - Impact on joint health
 - Monitoring and follow-up
 - Prevention and treatment
- Based on these key domains an educational [series of five podcasts](#), featuring lead author Dr Maria Elisa Mancuso and co-authors or expert guest speakers, is available to healthcare professionals

This slide deck provides supporting information for [Episode 3. Impact on joint health](#) of the podcast series on synovitis in haemophilia



An overview of synovitis in haemophilia

- Synovitis is defined as inflammation of synovial tissue within the joint¹
- It is common in patients with haemophilia in response to blood within joints and is the first step towards the development of chronic arthropathy¹
- One bleeding episode can initiate synovial inflammation, which may develop into chronic synovitis if bleeds recur frequently and are not adequately prevented²
- Synovitis is highly relevant to joint health in haemophilia; however, knowledge gaps exist regarding definition, pathophysiology, diagnosis, prevention, follow-up and treatment³
- Delphi methodology, which is often used to produce best-practice guidelines where evidence is missing, was employed to conduct a European e-Delphi consensus study on synovitis in haemophilia³

1. van Vulpen L, et al. Haemophilia. 2021;27(Suppl. 3):96–102; 2. van Vulpen L, et al. Osteoarthritis Cartilage. 2015;23:63–9;
3. Mancuso M, et al. Haemophilia. 2023;29:619–28

e-Delphi consensus article

Domain: Impact of synovitis on joint health (statements 9–11)

Impact on joint health of synovitis in haemophilia

e-Delphi consensus statements 9–11: Background

- Synovitis plays a major role in the development of joint damage, with the presence of intra-articular blood as the main trigger^{1–6}
- Detection of synovitis in asymptomatic joints during routine musculoskeletal ultrasound assessment for synovial hypertrophy has been attributed to silent bleeds or microbleeds, although there is no direct evidence for such phenomena^{7–11}

1. van Vulpen L, et al. Haemophilia. 2017;23:521–7; 2. Jansen N, et al. Arthritis Rheum. 2007;56:199–207; 3. Jansen N, et al. Osteoarthritis Cartilage. 2009;17:433–40; 4. Madhok R, et al. Arthritis Rheum. 1988;31:1148–55; 5. Roosendaal G, et al. Haemophilia. 2008;14(Suppl. 6):4–10; 6. Valentino L, et al. Haemophilia. 2007;13(Suppl. 3):10–13; 7. Puetz J, et al. J Thromb Haemost. 2018;16:1914–17; 8. Wharton R, et al. Hamostaseologie. 2017;37:104–6; 9. Manco-Johnson M, et al. N Engl J Med. 2007;357:535–44; 10. Olivieri M, et al. Haemophilia. 2012;18:369–74; 10. De la Corte-Rodriguez H, et al. Expert Rev Hematol. 2018;11:253–61; 11. Seuser A, et al. Sensors (Basel). 2018;18:518

Impact on joint health of synovitis in haemophilia

e-Delphi consensus statements 9–11

9 Synovitis is the major cause for haemophilic arthropathy

10 A single joint bleed can lead to synovitis and subsequent joint damage irrespective of haemophilia severity

11 In asymptomatic joints, presence of synovitis is indicative of silent bleeds or microbleeds

Podcast discussion points

Synovitis in Haemophilia: A Factor Think Tank Podcast Series
Episode 3. Impact on joint health

Episode 3. Impact on joint health

- This episode focuses on six topics relevant to the impact of synovitis on joint health in haemophilia:
 - Clinical course of synovitis
 - Joints typically affected
 - Surrounding bone and tissue
 - Impact on joint function
 - Number of bleeding events required for synovitis and joint damage
 - Synovitis in asymptomatic joints
- Host Dr Maria Elisa Mancuso leads the discussion with Factor Think Tank member Dr Sébastien Lobet



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Dr Sébastien Lobet, Sports Physiotherapist, Doctor in motor science and a researcher at the Cliniques Universitaires Saint-Luc in Brussels, Belgium

Topic 1. Clinical course of synovitis (1)

- Synovitis occurs in response to joint bleeds, representing the first milestone in chronic arthropathy
- Painless swelling can occur with range of motion typically preserved in the early stages
- Repeated intra-articular bleeds expose the synovium to blood components, resulting in inflammation, proliferation and neovascularisation of the synovial tissue, which becomes more vulnerable to subsequent bleeding events since the highly vascular and hypertrophic tissue is more likely to be impinged between the articular surfaces of the joint
 - For example, the synovial membrane in the ankle is frequently pinched during dorsiflexion in patients who have severe arthropathy and an osteophyte on the anterior part of the tibia and talus
- Without adequate treatment for joint bleeds, a vicious cycle of bleeding and synovitis can occur, leading to chronic synovitis

Topic 1. Clinical course of synovitis (2)

- In chronic synovitis:
 - Joint function can become mildly impaired and in some cases range of motion can be moderately affected
 - Muscle atrophy and loss of proprioception can also occur
 - Pain is often associated with more advanced stages
- The e-Delphi consensus study concluded that synovitis is the major cause of haemophilic arthropathy
- Repeated joint bleeding and pathological changes to the synovium contribute to end-stage degeneration and haemophilic arthropathy

“Without adequate treatment for joint bleeds, a vicious cycle of bleeding and synovitis can occur, leading to chronic synovitis”

Topic 2. Joints typically affected

- As haemarthrosis primarily affects the large synovial joints, synovitis typically occurs in the knees, elbows and ankles
- As synovitis in haemophilia typically only affects a few large synovial joints, joint damage and inflammation are easier to quantify than in systemic inflammatory diseases, such as osteoarthritis or rheumatoid arthritis

“Synovitis typically occurs in the knees, elbows and ankles”

Topic 3. Surrounding bone and tissue

- The important role of synovitis in joint damage has been clearly shown from basic and clinical research
- Repeated joint bleeding and synovitis can result in progressive destruction of the cartilage and bone
 - Synovial tissue proliferates and becomes invasive, leading to articular cartilage destruction of the affected joint
 - Direct contact between blood and cartilage can induce chondrocyte apoptosis and tissue degeneration, leading to irreversible joint damage
- In the early stages of synovitis, osteochondral damage likely occurs due to the negative impact of blood and iron on chondrocytes
- In more advanced stages, further osteochondral damage can occur due to pro-inflammatory factors and altered bone homeostasis, contributing to increased bone resorption and subchondral damage

“Repeated joint bleeding and synovitis can result in progressive destruction of the cartilage and bone”

Topic 4. Impact on joint function (1)

- Assessing the impact of early synovitis on joint function is challenging due to substantial variation within the general population in terms of range of motion, strength and gait; pathological function is easier to classify in the later stages of synovitis
- Most aspects of joint function (strength, gait and viscoelastic properties) are preserved in children and young adults with early synovitis
- Children and young adults can have repeated joint bleeding without reduced muscle strength, suggesting a latency period between structural and functional impairments, however, it can be difficult to classify patients as having normal or deficient strength based on age

Topic 4. Impact on joint function (2)

- Structural lesions may remain subclinical with respect to functional activities of moderate intensity, such as walking
- Proprioception seems to be affected in children and young adults with synovitis; mechanoreceptors located in the joint capsule near the synovial tissue are likely to impact proprioception by affecting coordination of muscle contraction
- It is important to start rehabilitation after each bleeding episode to restore proprioception in children and young adults with synovitis

“It is really challenging to assess and quantify the impact of early synovitis on joint function”

Topic 5. Number of bleeding events required for synovitis and joint damage

- The presence of blood in the joints can cause rapid articular cartilage damage
- A single joint bleed can lead to synovitis and subsequent joint damage, irrespective of haemophilia severity

“A single joint bleed can initiate a pathological cascade resulting in fast progressive arthropathy”

Topic 6. Synovitis in asymptomatic joints

- In asymptomatic joints, synovitis is indicative of potential silent bleeds or microbleeds (microscopic amounts of blood leaking into a joint)
- These can still trigger a vicious cycle of biochemical and biomechanical reactions, leading to irreversible, long-term joint damage
- Joint microbleeding can result in haemophilic arthropathy even if patients are receiving the most advanced forms of treatment for haemophilia

“Even in the presence of microscopic amounts of blood in the joint cavity, silent bleeds can still trigger a vicious cycle”

Conclusions

- Synovitis occurs in response to joint bleeds, even one of which may be sufficient to initiate the inflammatory process in the synovium
- Synovitis can be initially asymptomatic, but if persistent can impact joint function and impair range of motion
- Persistence of inflamed synovium leads to irreversible osteochondral damage
- In asymptomatic patients, synovitis may indicate silent bleeds that may require better haemostatic coverage

Listen to the whole series

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More in the series

- If you enjoyed this podcast and want to find out more about the Factor Think Tank, please visit the website: www.factorthinktank.com
- All episodes in the series can be found here:
 - Episode 1. Definition and pathophysiology (Dr Maria Elisa Mancuso and Dr Robert Klamroth)
 - Episode 2. Diagnosis (Dr Maria Elisa Mancuso and Prof Dario Di Minno)
 - Episode 3. Impact on joint health (Dr Maria Elisa Mancuso and Dr Sébastien Lobet)
 - Episode 4. Monitoring and follow-up (Dr Maria Elisa Mancuso and Dr Katharina Holstein)
 - Episode 5. Prevention and treatment (Dr Maria Elisa Mancuso and Dr Gianluigi Pasta)