# From birth to breastfeeding and beyond with plasma-derived C1 inhibitor treatment

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# Financial disclosure

Dr. Thomas Buttgereit is or recently was a speaker and/or advisor for

AstraZeneca, BioCryst Pharmaceuticals, CSL Behring, GSK, Hexal, KalVista Pharmaceuticals, Medac, Novartis, Pharming, Roche, Sanofi, and Takeda

# General medical history

- **36-year-old** female with HAE-C1INH Type I, no comorbidities
- Initial manifestation of HAE attacks at **age of 11 years**
- Low C4↓, low C1INH levels/function↓, SERPING1 gene mutation
- Two children: one son (XXYY) and one daughter (healthy)


- **First pregnancy (2013):** 4 attacks/month, initiation of LTP with pdC1INH* IV†
- **Second pregnancy (2018):** 6 attacks/month, initiation of LTP with pdC1INH* IV†

*According to the Summary of Product Characteristics for plasma-derived C1INH products, there is limited data that indicate no increased risk from the use of plasma-derived C1INH in pregnant woman. Plasma-derived C1INH should be given to pregnant women only if clearly indicated.
†Intravenous pdC1INH indication for use in LTP varies by manufacturer.
C1INH, C1-esterase inhibitor; C4, complement component 4; HAE, hereditary angiodema; HAE-C1INH, HAE with C1INH deficiency; IV, intravenous; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1INH.

# Current medical history

- **February 2021:** Started LTP with lanadelumab, five injections up to September 2021
- **September 2021:** Patient expresses desire for a third child, discloses a spontaneous abortion in May 2021
  - **Stop lanadelumab and start on-demand therapy with pdC1INH concentrate IV**
- **February 2022:** Patient reports increased attack rate
  - On-demand therapy with pdC1INH concentrate every 4 days was needed
- **April 2022:** Third month of pregnancy the patient reports HAE attacks every 2–3 days
  - Switch to LTP with pdC1INH concentrate SC* twice per week
- Since then, **patient is attack free throughout pregnancy**

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HAE, hereditary angiodema; IV, intravenous; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1-esterase inhibitor; SC, subcutaneous.

# Preparation for labour, delivery, and breastfeeding

- **April – September 2022:**
  - Close monitoring via short telephone consultations

- **September 2022 (37th week of pregnancy):**
  - Discussion of the *individual treatment plan*

# HAE-C1INH – evidence for use during labour and delivery

- Delivery is associated with **substantial mechanical trauma**, however, **HAE attacks are rare during labour and delivery**
- HAE attacks may occur **either during labour or within 48 hours of delivery**
- **Vaginal delivery is preferred**, because surgery or general anasthesia may involve endotracheal intubaton causing HAE attacks
- It is recommended that **labour and delivery are managed in the hospital setting** (as opposed to at home) unless robust measures for the prompt and effective treatment of HAE attacks are available

HAE, hereditary angiodema; HAE-C1INH, HAE with C1-esterase inhibitor deficiency.

# Treatment recommendations for labour and delivery in patients with HAE

- STP with pdC1INH concentrate, and epidural anesthesia, is recommended before a cesarean section if this is planned

- STP before vaginal delivery is not mandatory, but recommended if:
  a) symptoms have been **recurring frequently during the 3rd trimester**
  b) patient's history includes **genital oedema caused by mechanical trauma**
  c) **forceps delivery/forceps extraction** is planned

- **pdC1INH concentrate** should always be available for immediate on-demand use

- STP with pdC1INH concentrate is mandatory if intubation is planned

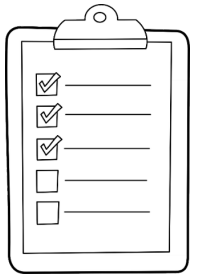
HAE, hereditary angiodema; pdC1INH, plasma-derived C1-esterase inhibitor; STP, short-term prophylaxis.
Maurer M, *et al. Allergy* 2022;77(7):1961–1990.

# Preparation for labour, delivery, and breastfeeding

- **April – September 2022:**
  - Close monitoring via short telephone consultations

- **September 2022 (37th week of pregnancy)**
  - Discuss the patient's *individual treatment plan*

- **Individual treatment plan for labour/delivery:**
  - **LTP:** Continuation of pdC1INH SC at least 2x/week until delivery
  - **STP:** Consideration of pdC1INH IV 20 IU/kg in case of surgery
  - **On-demand therapy:** pdC1INH IV (sufficient to treat at least two attacks) on hand



- Call with birth clinic obstetrics team to discuss the patient's management plan

IU, international unit; IV, intravenous; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1-esterase inhibitor; SC, subcutaneous; STP, short-term prophylaxis.

# Labour and delivery

**October 2022: Onset of labour and journey to hospital:**

- Patient was brought to hospital by her husband and provided with 1x STP and 2x on-demand therapy with pdC1INH concentrate, respectively
- HAE pass

**Delivery:**

- Complication free and spontaneous vaginal delivery (full-term)
- Patient had **no HAE attacks**
- Healthy boy, 3760g, 53cm

Patient did not want to continue LTP with pdC1INH concentrate postpartum

HAE, hereditary angiodema; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1-esterase inhibitor; STP, short-term prophylaxis.

# HAE-C1INH – evidence for use in breastfeeding, and treatment recommendations

- Breastfeeding may be associated with an **increased frequency of HAE attacks**, especially **abdominal** attacks[1,2]
- Increased attack rate may be due to **elevated serum prolactin levels** during lactation[3]
- Lactation is recommended based on **benefits provided to the infant**[1]
- **pdC1INH concentrate is recommended as 1st line** treatment for on-demand therapy, STP and LTP when indicated during lactation*[1]

*There is no information regarding the excretion of pdC1INH in human milk, the effect on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for pdC1INH and any potential adverse effects on the breastfed infant from pdC1INH or from the underlying maternal condition.

HAE, hereditary angioedema; HAE-C1INH, HAE with C1-esterase inhibitor deficiency; pdC1INH, plasma-dervied C1-esterase inhibitor; LTP, long-term prophylaxis; STP, short-term prophylaxis.

1. Maurer M, *et al. Allergy* 2022;77(7):1961–1990; 2. Martinez-Saguer I, *et al. Am J Obstet Gynecol* 2010;203(2):131.e1–7; 3. Czaller I, *et al. Eur J Obstet Gynecol Reprod Biol* 2010;152(1):44–49.

# Lactation and breastfeeding

- Patient was **monitored in hospital for 3 days postpartum**, with **no HAE attacks**

**Since week 3 postpartum:**

- Patient reported an increased frequency of maternal HAE attacks
- These were reported as 1 abdominal attack/week
- pdC1INH concentrate IV on-demand therapy was frequently used

**Week 8 postpartum:**

- **Re-initiation of LTP with pdC1INH concentrate** SC 2x/week
- Patient was attack free with excellent tolerability

HAE, hereditary angioedema; IV, intravenous; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1-esterase inhibitor; SC, subcutaneous.

# Testing newborns for HAE

- Newborns with a positive family history of HAE are considered at risk and **must be tested as early as possible**
- Complement testing in children <1 year old lacks reference values, but **measurement of C1INH levels may be more meaningful than measuring C4 levels**
- Early complement testing should be repeated after the age of 1 year
- **Genetic testing increases the diagnostic reliability** and may be helpful where biochemical measurements are inconclusive, and the genetic mutation of the parent is known

C1INH, C1-esterase inhibitor; C4, complement component 4; HAE, hereditary angioedema.
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# Take-home messages

- HAE attacks are rarely reported during labour and delivery, but may occur either during labour or within 48h of delivery
- Breastfeeding may be associated with an increased number of maternal HAE attacks, but is recommended based on benefits provided to the infant
- pdC1NH concentrate is safe and effective and recommended as 1st line treatment for on-demand therapy, STP and LTP during labour, delivery and lactation and breastfeeding
- **Pregnant women with HAE need an individual treatment and management plan**

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