Rigshospitalet

Department of oto-rhino-laryngology, head and neck surgery and audiology

Hereditary angioedema

What is it, how does it manifest and how do we treat it?

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Disclosures

Eva Rye Rasmussen has received research grant support and/or speaker fees from Shire, CSL Behring, Viropharma, Roche and MSD Norway.

Curriculum vitae

- Specialty registrar in oto-rhino-laryngology in Copenhagen, Denmark
- Published 42 papers since 2012, hereof 22 about angioedema
- Special interest in patients with angioedema with and without complement C1 deficiency
- Defended my PhD thesis on ACE-inhibitor induced angioedema in September 2018

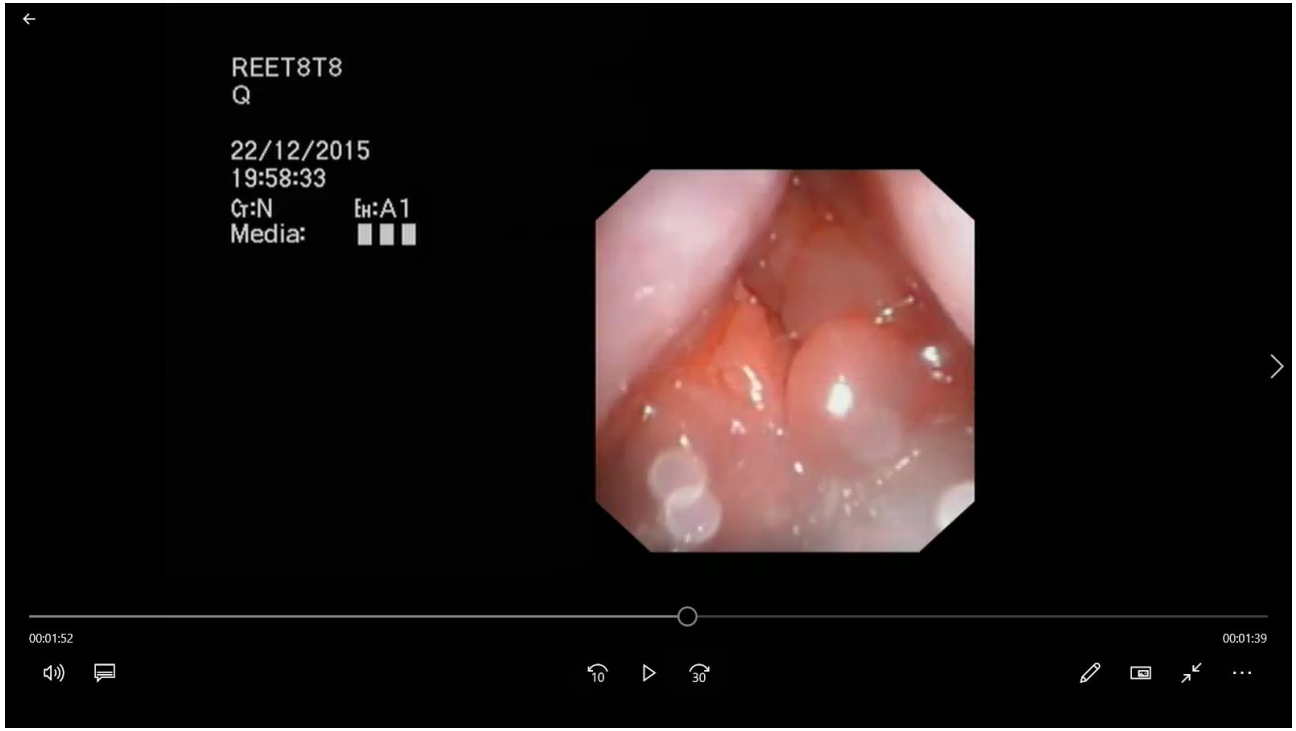
Today's programme

- Hereditary angioedema – what is it?
- Epidemiology and pathophysiology
- Genetic causes – new types of HAE emerging

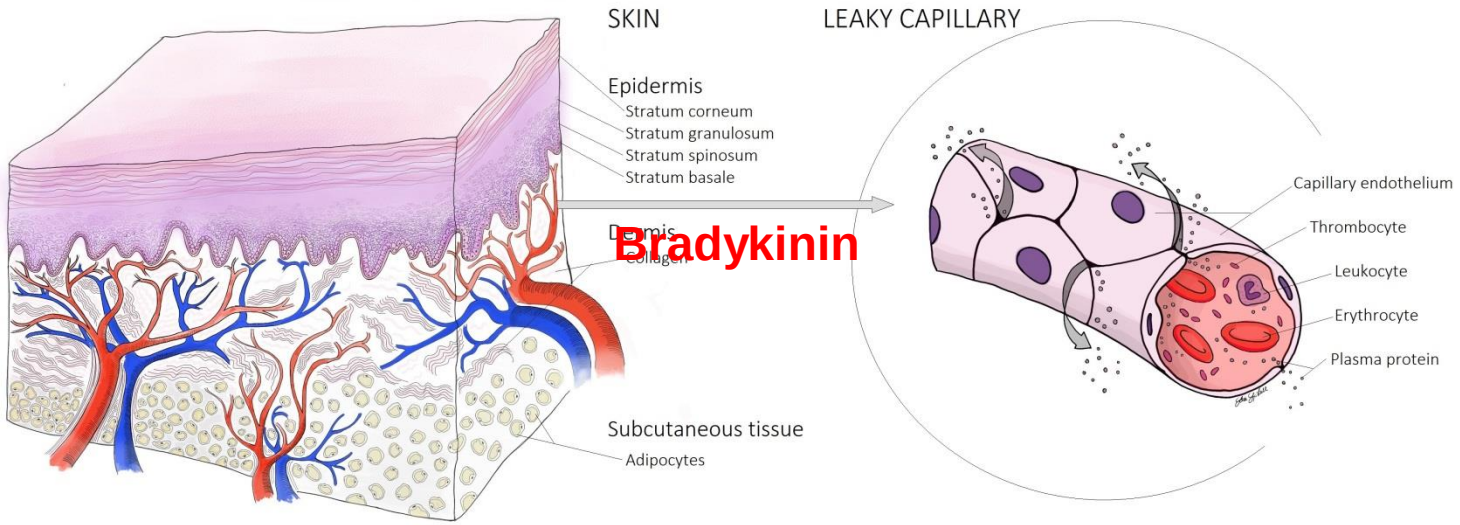
Today's programme

- Treatment – current and those in pipeline
- Future perspectives
- Questions from the audience

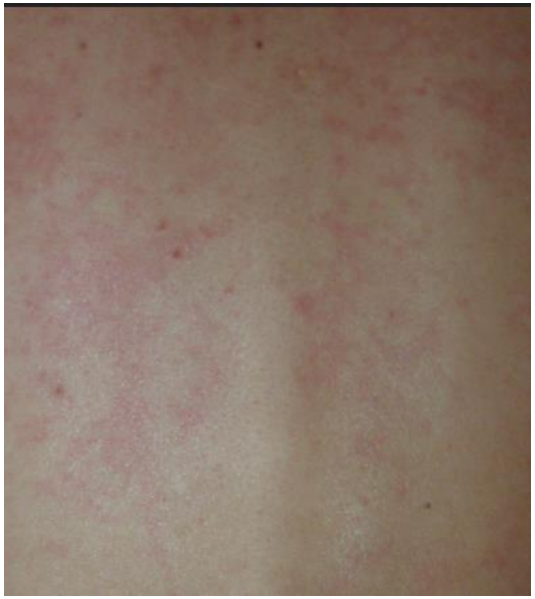
Hereditary angioedema is a genetic disease causing C1 INH deficiency → recurrent swelling episodes



Plasma leakage from capillaries → angioedema



Thanks to Dr. Sannia Sjöstadt for producing this figure



Symptoms

- Erythema marginatum
- Swellings of abdomen
- Recurrent episodes throughout life
- Debut in childhood or teenage years
- Other symptoms: tiredness, irritability, smelly urine…

Rasmussen ER, Valente De Freitas P, Bygum A. *Acta Derm Venereol* 2016

Epidemiology and background

- In 1882 Dr. Quincke described the angioedema-symptom in a familie with hereditary angioedema
- Prevalence 1:50.000-100.000 inhabitants
- In Denmark a multi ethnic cohort
- Autosomal dominant disease in most cases

Epidemiology and background

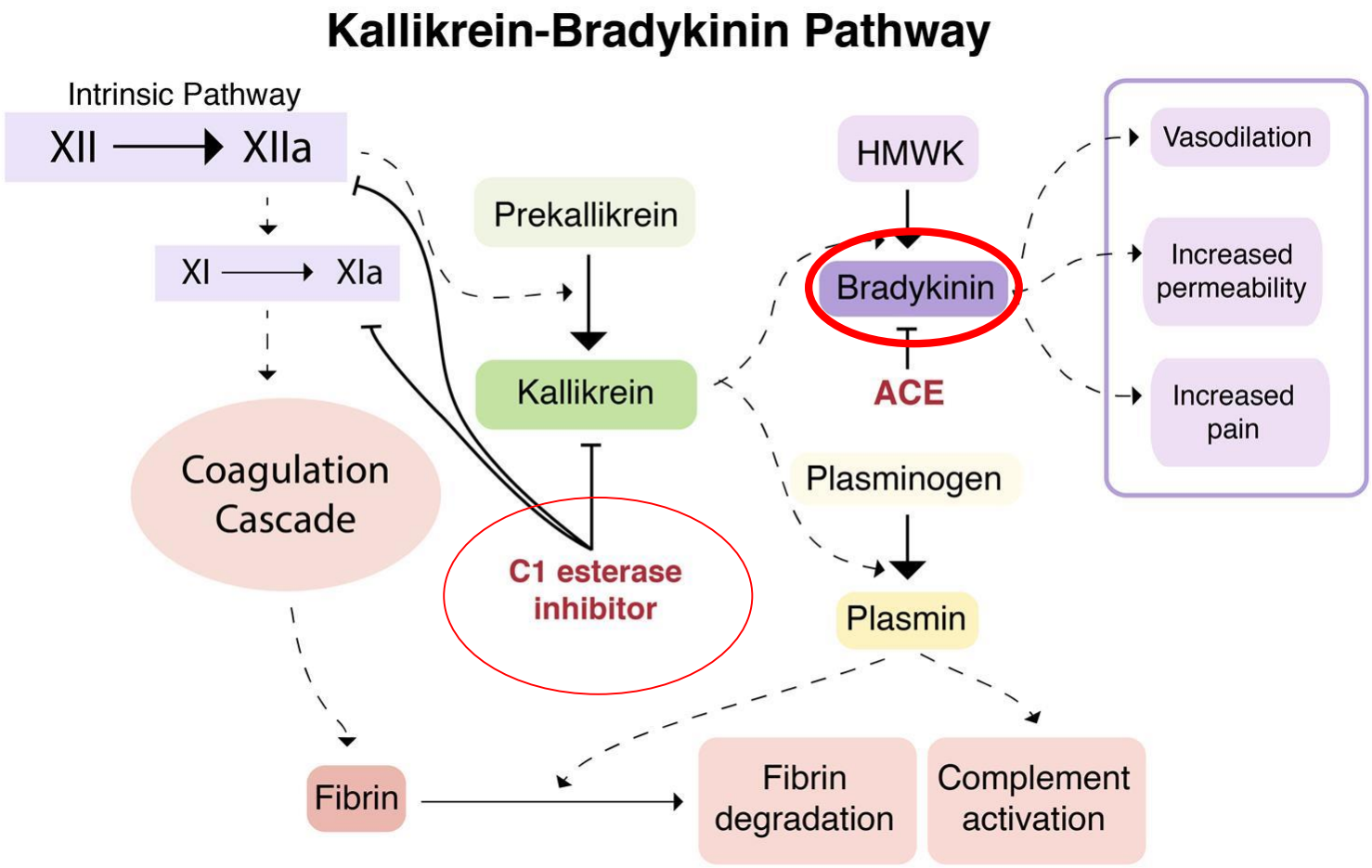
- Before effective treatment risk of death 20-25%
- Increased risk
    - Surgery
    - Dental treatment
    - Stress
    - Menstruation
    - Many more – individual factors

Epidemiology and background

- 25% are new mutations – hence no family history
- Males and females equally inflicted

Pathophysiology

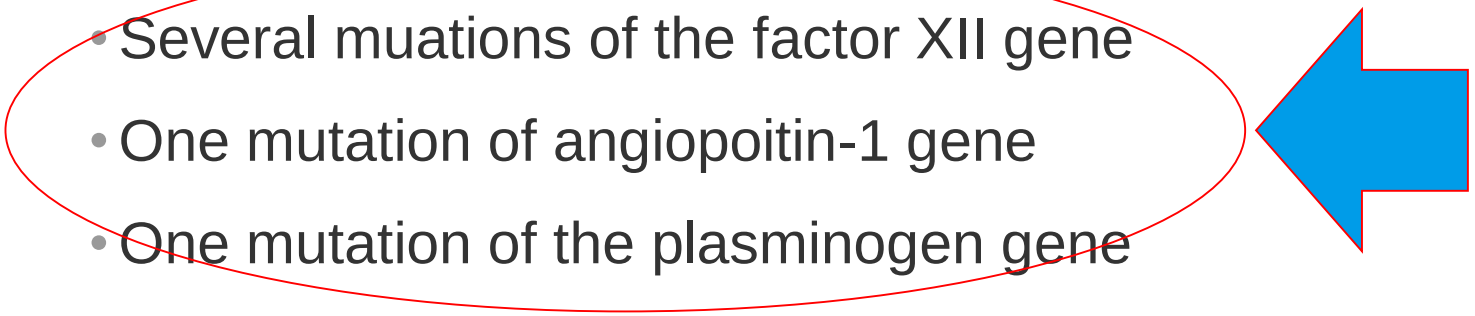
- Two types with low concentration or function of complement C1 inhibitor
- Estrogen dependent factor XII associated HAE
- Hereditary angioedema with normal C1 inhibitor



https://step1.medbullets.com/immunology/105011/hereditary-angioedema

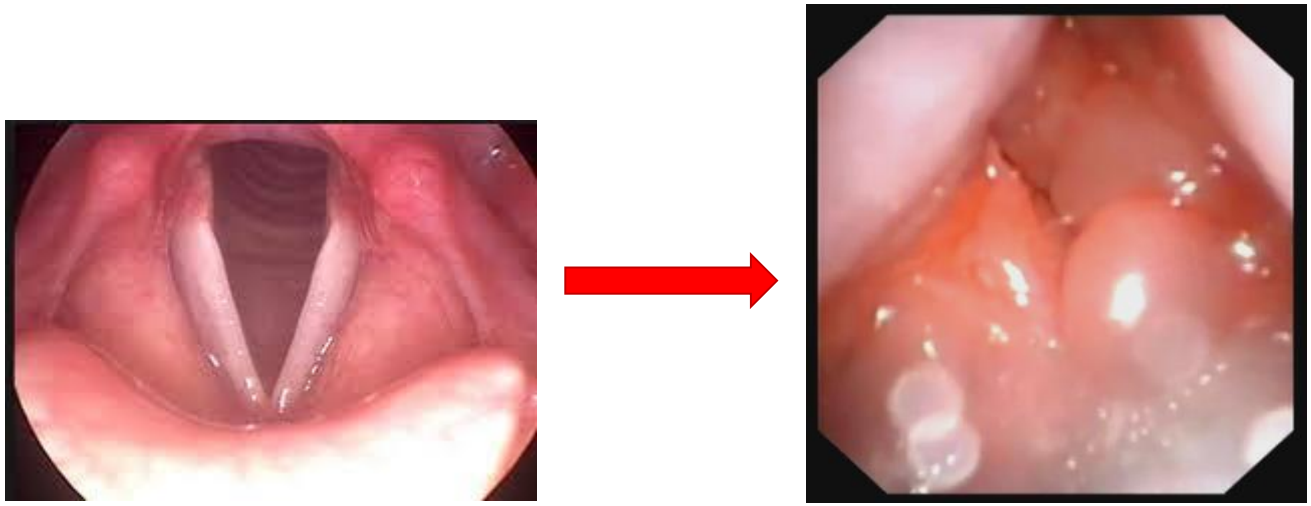
Genetic causes

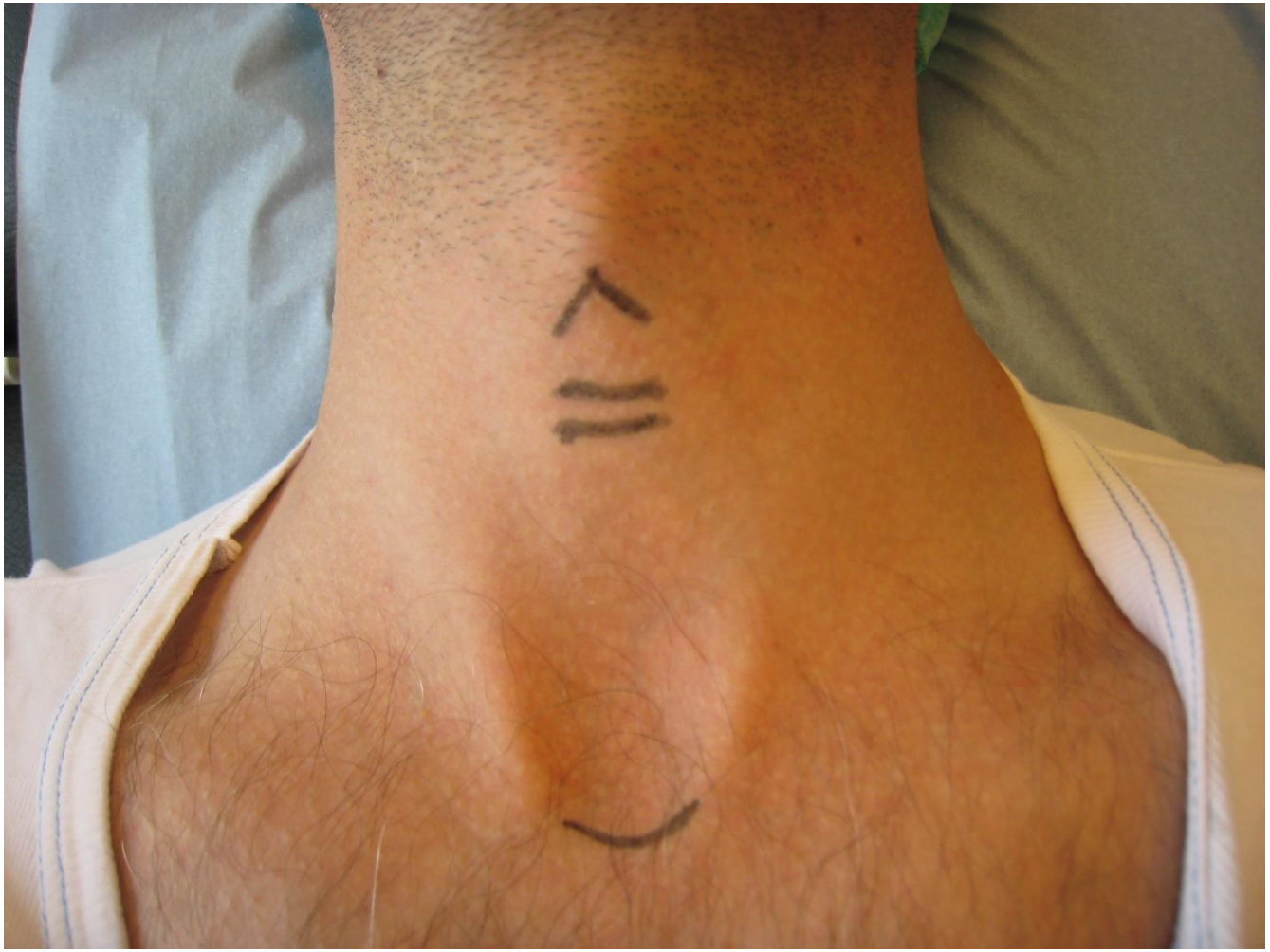
- More than 400 mutations of the *SERPING1* gene
- Several muations of the factor XII gene
- One mutation of angiopoitin-1 gene
- One mutation of the plasminogen gene

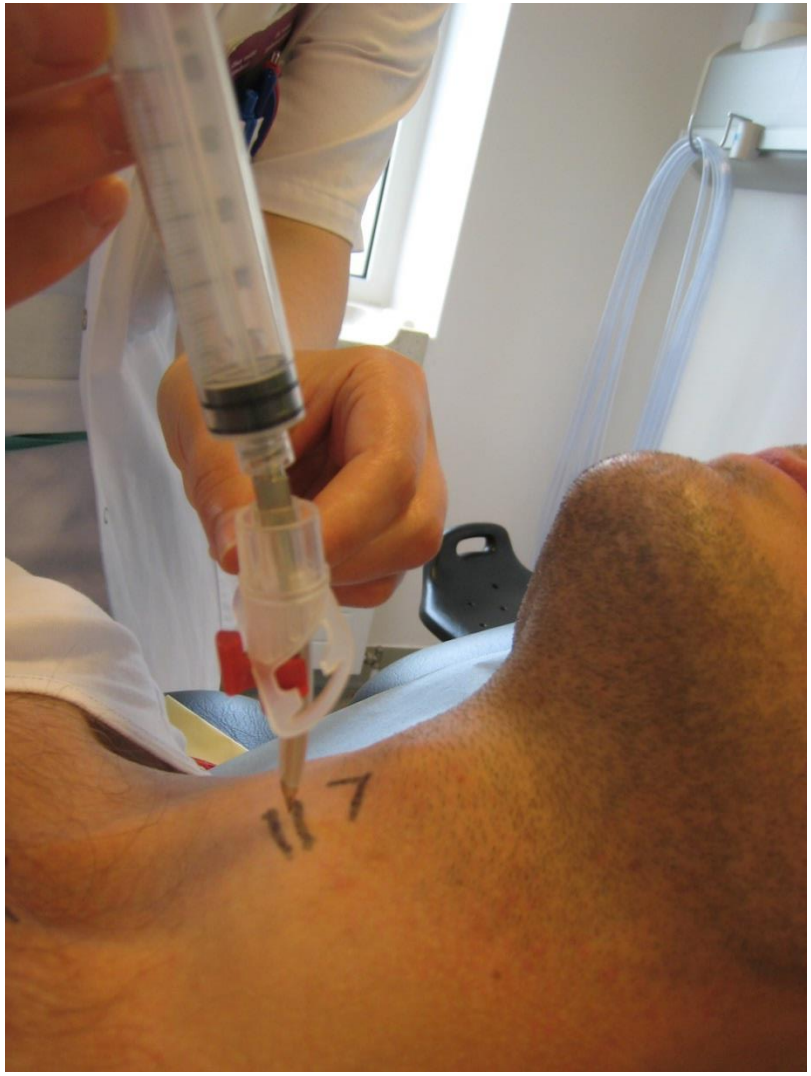


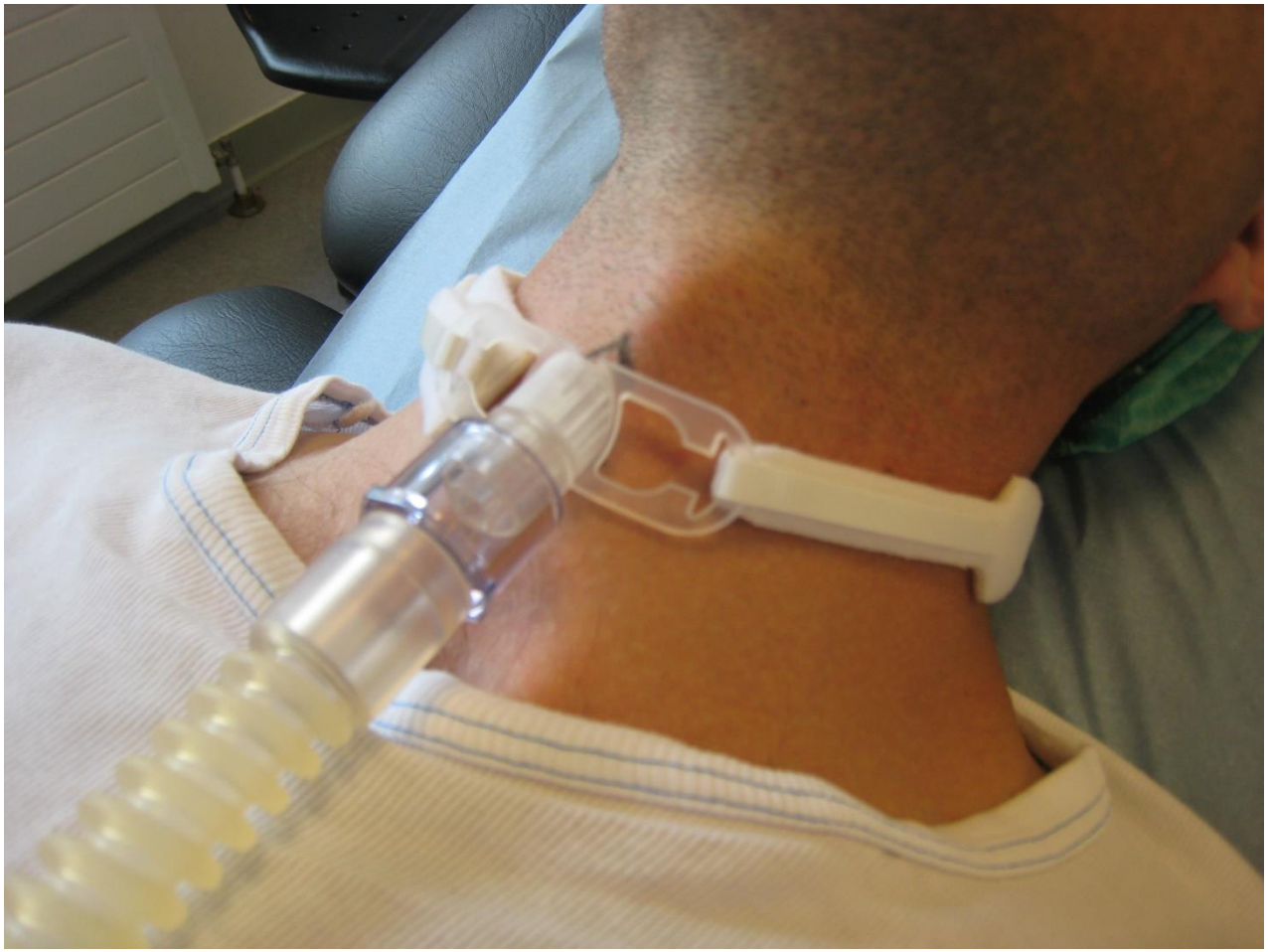
The HAE patient in the emergency situation: manage the airway

- Intubation (oral or fiberoptic nasal) or emergency tracheotomy?
- Progresses rapidly









Pharmacological treatment

- Anti-allergic medications have no effect
- Bradykinin receptor type 2 antagonist – icatibant (Firazyr®)
- Complement C1 inhibitor concentrate (Berinert®, Ruconest® or Cinryze®)
- In the US: kallikrein inhibitor (ecallantide®)

Sinert R *et al. Acad Emerg Med* 2015;22:S3–425
Bas M *et al*. *Ann Emerg Med* 2010;56:278–82.
Baş M *et al. N Engl J Med* 2015;372:418–25

More treatment options are coming

- Subcutaneus complement C1 inhibitor concentrate
- Lanadelumab – monolonal antibody targeting kallekrein

The future is bright

- Most Danish patients home treat
- Also children
- More effective medication
- But they do forget medication
- And there are new cases

To sum up

- Hereditary angioedema is a genetic disease
- The coagulation cascade is affected – but no bleeding
- Bradykinin and substance P are the mediatiors
- Airway management is essential
- Intermittent abdominal pain

Questions and answers

Thank you for your time

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