Proposed case-definition of VITT and treatment algorithm

Jakob Stensballe

MD, PhD, Consultant Transfusion Medicine & Anaesthesiology

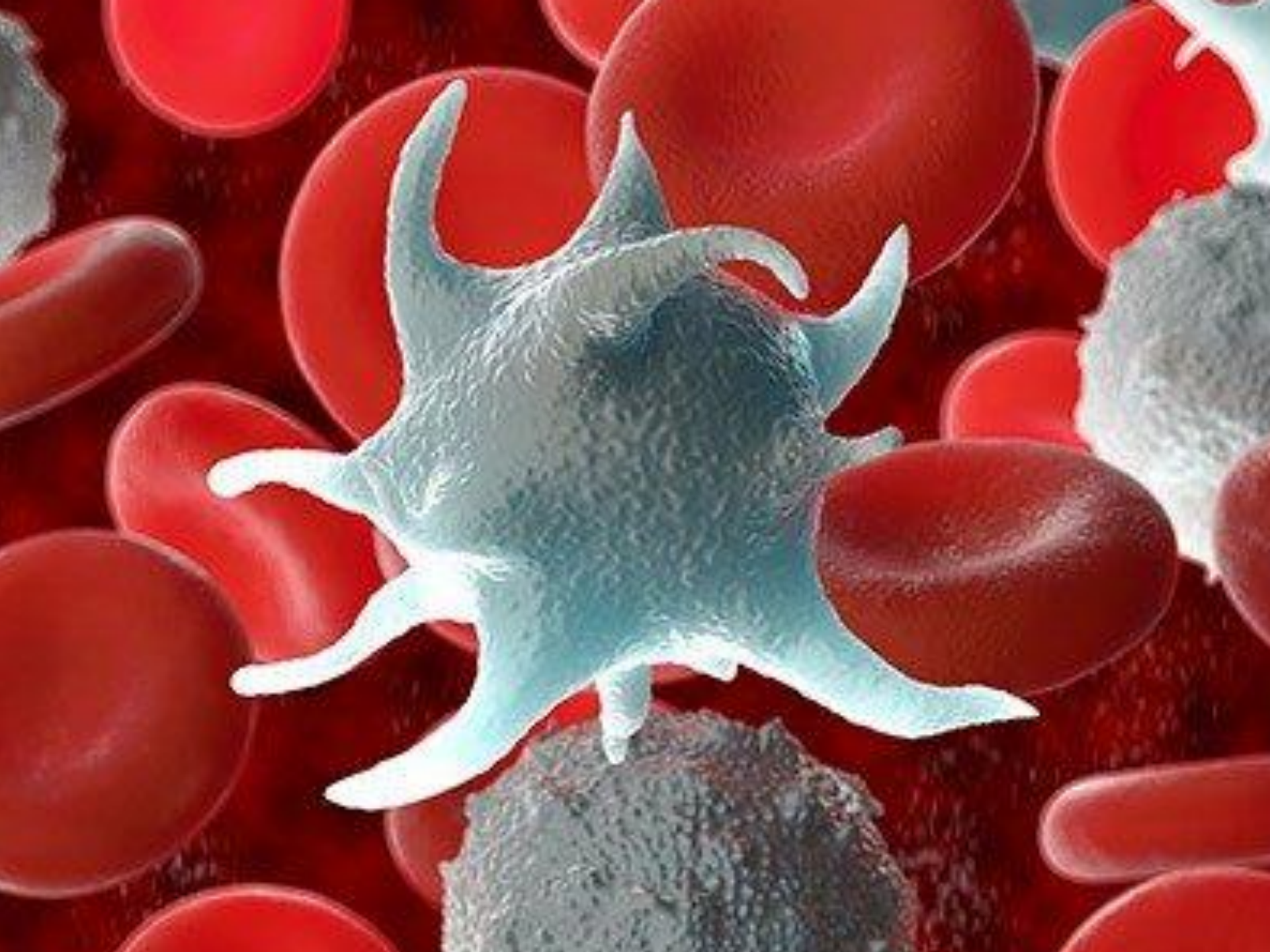
Section for Transfusion Medicine, Capitol Region Blood Bank

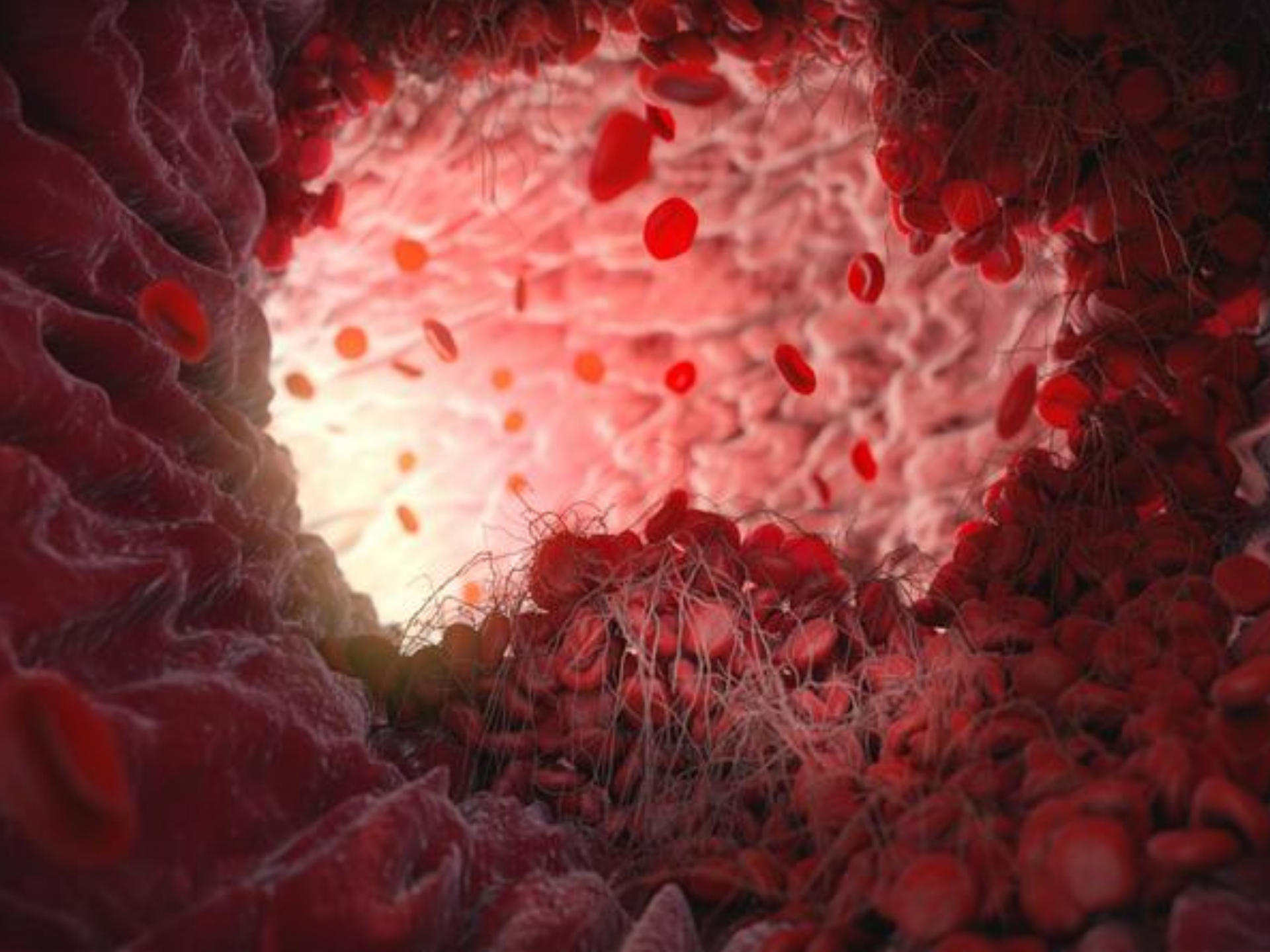
&

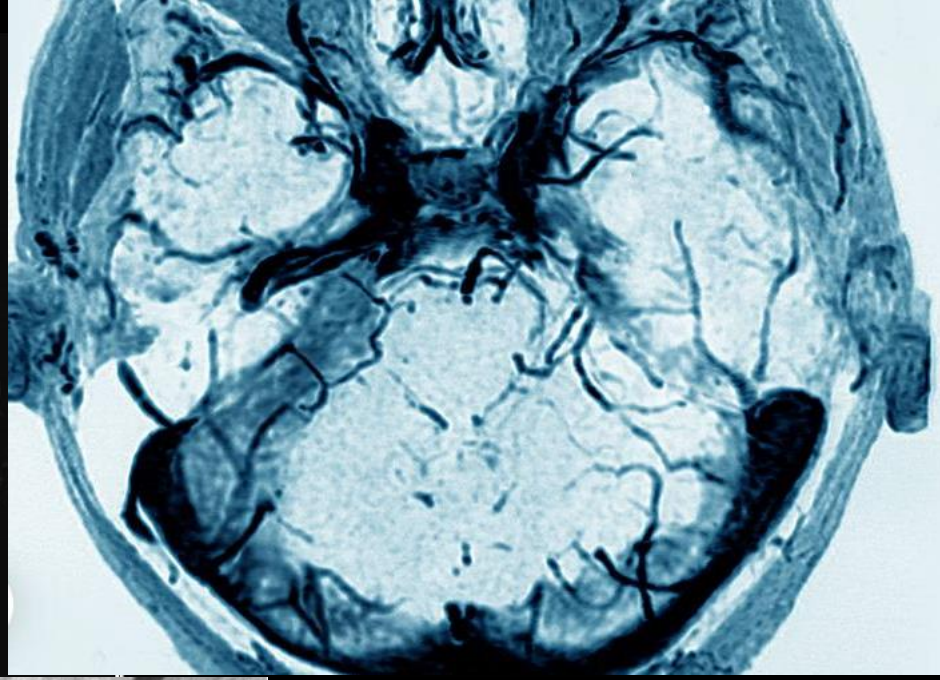
Department of Anaesthesiology and Trauma Centre

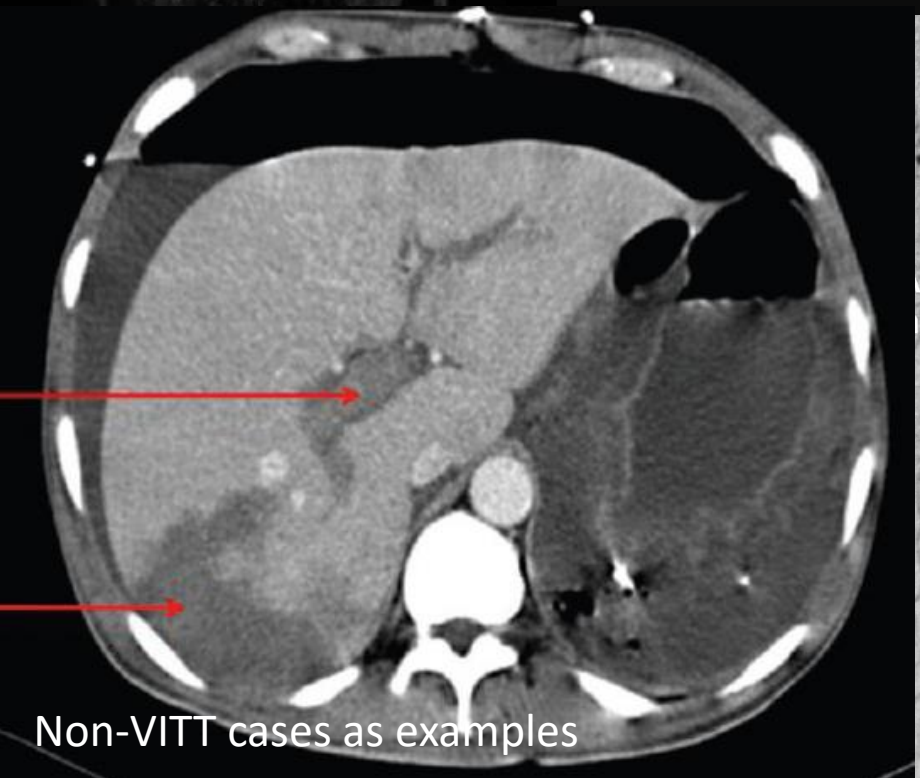
Copenhagen University Hospital, RIgshospitalet

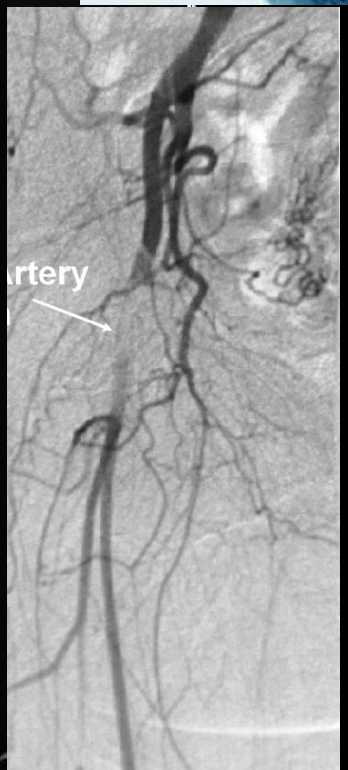
COI: None

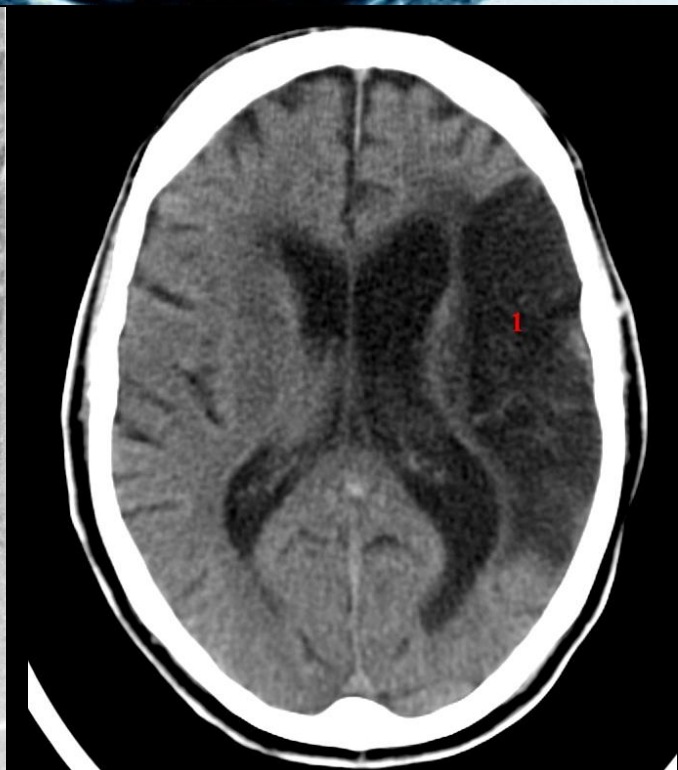




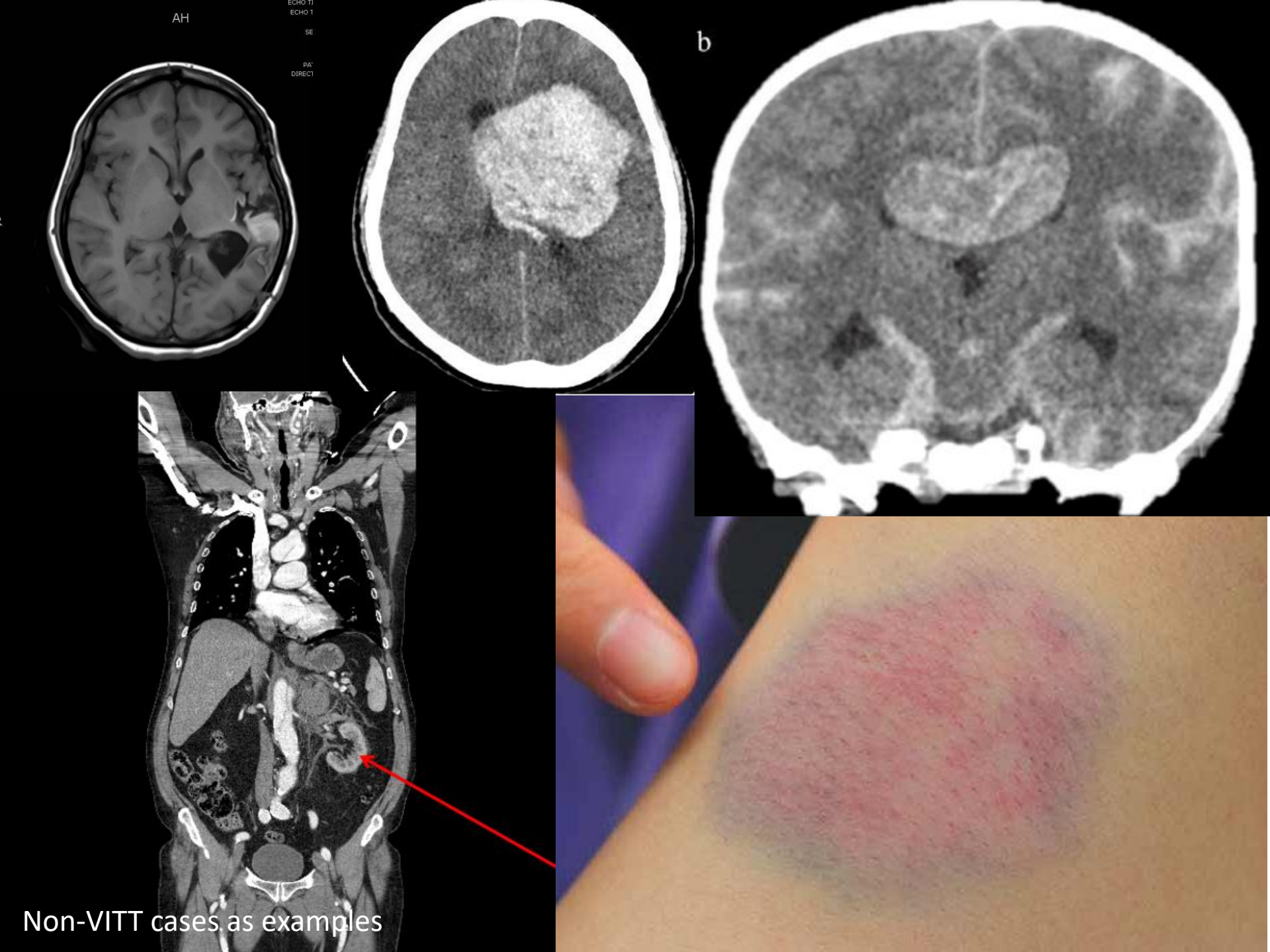








Non-VITT cases as examples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Non-VITT cases as examples


Phenotypes ?

Vaccine	Country	No	Thrombosis	Bleeding	PLT	Mortality
AZ	Norway	5	4 CVST 1 Portal	> 80%	27	60%
AZ	Germany Austria	11	9 CVST 1 PE	> 8%	45	55%
AZ	UK	23	13 CVST 4 PE 1 DVT 2 MCA stroke 2 Portal	> 10%	34	30%
JJ	USA	16	13 CVST Portal, GI PE, DVT, Carotid, Femoral & Iliac artery	?	< 50	20-30%
AZ	Denmark	> 1	CVST, Portal, Mesentery etc	> 30%	< 50	20-30%

International guidelines : fasttrack....

World Health Organization

ISth

18/3 19/3 1/4 7/4 9/4

DANISH HEALTH AUTHORITY

Vaccination against SARS-CoV-2 and vaccine-induced immune thrombotic thrombocytopenia (VITT)

GTH

GTH Geschäftsstelle – Gertrudenstr. 9 - 50667 Köln / Germany

GTH
Gesellschaft
für Thrombose- und
Hämostaseforschung
e.V.

GTH Geschäftsstelle
Haus der Verbände Köln
Gertrudenstr. 9
50667 Köln / Germany

Telefon +49 221 423346 26
mail@gth-online.org
www.gth-online.org

Vorstand
Vorsitzender
Prof. Dr. J. Oldenburg
Stellvertr. Vorsitzender
PD Dr. R. Klamroth
Sekretär
Prof. Dr. F. Langer
Schatzmeisterin
Dr. C. von Auer
Weitere Mitglieder
Prof. Dr. M. Albisetti
PD. Dr. C. Ay
Prof. Dr. W. Korte

Köln, den 19.03.2021

Aktualisierte Stellungnahme der GTH nach dem Beschluss der EMA, die Impfungen mit dem AstraZeneca COVID-19 Vakzin fortzusetzen

Am Freitag, 19. März 2021, werden die Impfungen mit dem COVID-19 Vakzin der Firma AstraZeneca in Deutschland wieder aufgenommen. Vom Paul-Ehrlich-Institut wurden bei > 1,6 Million verabreichten Impfdosen der Firma AstraZeneca mittlerweile über 13 Fälle einer Sinus- oder Hirnvenenthrombose berichtet. Die Thrombosen traten 4–16 Tage nach der Impfung mit dem AstraZeneca COVID-19 Vakzin bei zwölf Frauen und einem Mann im Alter von 20–63 Jahren auf. Bei den Patienten lag gleichzeitig eine Thrombozytopenie vor, die auf ein immunologisches Geschehen als Ursache der Thromboseneigung hinweist.

Ein wichtiger Pathomechanismus wurde mittl
unter Führung der Greifswalder Arbeitsgrupp
aufgeklärt. Durch die Impfung kommt es wahr
inflammatorischen Reaktion und Immunstimu
Antikörperbildung gegen Plättchenantigene. D
dann abhängig oder unabhängig von Heparin
massive Thrombozytenaktivierung in Analogie
Thrombozytopenie (HIT). Dieser Mechanismus
Patienten mit einer Sinus-/Hirnvenenthrombo
AstraZeneca COVID-19 Vakzin im Labor von A
Kooperation mit anderen GTH Mitgliedern na
der klassischen HIT treten diese Antikörper 4–
auf. Dieser Pathomechanismus schließt zwar
/Hirnvenenthrombosen nach Impfung mit den
Vakzin auch andere Ursachen zugrunde liegen
für die folgenden aktualisierten Feststellunge

ISTH
International Society on Thrombosis and Haemostasis

ISTH Headquarters
610 Jones Ferry Road
Suite 205
Carrboro, NC 27510 USA

Tel: +1 919 929 3
Fax: +1 919 929 3
headquarters@ist
www.isth.org

ISTH Interim Guidance for the Diagnosis and Treatment on Vaccine-Induced Immune Thrombotic Thrombocytopenia (Updated 20 April, 2021)

Step 1: Who is at risk for VITT?

1) COVID-19 vaccination 4-28 days prior to onset of symptoms?
   - VITT has only been identified following AstraZeneca or Johnson & Johnson vaccine. It has not been identified after other vaccines.
2) Signs/symptoms suggestive of thromboembolism?
   Examples include (but not limited to) NEW ONSET:
   - Severe, persistent headache +/- vision change, seizure-like activity
   - Severe, persistent abdominal pain
   - Leg swelling or pain
   - Chest pain and/or shortness of breath

If answers to questions 1 and/or 2 are no, then this is not VITT. Manage clinical presentation according to standard practice.

- If answers to both questions are yes, then proceed to Step 2.

Step 2: How to screen for VITT in at risk patients?

- Order appropriate imaging tests to confirm thromboembolism based on symptom presentation (e.g., CT venogram head for headache, CT venogram abdomen for abdominal pain).
- Order an urgent complete blood count.

If no thrombosis on imaging → this is not VITT.

If platelet count ≥ 150 x 10^9/L → VITT unlikely.

If there is evidence of acute thrombosis AND p
VITT proceed to Step 3.

Step 3: Initial evaluation

tion laboratory studies (

platelet factor 4 (PF4) a
the most reliable).

COVID-19 VACCINES
VIPIT INTERIM GUIDANCE
12 APRIL 2021

Interim Guidelines: Diagnosis and Management of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (following AstraZeneca COVID-19 Vaccinations

12 April 2021

Introduction

Rare cases of blood clots with low platelets after receipt of AstraZeneca (AZ) COVID-1
been reported. At present there is no clear signal of risk factors for this condition. This
provides guidance to UN medical staff globally on the diagnosis, management and rep
vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) cases. **UN medical
be alert for this syndrome and arrange for early referral to local hospitals or hae
and/or consider early medical evacuation for further lab confirmation and treatm
condition.**

For any questions, contact DHMOSH Public Health at dos-dhmosh-public-health@un
this is a living document which will be updated as more information emerges.

Current Situation Update

At the time of writing, the AstraZeneca vaccine is currently being authorized for us
several other countries, including the UK, Canada and India. Based on a multinatio
the vaccine had 70.4% efficacy in preventing symptomatic COVID-19 at/after 14 d
dose. Although there is some concern about vaccine efficacy against certain

Thrombosis Canada
Thrombose Canada

VACCINE-INDUCED PROTHROMBOTIC IMMUNE THROMBOCYTOPENIA (VIPIT)

Objective:

To assist health care professionals in the diagnosis and management of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT).

Background:

Vaccines are a critical tool in the management of the COVID-19 pandemic resulting from SARS-CoV-2. Several vaccines have been rapidly developed and subsequently approved by Health Canada and deployed across Canada. Among those is the ChAdOx1 nCoV-19 vaccine (AZD1222) developed at Oxford University and produced by AstraZeneca and the Serum Institute of India.

Recently, after widespread vaccination with the AstraZeneca vaccine in Europe, there have been reports of some vaccine recipients developing unusual thrombotic events and thrombocytopenia. Investigators have concluded that the AstraZeneca vaccine is associated with development of a prothrombotic disorder that clinically resembles heparin-induced thrombocytopenia (HIT). [See **Clinical Guide Heparin Induced Thrombocytopenia.**]

Diagnosis of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT):

Patients presenting with the following blood clotting symptoms should be asked about their vaccine history:

- a persistent and severe headache
- focal neurological symptoms or visual changes, including blurred or double vision, or

Guidance from the Expert Haematology Panel (EHP) on Covid-19 Vaccine-induced Immune Thrombocytopenia and Thrombosis (VITT)

Updated Guidance on Management. Version 1.7 **20 April 2021**

Note this is a live document and is updated frequently as further information comes to light

There are currently no robust data to inform management of this condition. In the absence of published evidence, these are pragmatic guidelines based on experience of managing the initial cases, alternative similar conditions and the theoretical risks and benefits of interventions. As evidence emerges, recommendations are expected to change. Patient management should be individualised according to specific circumstances.

A rare syndrome of immune-driven thrombosis, often cerebral venous sinus thrombosis, and thrombocytopenia has been reported after COVID-19 vaccination and is highlighted as affecting patients of all ages and both genders; at present there is no clear signal of risk factors.

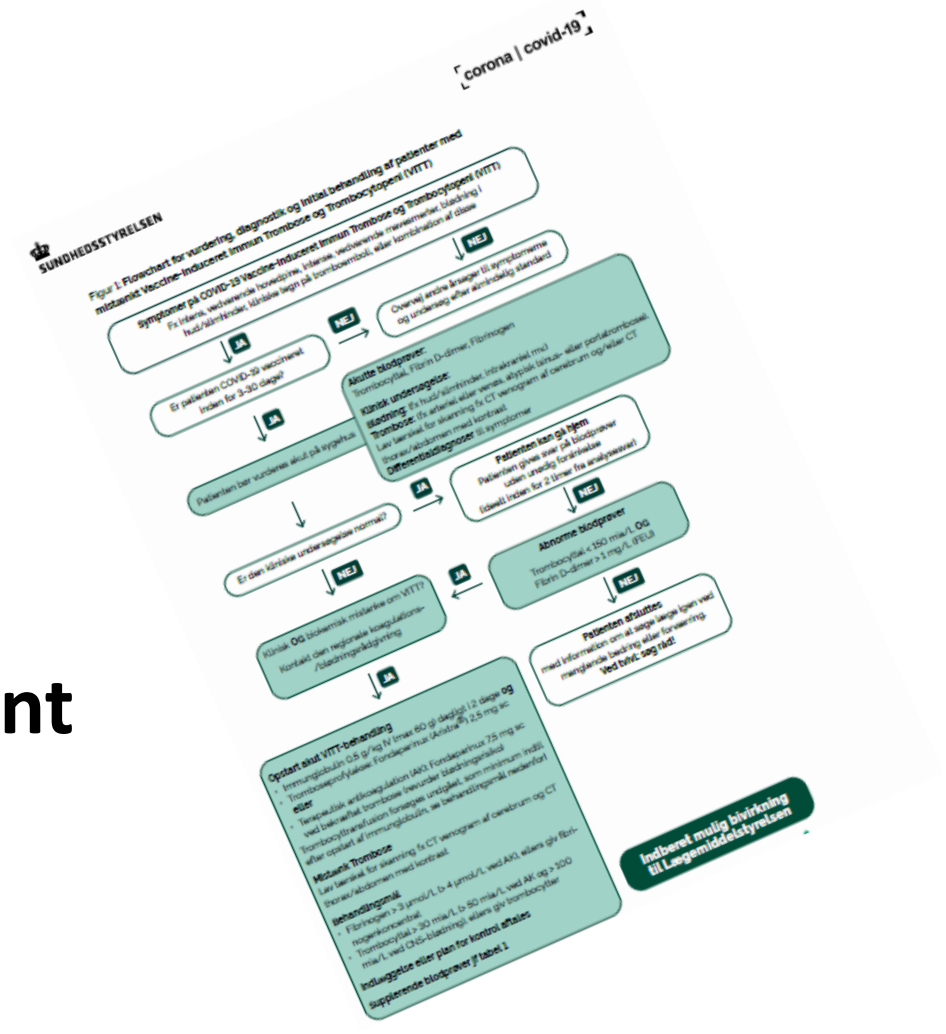
Clinicians need to be on alert for this syndrome, to understand how to make the diagnosis and to note the specifics of how to treat it. The Expert Haematology Panel (EHP) offers MDT support for management of cases

Probable cases must be reported to the EHP and Public Health England via this link https://cutt.ly/haem_AE. Additionally, all cases of thrombosis or thrombocytopenia occurring within 28 days of COVID-19 vaccine must be reported to the MHRA via the online yellow card system https://coronavirus-yellowcard.mhra.gov.uk/

Please also note that new or relapsed post-vaccine ITP cases can also be reported to Public Health England through the same initial link which diverts down a different line of questioning (https://cutt.ly/haem_AE)

Key points on a VITT guideline

- **Simple**
- **Evidence-based**
- **Early capture & treatment of patients**



VITT case definition

Possible

↓

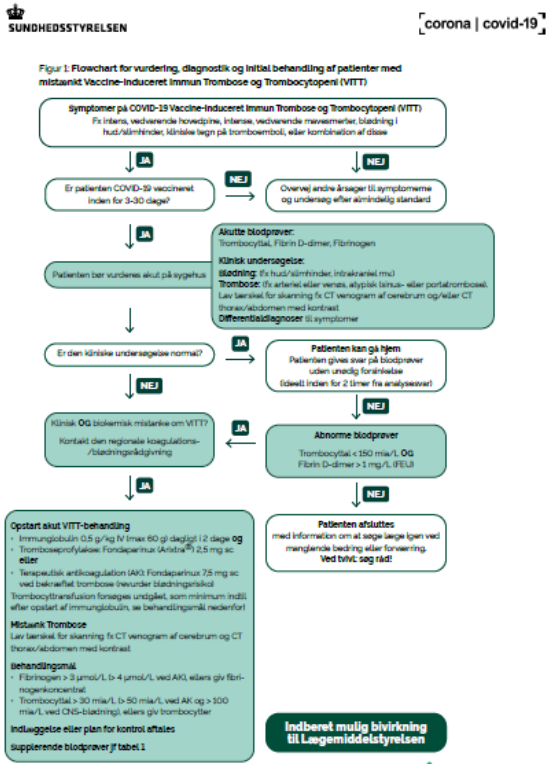
Probable → **Early treatment**

↓

Confirmed

↘

Unlikely



SUNDHEDSSTYRELSEN

corona | covid-19

Figur 1. Flowchart for vurdering, diagnostik og initial behandling af patienter med mistænkt Vaccine-induceret immun Trombose og Trombocytopeni (VITT)

Symptomer på COVID-19 Vaccine-induceret immun Trombose og Trombocytopeni (VITT)
Fx intens, vedvarende hovedpine, intense, vedvarende mavesmerter, blødning i hud/slimhinder, kliniske tegn på tromboemboli, eller kombination af disse

JA / NEJ

Er patienten COVID-19 vaccineret inden for 3-30 dage?

NEJ: Overvej andre årsager til symptomerne og undersøg efter almindelig standard

JA

Patienten bør vurderes akut på sygehus

Akutte blodprøver:
Trombocyttal, Fibrin D-dimer, Fibrinogen
Klinisk undersøgelse:
Blødning: Fx hud/slimhinder, intrakranielt mv.
Trombose: Fx arterielt eller venøs, atypisk (sinus- eller portatrombose).
Lav tærskel for skanning fx CT venogram af cerebrum og/eller CT thorax/abdomen med kontrast
Differentialdiagnoser til symptomer

Er den kliniske undersøgelse normal?

JA: Patienten kan gå hjem
Patienten gives svar på blodprøver uden unødig forsinkelse (ideelt inden for 2 timer fra analysesvar)

NEJ

Klinisk OG biokemisk mistanke om VITT?
Kontakt den regionale koagulations-/blødningsrådgivning

JA

Abnorme blodprøver
Trombocytal < 150 mia/L OG Fibrin D-dimer > 1 mg/L (FEU)

NEJ

Opstart akut VITT-behandling
- Immunglobulin 0,5 g/kg IV (max 60 g) dagligt i 2 dage og
- Tromboseprofylakse: Fondaparinux (Arixtra®) 2,5 mg sc eller
- Terapeutisk antikoagulation (AK): Fondaparinux 7,5 mg sc ved bekræftet trombose (nedsat blødningsrisiko)

Trombocyttransfusion forsøges undgået, som minimum indtil efter opstart af immunglobulin, se behandlingsmål nedenfor!

Mistænk Trombose
Lav tærskel for skanning fx CT venogram af cerebrum og CT thorax/abdomen med kontrast

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- Fibrinogen > 3 µmol/L (> 4 µmol/L ved AK), ellers giv fibrinogenkoncentrat
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Indlæggelse eller plan for kontrol aftales

Supplerende blodprøver jf tabel 1

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Ved tvivl: søg råd!

Indberet mulig bivirkning til Lægemiddelstyrelsen

VITT case screening

Possible

↓

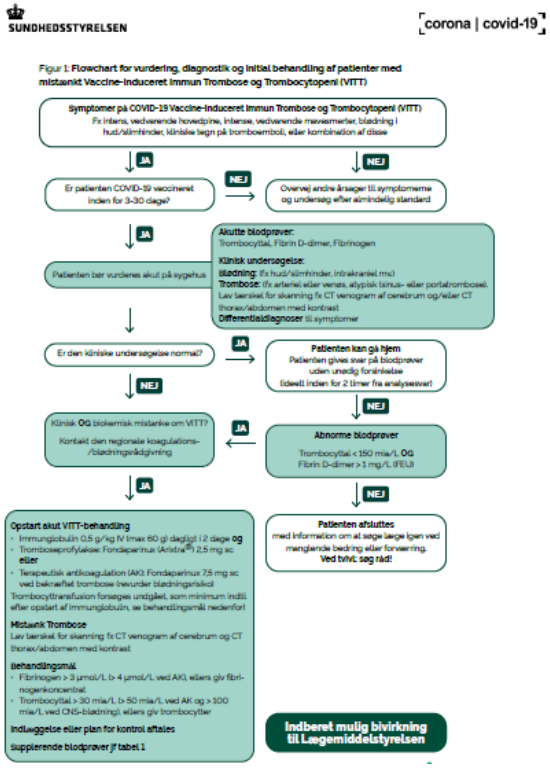
Probable

3-30 days (COVID19 vacc)

Severe, persistent headache / abdominal pain

PLT↓ D-Dimers ↑

Thrombosis / Bleeding ?



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Trombocyttransfusion forsøges undgået, som minimum indtil efter opstart af immunglobulin, se behandlingsmål nedenfor!

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Behandlingsmål
- Fibrinogen > 3 µmol/L (> 4 µmol/L ved AK) eller giv fibrinogenkoncentrat
- Trombocyttal > 30 mia/L (> 50 mia/L ved AK og > 100 mia/L ved CNS-blødning), ellers giv trombocytter

Indlæggelse eller plan for kontrol aftales

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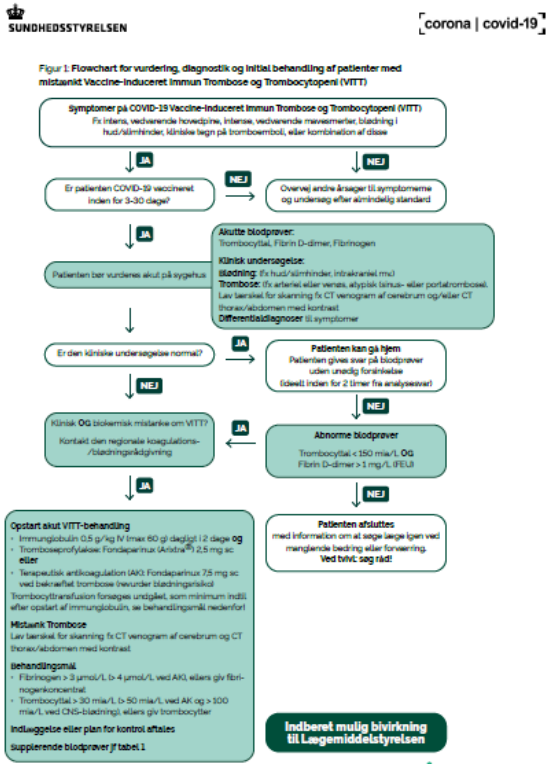
med information om at søge læge igen ved mangelende bedring eller forværring.
Ved tvivl: søg råd!

Indberet mulig bivirkning til Lægemiddelstyrelsen

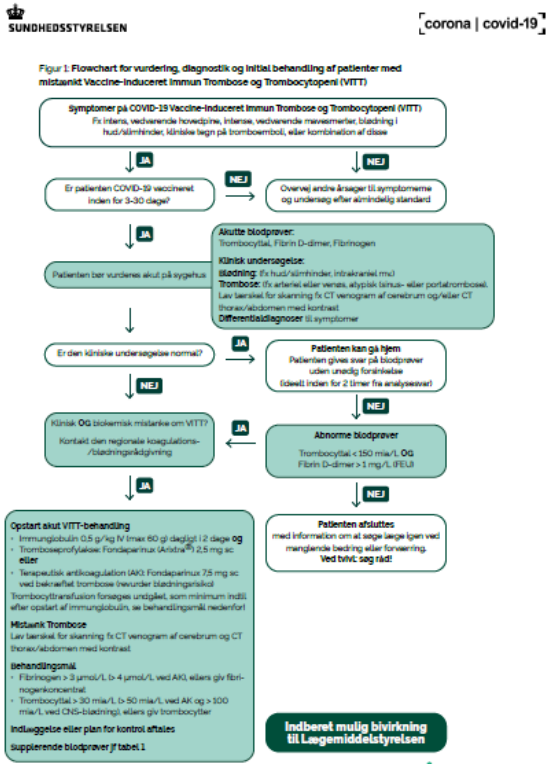
Probable VITT early treatment

- Consult ASAP with local specialist (Don't delay)
- Immunoglobulin 0.5 g/kg (max 60 g) IV
- Fondaparinux 7.5 mg (2.5 mg)
- Avoid PLT transfusion (unless severe bleeding phenotype)
- Dexamethasone 40 mg (if PLT < 50)
- Locate that thrombosis !



Early goals of VITT management

- **Fibrinogen > 1.5 g / L**
- **PLT > 30 x10^9 / L (50 or 100 in bleeding phenotypes)**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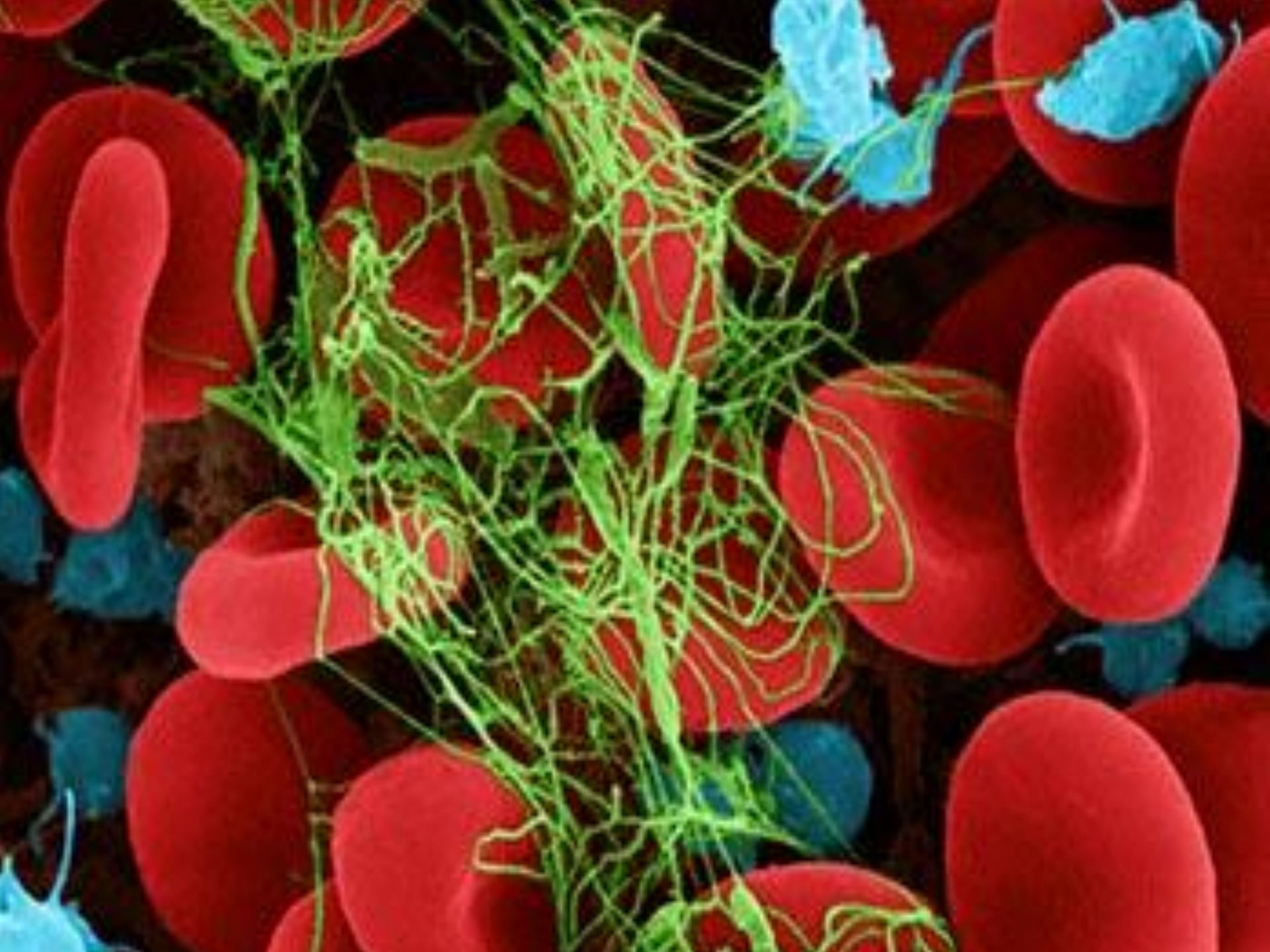

Key remarks

- National guidelines….live update!
- Early → Screening, Identification & Treatment
- Phenotype → Thrombosis (& bleeding risk)
- Strong collab at all levels → National & International

DANISH HEALTH AUTHORITY

LÆGEMIDDELSTYRELSEN
DANISH MEDICINES AGENCY

DSTH

Danish Society of Thrombosis & Haemostasis www.dsth.dk

DSKI
Dansk Selskab for Klinisk Immunologi

Danish Society of Clinical Immunology www.dski.dk

Dansk Hæmatologisk Selskab

Danish Society of Hematology www.hematology.dk