STROKE SYNDROMES

BY Aaron Gaekwad

Stroke Fellow

DISCLAIMER

This talk is for medical interns at POWH

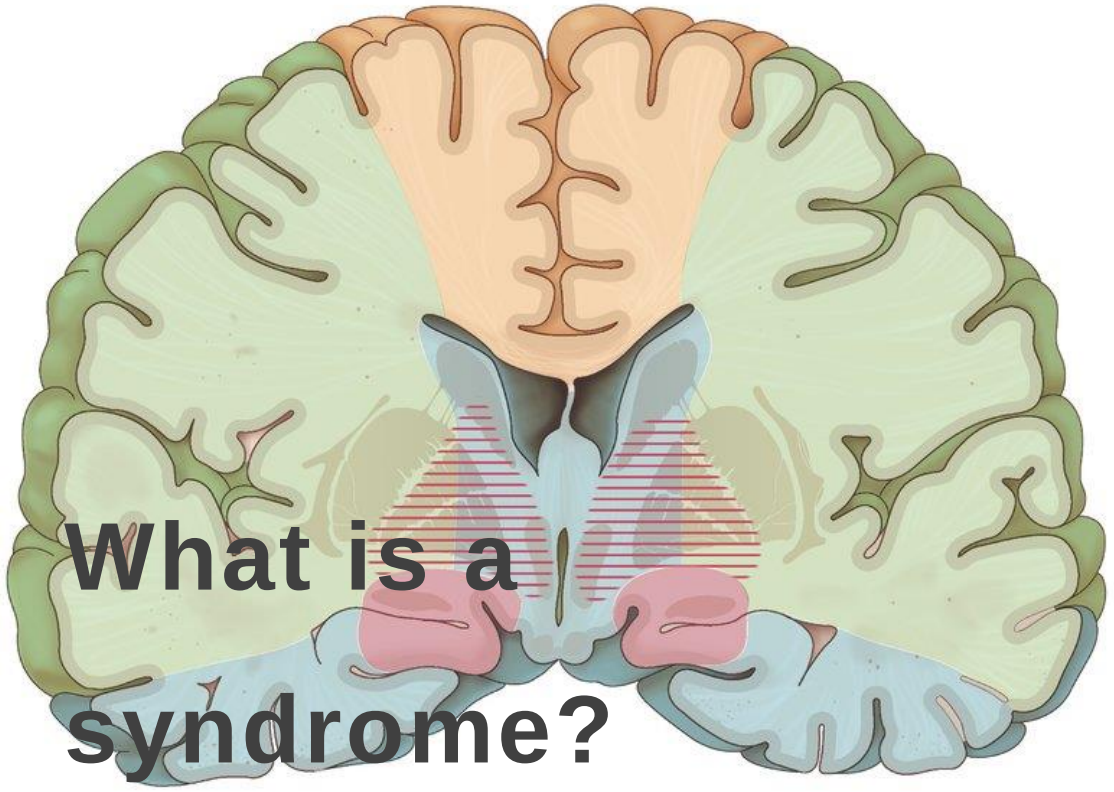
This talk covers certain relevant and interesting topics in regards to stroke

For diagnosis and management of stroke please see hospital protocols for more conclusive local protocols

The opinions on this presentation are my own

Any questions about this presentation can be asked at the presentation time permitting or via email Aaron.Gaekwad@health.nsw.gov.au

What is a syndrome?



Anterior cerebral artery
Middle cerebral artery
Partially supplied by posterior communicating artery
Posterior cerebral artery
Anterior choroidal artery
Anterior choroidal artery

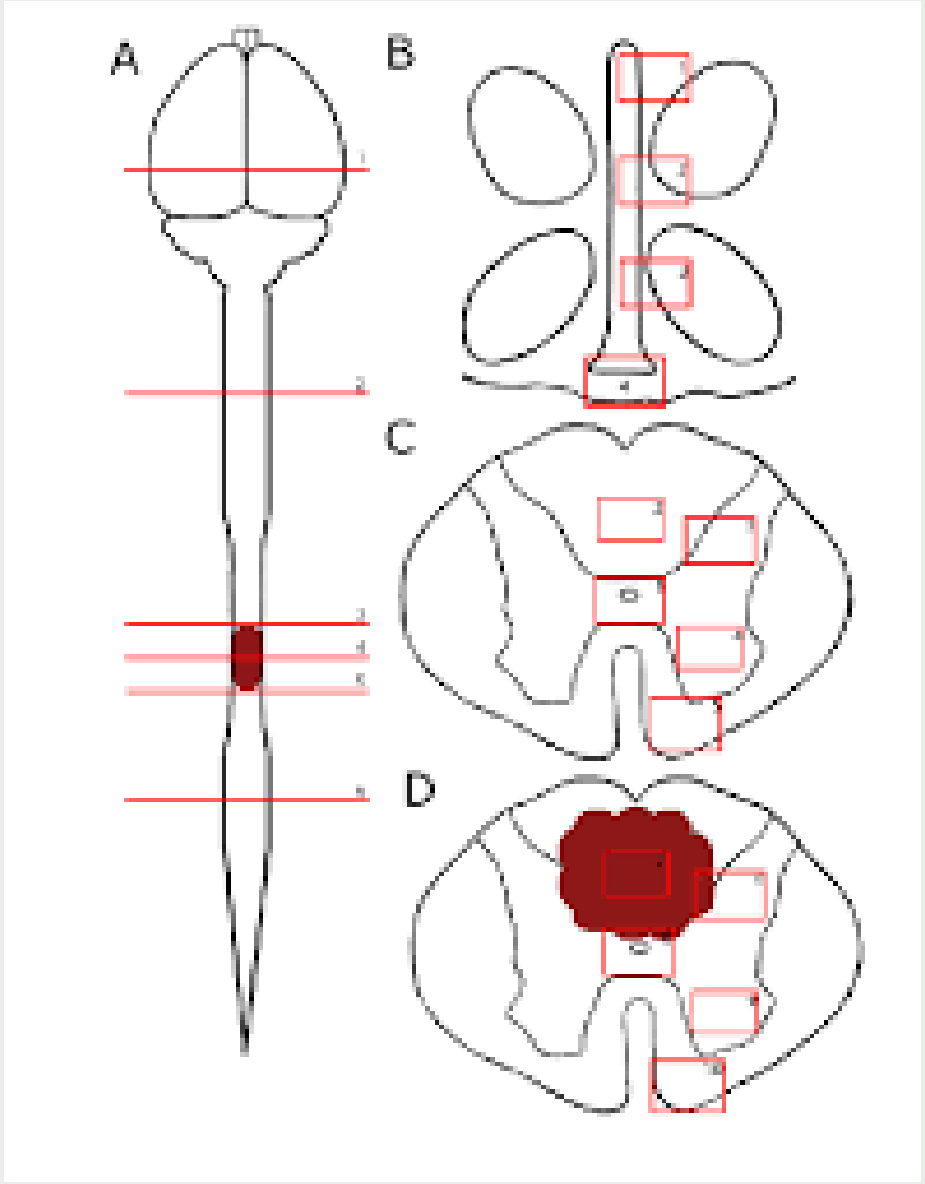
A group of symptoms which consistently occur together, or a condition characterized by a set of associated symptoms

An aetiology is not in the definition of a syndrome

Why is history and examination so important in Neurology

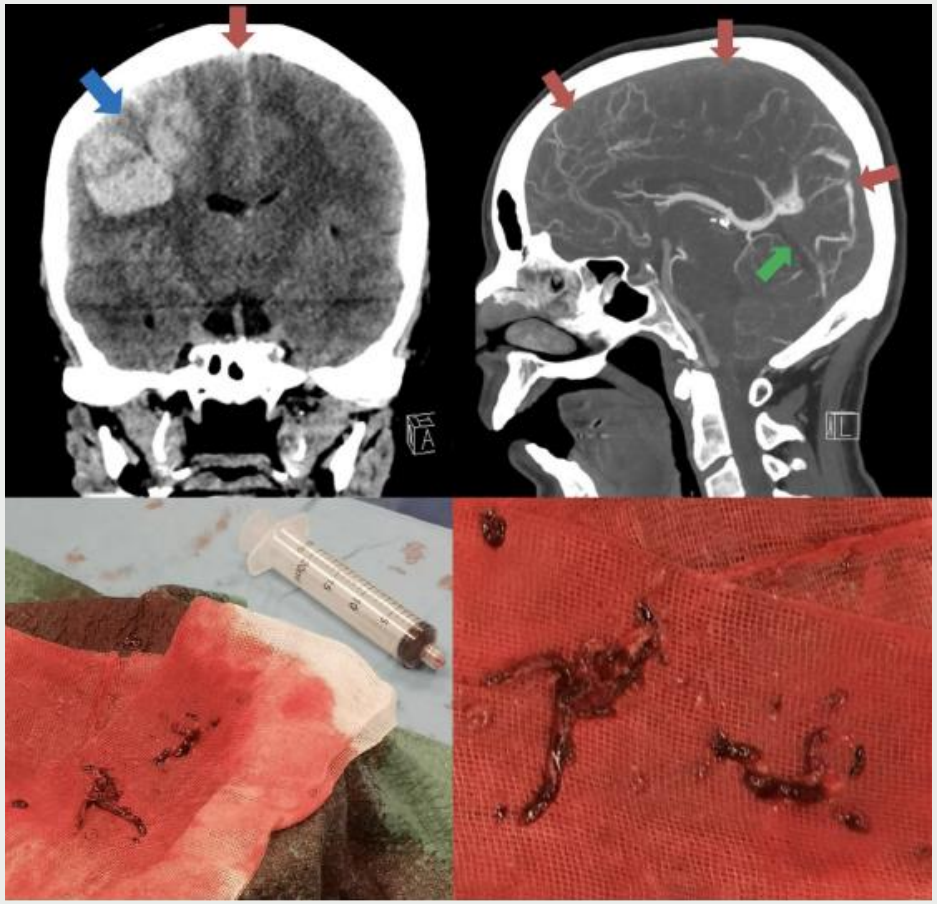
Examination gives you the location of the disease

History gives you the type of disease



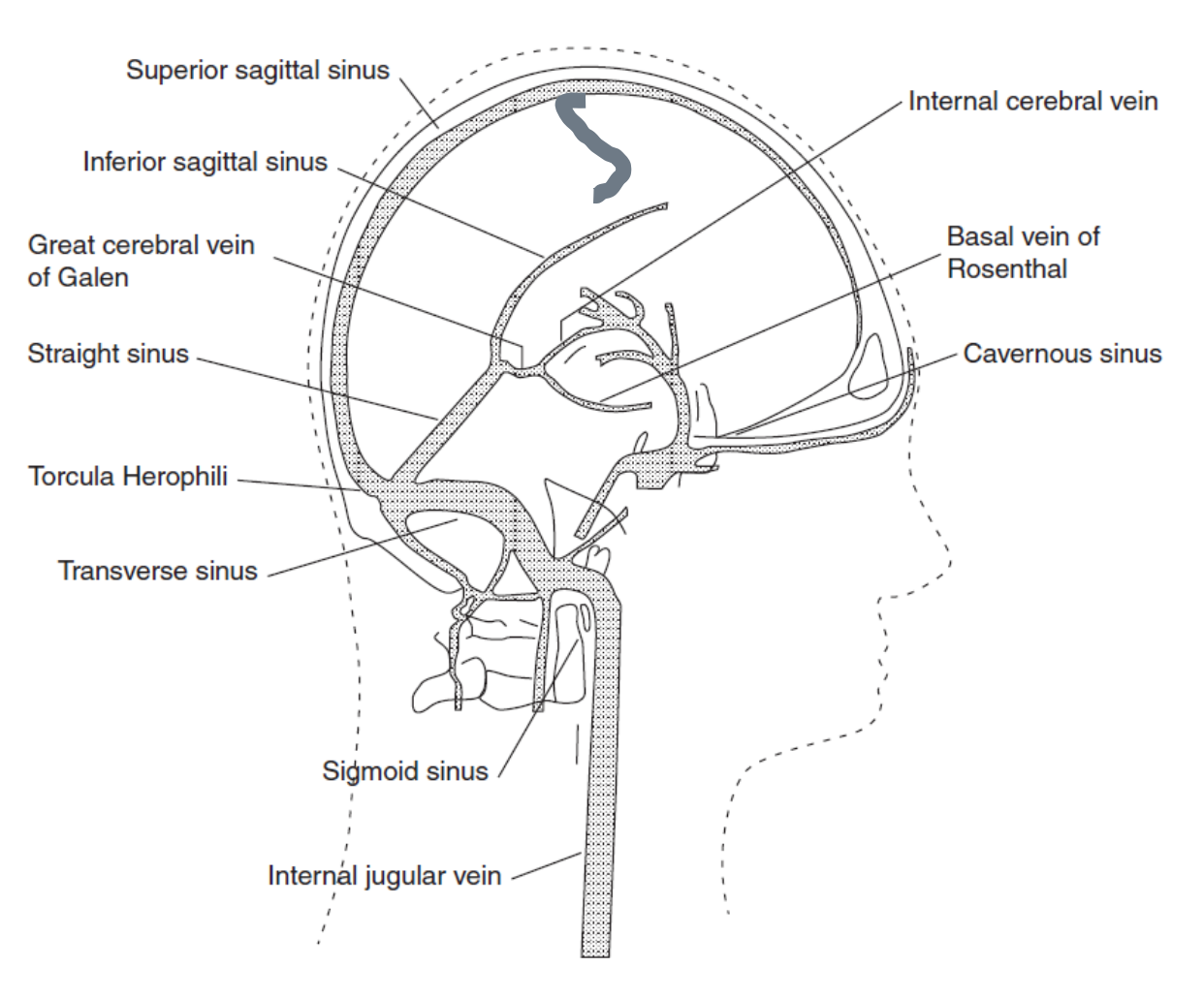
What is this?

Tell me what you see



Cerebral Venous Thrombosis (CVT)

- Rare
- Large Clinical spectrum
- Numerous causes
- Numerous risk factors



Cortical Veins - Variability

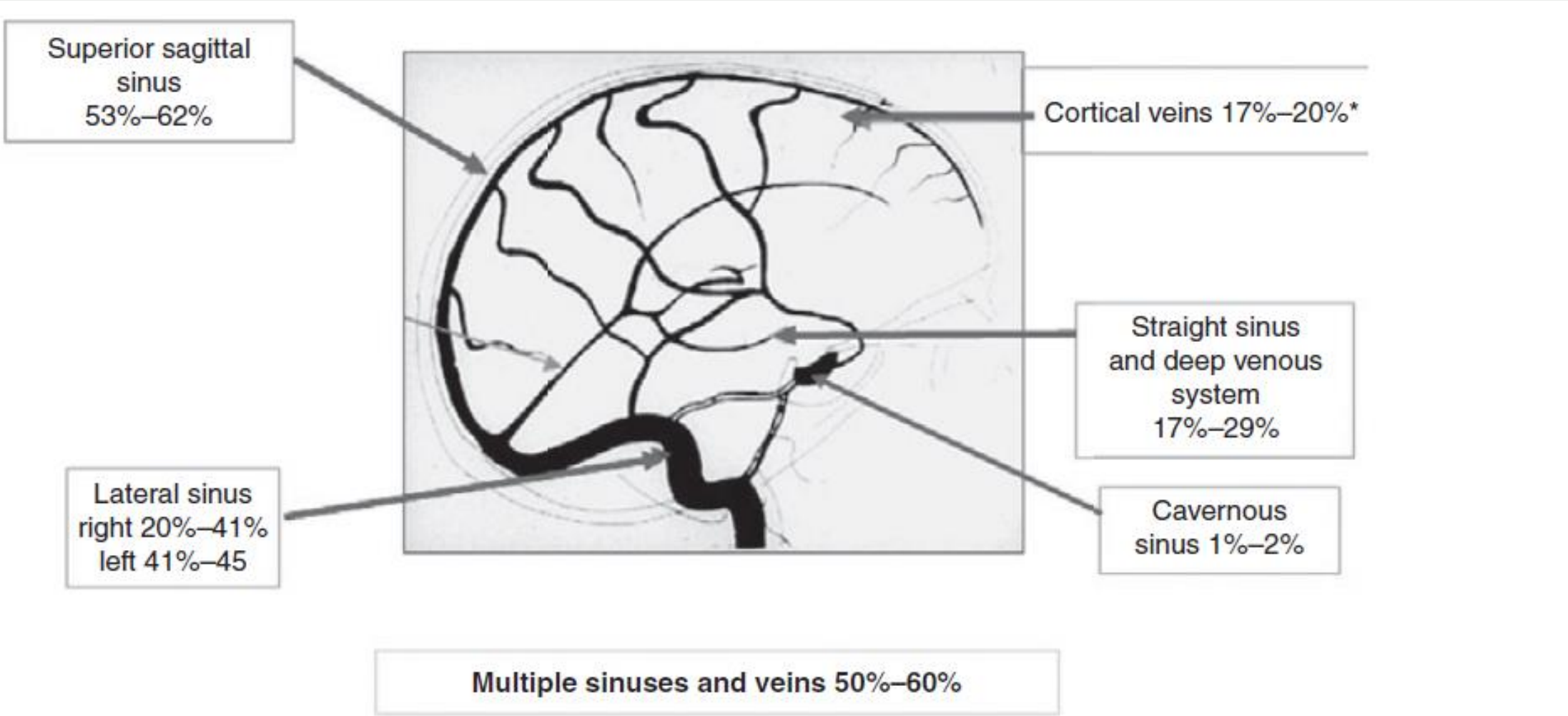
- Drain upwards to SSS
- Drian into CS
- Numerous anastomoses
- No valves
- Multi-direction flow and dilation

Deep Cerebral Veins – Less variability

- Drain white matter
- Drain basal ganglia
- Vein of Galen then SS

Posterior fossa Veins

- Drainage superior, anterior and posterior drainage
- Variable +++


Superior sagittal sinus 53%–62%
Cortical veins 17%–20%*
Straight sinus and deep venous system 17%–29%
Lateral sinus right 20%–41% left 41%–45
Cavernous sinus 1%–2%
Multiple sinuses and veins 50%–60%

Cerebral Thrombosis Pathology

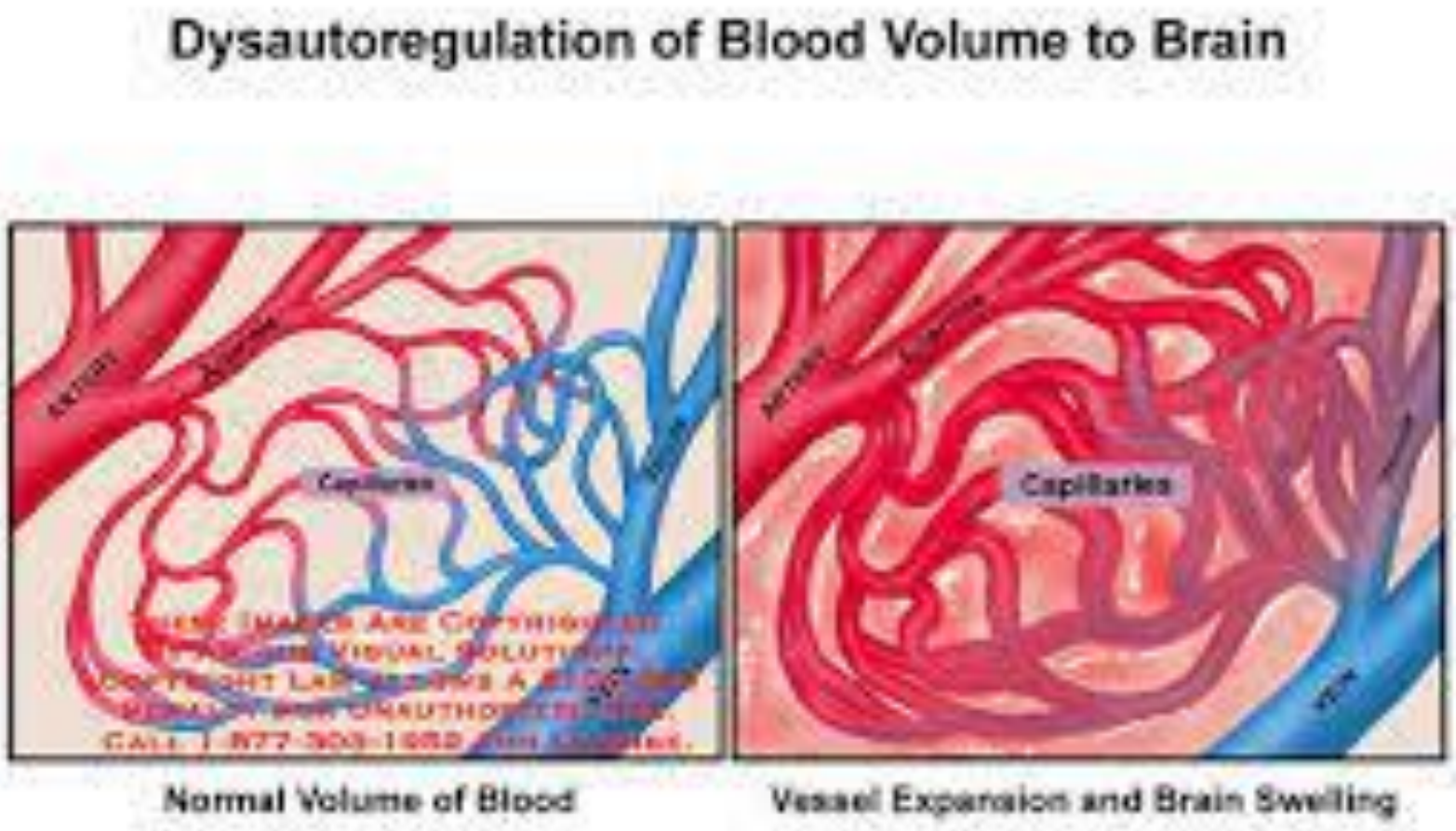
Dynamic

Propagation – forward or backward in vein

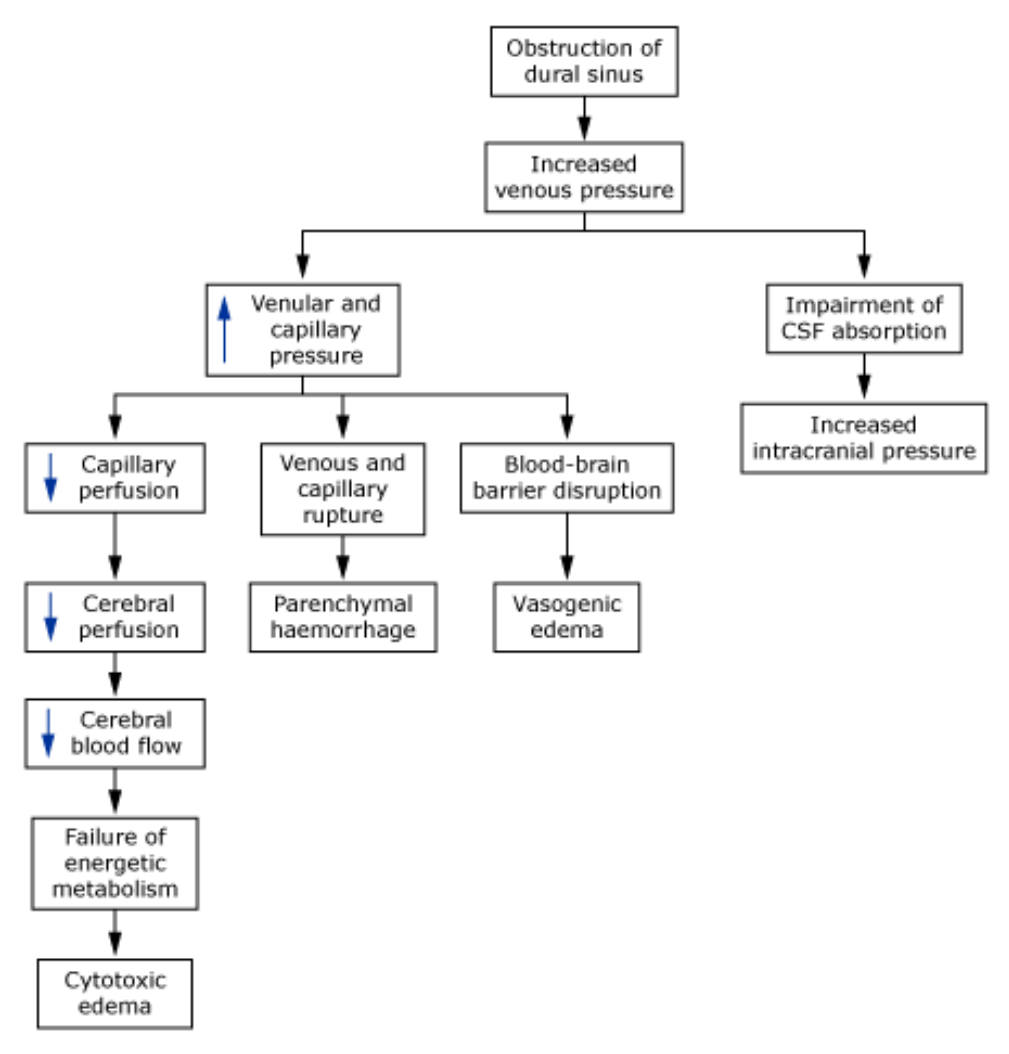
Sequalae

- Asymptomatic

-Elevated cerebral venous pressure→ dilated venous and capillary bed→ interstitial oedema--> rupture of cerebral veins→ IPH and/or SAH



PATHOPHYSIOLOGY



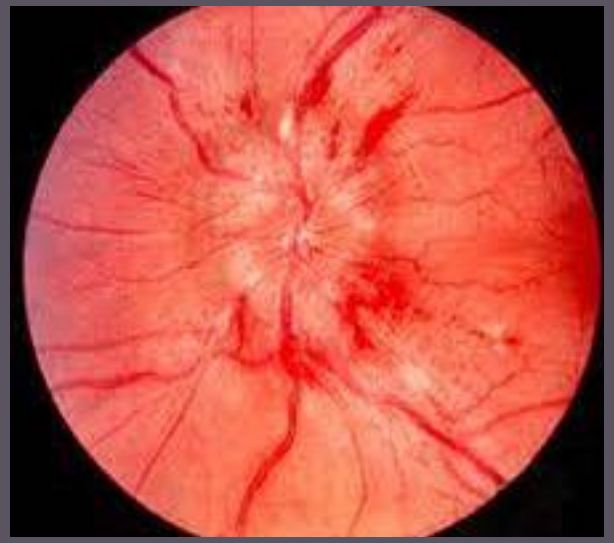
CVT SYMPTOMS

Characteristics	Consequences
Sinuses	
Rich innervation of the dura wall	Headache
Contain the arachnoid villi (CSF resorption)	Intracranial hypertension
Connection with ear, face, scalp veins	Septic or traumatic thrombosis
Anatomical variations: lateral sinus, torcular	Various drainage
Cortical veins	
Thin-wall, no defined muscle coat	Dilation, rupture with hemorrhages
No valves	Reversal of flow
Variable in number and location	No definite venous clinical syndromes
Sinuses and veins	
Numerous anastomoses	Collateral circulation
Venous drainage	Edema, hemorrhages, no real ischemia

CVT Aetiologies

- Local
- General infections
- Acquire Prothrombotic states
- Haematological conditions
- Systemic diseases
- Obstetric-Gynaecological
- Medications
- General conditions

Local causes	Direct septic trauma
Infectious	Intracranial infection: abcess, subdural empyema, orbital cellulites, tonsillitis, cutaneous cellulitis Head or neck tumors, neurosurgical procedures
Non-infectious	Head injury CSF hypotension (secondary or spontaneous) Jugular catheterization
General infections	Meningitis, systemic infectious disease
Thrombophilia/ Acquired prothrombotic states	Factor V Leiden mutation, G20210A prothrombin mutation, hyperhomocysteinemia and MTHFR mutation Antithrombin, protein S, protein C deficiencies Disorders of fibrinolysis Antiphospholipid antibodies Paroxysmal nocturnal hemoglobinuria Disseminated intravascular coagulation
Hematological conditions	Polycythemia, thrombocythemia Iron deficiency anemia Leukemia, lymphoma
Systemic diseases	Systemic lupus erythematosus, Behcet's disease, Wegener's granulomatosis, inflammatory bowel diseases, sarcoidosis, thyroiditis Cancers
Gyneco-obstetrical conditions	Postpartum, pregnancy Oral contraceptives
Medications	Corticoids, L-asparaginase, epsilon aminocaproic acid, thalidomide, tamoxifen, erythropoetin
General conditions	Postsurgery Severe dehydration (especially in children) Nephrotic syndrome Cardiac insufficiency Hypoxy, high altitude



CVT SYNDROMES

Have a guess at the syndromes

CVT Syndrome Patterns

Pathology	Neurological Syndrome
Isolated intracranial hypertension	Headache, papilloedema, 6th nerve palsy
Focal syndrome	Focal neurologicall deficits and/or partial seizures
Subacute encephalopathy	Depressed level of consciousness+/- Seizures
Cavernous sinus syndrome	Orbital pain, chemosis, proptosis, oculomotor palsies

Variable signs and symptoms

	ISCVT study N = 624 patients (%)	Authors'series N = 332 patients (%)
Headaches	553 (89%)	320 (96%)
Papilledema	174 (28%)	118 (37%)
Motor deficit	232 (37%)	80 (24%)
Sensory deficit	34 (5%)	23 (7%)
Aphasia	119 (19%)	50 (15%)
Altered consciousness/coma	137 (22%)	73 (22%)
Seizures before diagnosis	245 (39%)	116 (35%)
– Generalized seizures		60 (18%)
– Focal +/– generalization		58 (18%)
Other focal cortical signs	21 (3%)	11 (3%)
Bilateral signs		11 (3%)

Neuroimaging

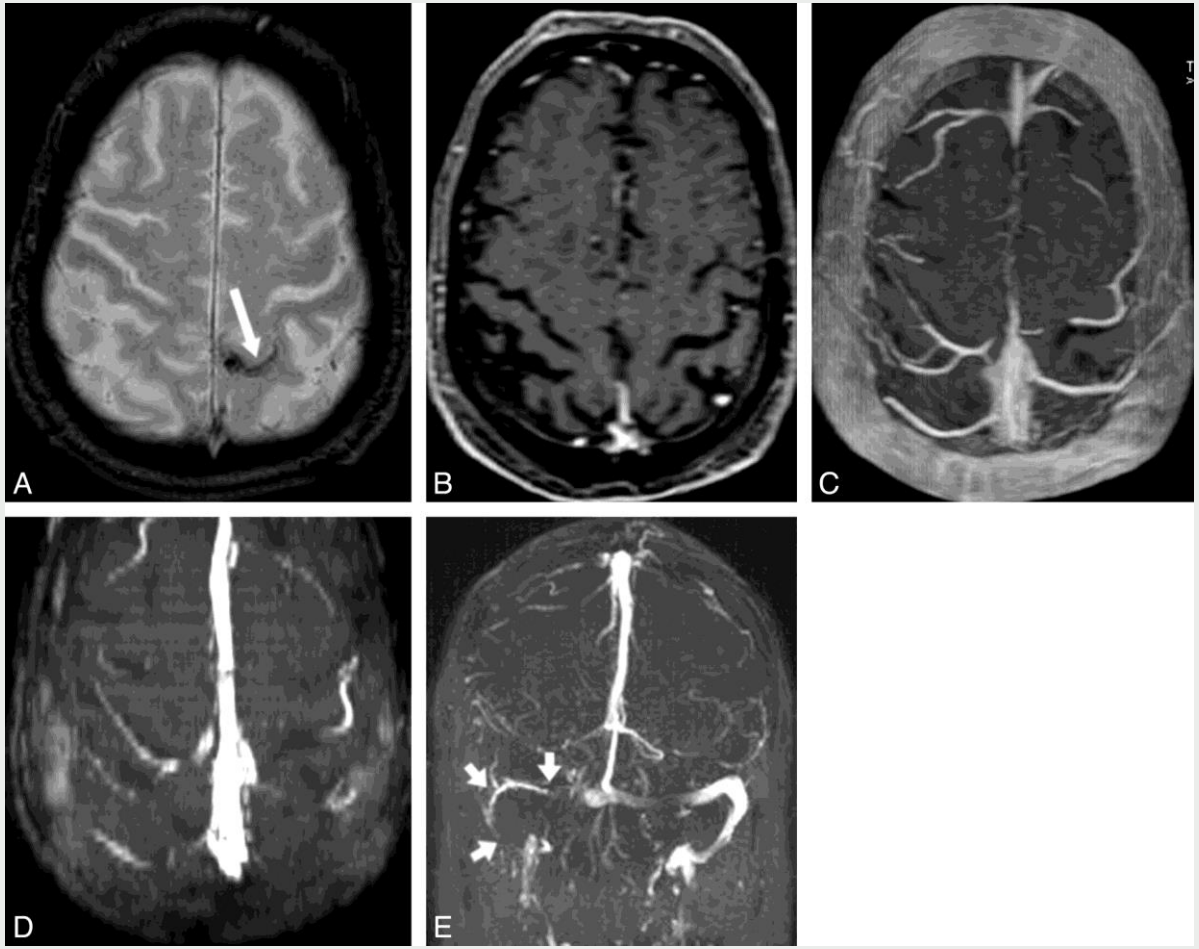
Neuroimaing has provided insight into CVT

Both venous and parenchymal imaging is done to look fot CVT and look for CVT mimics which may often be other parenchymal lesions

Visualisation of thrombus is key to diagnosis

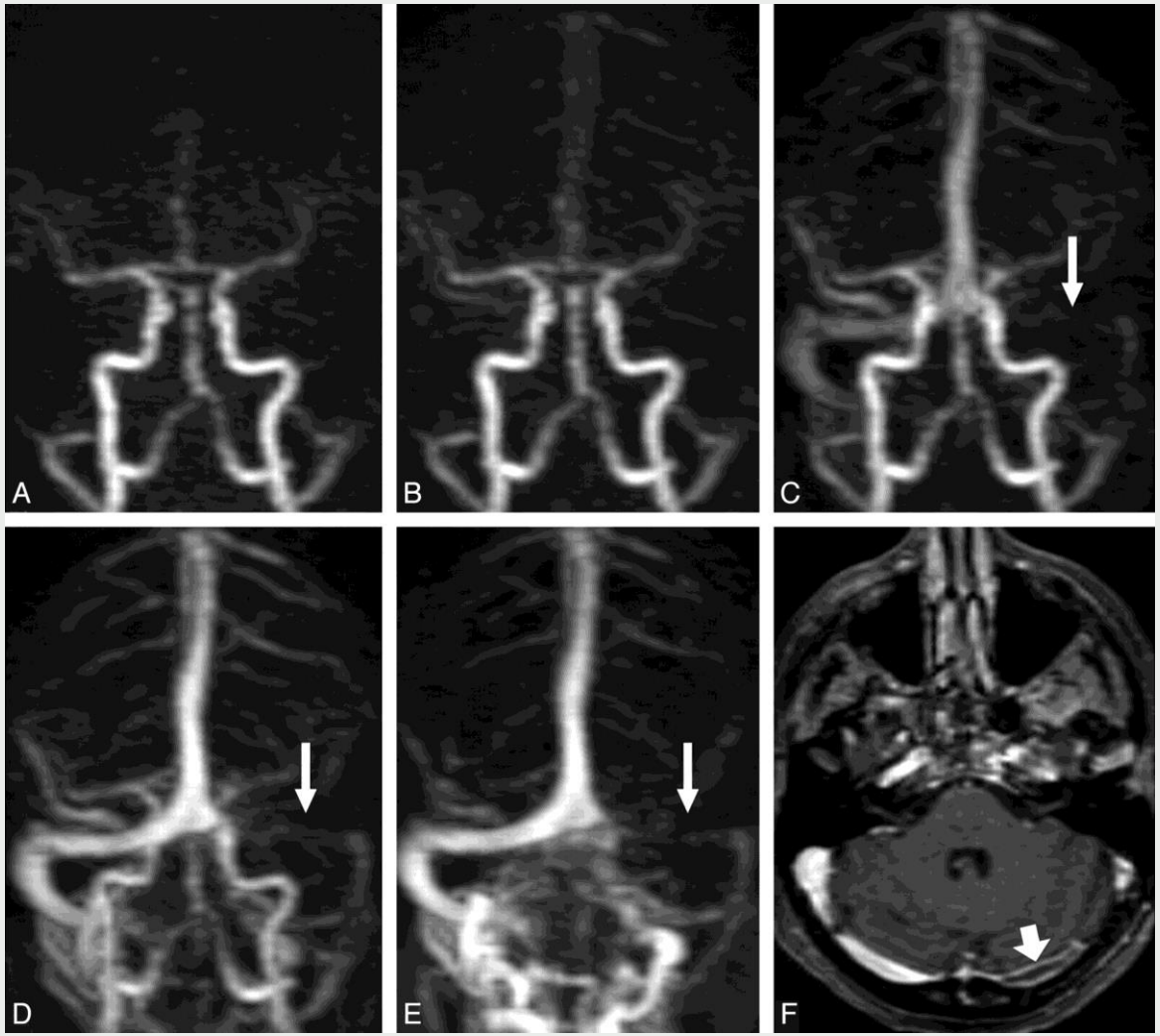
NEUROIMAGING

Imaging Modality	Notes
Non Contrast CTB	Normal in 30% Dense triangle Sign Empty Delta Sign Cord Sign Indirect signs: Haemorrhagic lesions Hypodensities (oedema/venous infarction)
CT Venogram	Can demonstrate filling defects, sinus wall enhancement, and increased collateral venous drainage CVT = MRV Quicker Can delinate acute from chronic (thrombus density) Dependent on vein site
MRI Brain	Most sensitive T2 Parenchymal indirect effects
MR venogram	Most sensitive Parenchymal indirect effects Dependent on vein site



MRV Cortical Vein thrombosis
Lateral sinus thrombosis

Meckel, S., Reisinger, C., Bremerich, J., Damm, D., Wolbers, M., Engelter, S., Scheffler, K., Wetzel, S.G., 2010. Cerebral Venous Thrombosis: Diagnostic Accuracy of Combined, Dynamic and Static, Contrast-Enhanced 4D MR Venography. American Journal of Neuroradiology 31, 527–535.. doi:10.3174/ajnr.a1869



MRV Left Proximal lateral sinus thrombosis

F- filling defect

Meckel, S., Reisinger, C., Bremerich, J., Damm, D., Wolbers, M., Engelter, S., Scheffler, K., Wetzel, S.G., 2010. Cerebral Venous Thrombosis: Diagnostic Accuracy of Combined, Dynamic and Static, Contrast-Enhanced 4D MR Venography. American Journal of Neuroradiology 31, 527–535.. doi:10.3174/ajnr.a1869

MRV/MR work up for posterior fossa haemorrhage

B- hypoplastic sinus (no thrombus)

Meckel, S., Reisinger, C., Bremerich, J., Damm, D., Wolbers, M., Engelter, S., Scheffler, K., Wetzel, S.G., 2010. Cerebral Venous Thrombosis: Diagnostic Accuracy of Combined, Dynamic and Static, Contrast-Enhanced 4D MR Venography. American Journal of Neuroradiology 31, 527–535.. doi:10.3174/ajnr.a1869

Thoughts?

Case

Next steps?

54 year old female

Presents with wake up stroke like symptoms	Left sided hemiparesis
	Headache
	1 week post ChAdox1 Vaccination
	PMHx:
	HTN – on antihypertensives
	HRT

Thoughts?

Case

History:

Felt unwell 5 days after vaccination. Never had COVID19 before

Headache started on day 6

Today awoke with left sided weakness

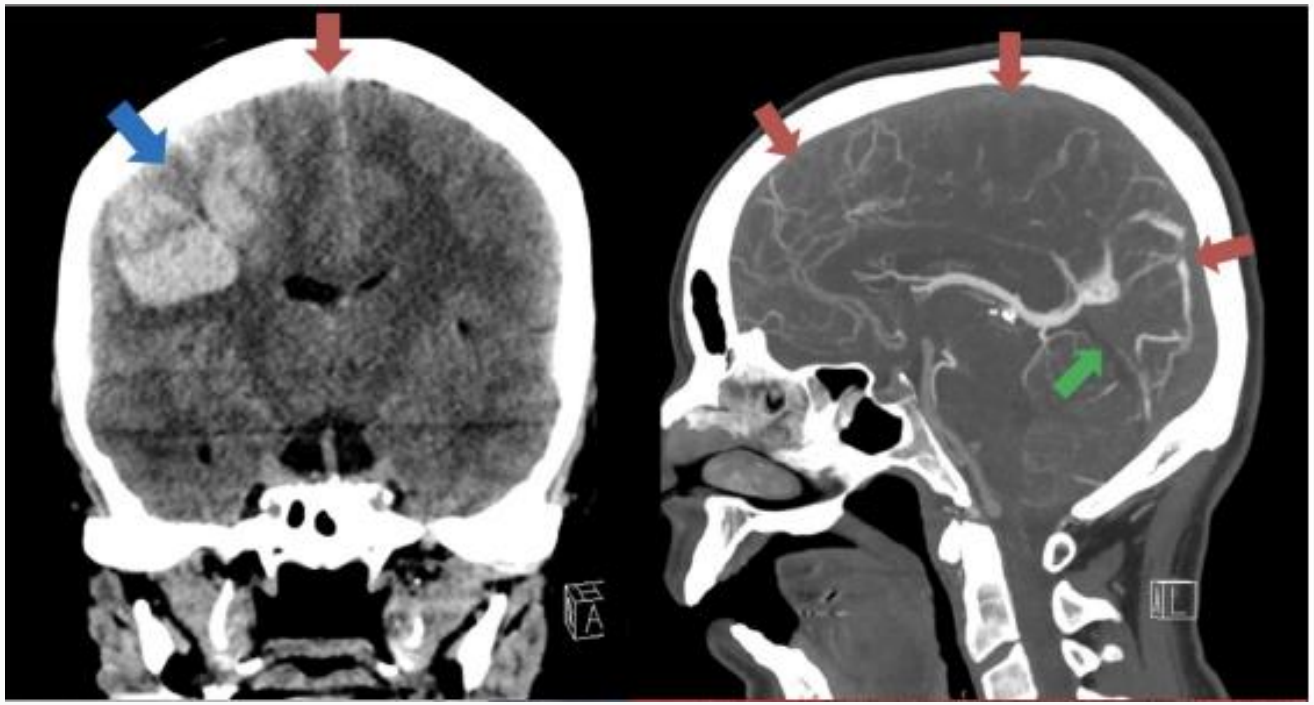
Never had this before

Examination:

NIHSS = 7

Next steps?

LABS AND NEUROIMAGING



Platelets 19
D-Dimer >35
INR 1.1
APTT 29
Fibrinogen 1.2
SarsCoV2 AB – Nucleocapsid protein negative, Spike protein positive

Thoughts?

The next few days

Platelet transfusion

Methylprednisolone

IVIG

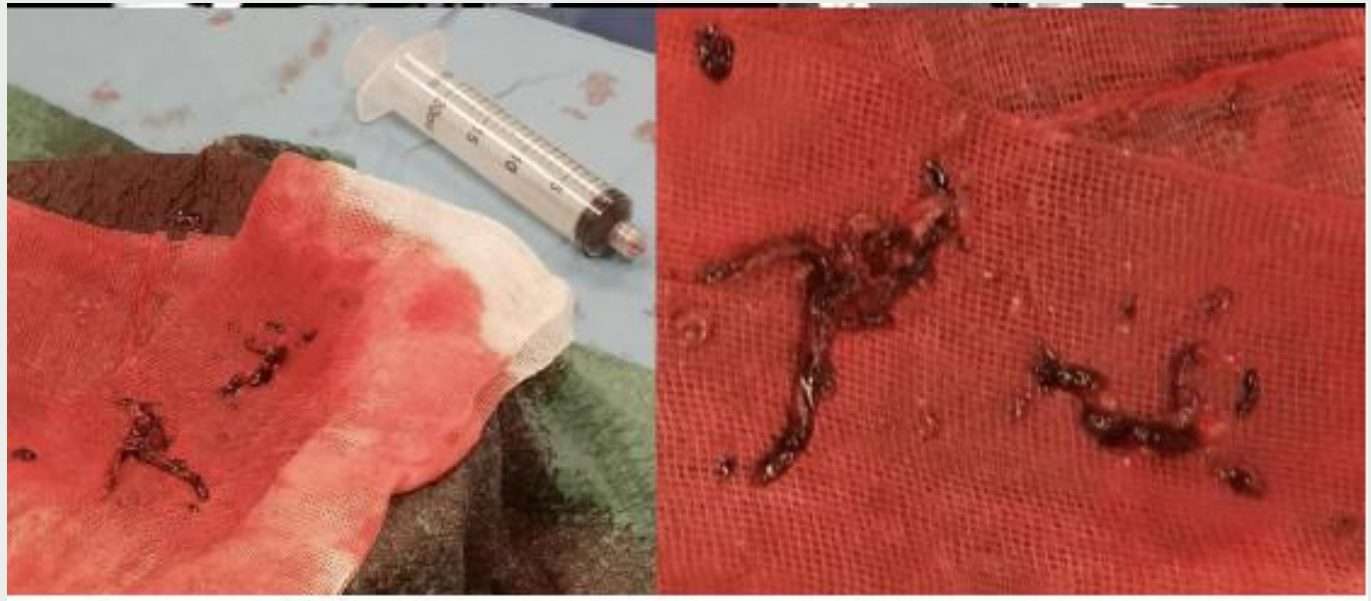
Endovascular thrombectomy with UFH

Demcompressive hemicraniectomy for raised ICP

Refractory raised ICP

Death

Thoughts?

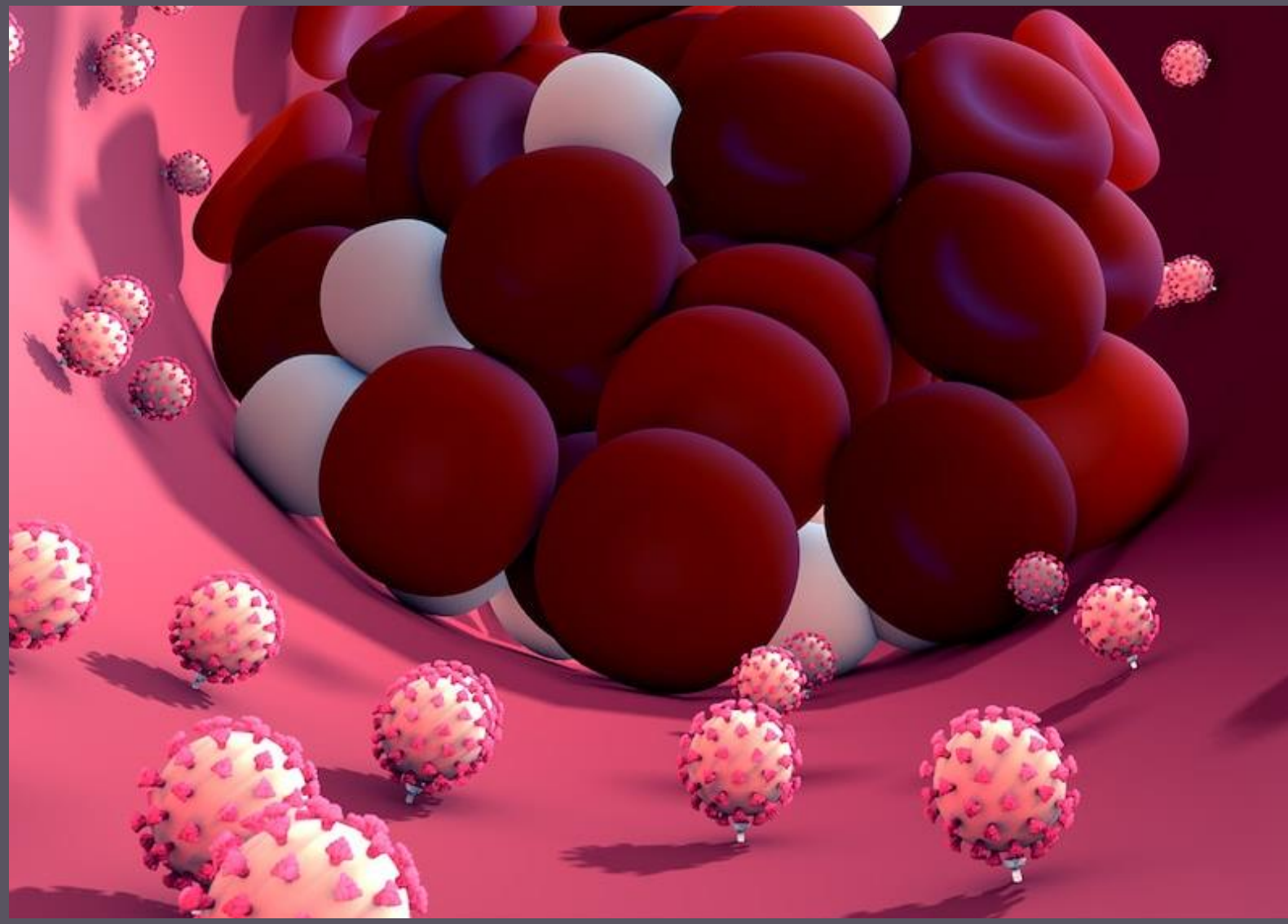


VITT

Vaccine induced immune thrombotic thrombocytopenia

Proposed as an association with ChAdox1 Vaccination

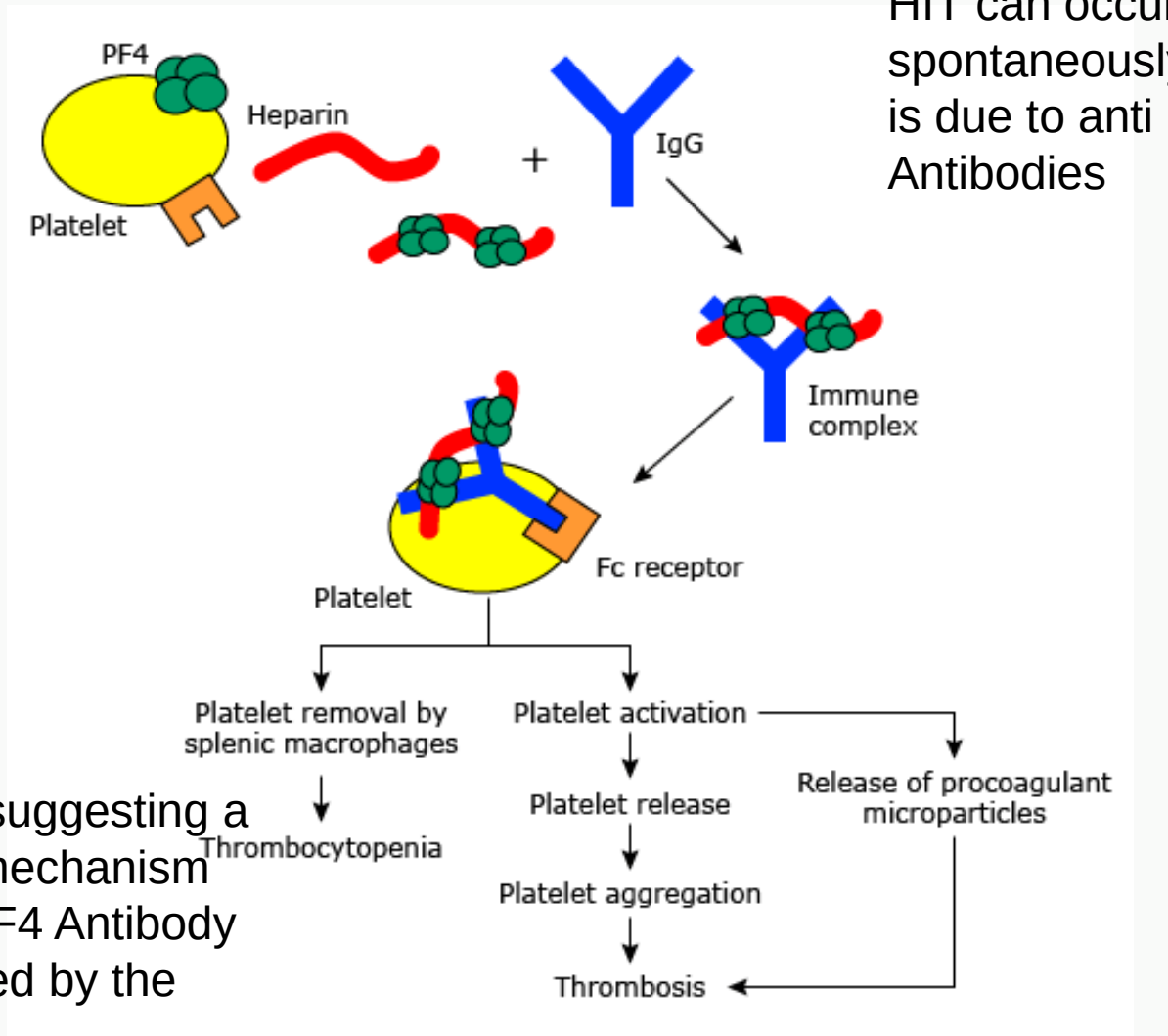
Not limited to cerebral circulation



VITT PROPOSED PATHOPHYSIOLOGY

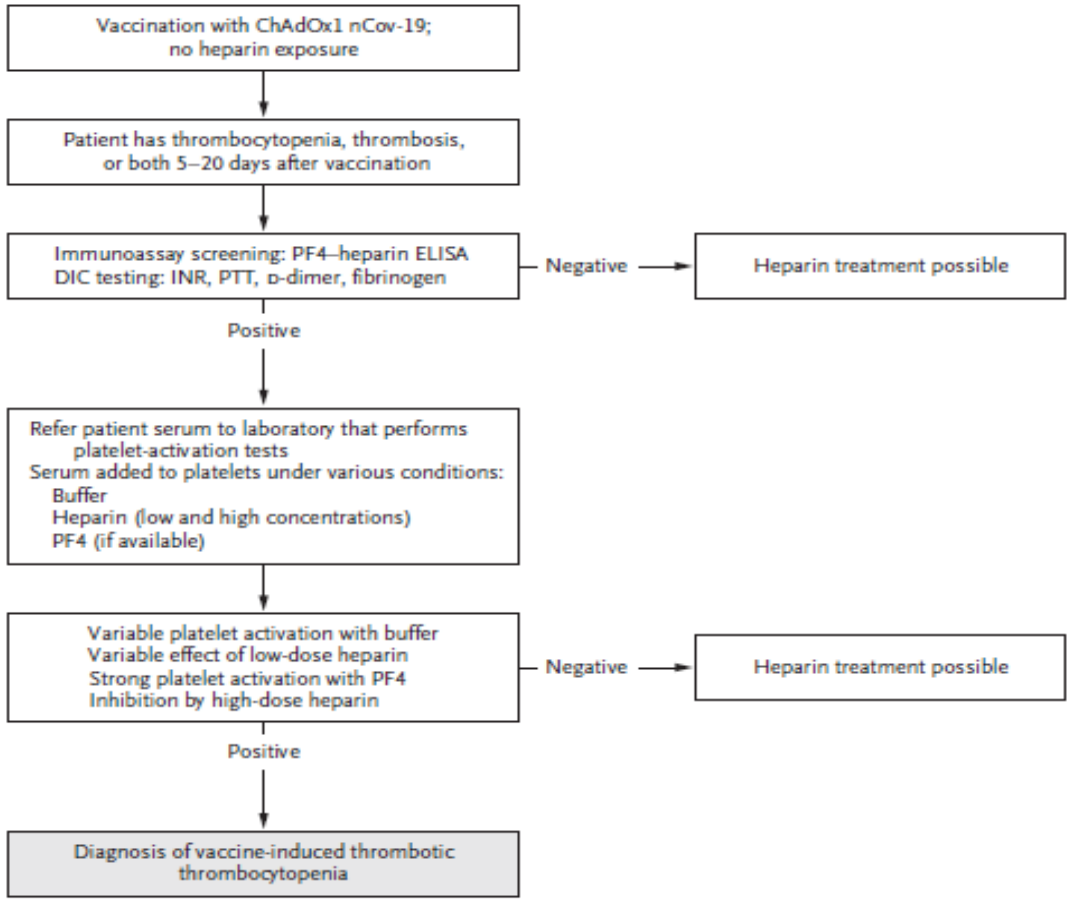
VITT links thrombosis with immune

Heparin is physiological HIT can occur spontaneously and is due to anti PF4 Antibodies



VITT is suggesting a similar mechanism with a PF4 Antibody stimulated by the Vaccine

VITT MANAGEMENT



Treatment Options	Comment
High-dose intravenous immune globulin (1 g per kg for 2 days)	Raises platelet count and decreases hypercoagulability (by analogy with autoimmune HIT); inhibits platelet activation by platelet-activating anti-PF4 antibodies (platelet Fcγ receptors)
Anticoagulants often used to treat heparin-induced thrombocytopenia	Direct oral Xa inhibitors (apixaban, rivaroxaban) Direct thrombin inhibitors (argatroban, bivalirudin) Indirect (antithrombin-dependent) Xa inhibitors: danaparoid (not available in U.S.), fondaparinux
Platelet transfusions	Avoid unless presence of bleeding (theoretical prothrombotic risk)
Vitamin K antagonist	Contraindicated during acute thrombocytopenia and disseminated intravascular coagulation (microthrombosis associated with protein C depletion)

Figure 2. Potential Diagnostic and Therapeutic Strategies for Management of Suspected Vaccine-Induced Immune Thrombotic Thrombocytopenia.

WHAT NOW?
PHARMACOVIGILANCE

References

1. Caplan, L. R. and Van Gijn, J. (2012) *Stroke syndromes*. 3rd edn. Cambridge: Cambridge University Press (Cambridge medicine). Available at: INSERT-MISSING-URL (Accessed: April 19, 2021).

2.Meckel, S., Reisinger, C., Bremerich, J., Damm, D., Wolbers, M., Engelter, S., Scheffler, K., Wetzel, S.G., 2010. Cerebral Venous Thrombosis: Diagnostic Accuracy of Combined, Dynamic and Static, Contrast-Enhanced 4D MR Venography. American Journal of Neuroradiology 31, 527–535.. doi:10.3174/ajnr.a1869

3. Ferreo, JM. Cerebral venous thrombosis: Etiology, clinical features, and diagnosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2014.

4. Greinacher, A., Thiele, T., Warkentin, T.E., Weisser, K., Kyrle, P.A., Eichinger, S., 2021. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. New England Journal of Medicine.. doi:10.1056/nejmoa2104840

5. Schultz, N.H., Sørvoll, I.H., Michelsen, A.E., Munthe, L.A., Lund-Johansen, F., Ahlen, M.T., Wiedmann, M., Aamodt, A.-H., Skattør, T.H., Tjønnfjord, G.E., Holme, P.A., 2021. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. New England Journal of Medicine.. doi:10.1056/nejmoa2104882