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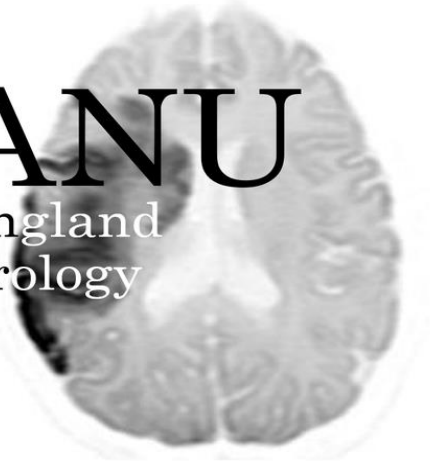

Neurological investigations… what are they good for?

Matt Jones

Chris Kobylecki

MANCHESTER 1824
The University of Manchester

Manchester Centre for Clinical Neurosciences

Salford Royal NHS
NHS Foundation Trust

Disclosures

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C Kobylecki

- Employment: Northern Care Alliance NHS Trust
- Grants: Parkinson's UK, Michael J Fox Foundation
- Lecture fees: Britannia Pharmaceuticals, Bial
- Trustee of Multiple System Atrophy Trust

M Jones

- Employment: Northern Care Alliance NHS Trust
- Lecture fees: Biogen
- Expert Advisor – BMJ best practice

Objectives

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- Understand the role of investigations in acute neurological presentations
- Neuroimaging and neurophysiology
- CSF and blood tests
- Limitations and cautions when using neurological investigations

Why do we image?

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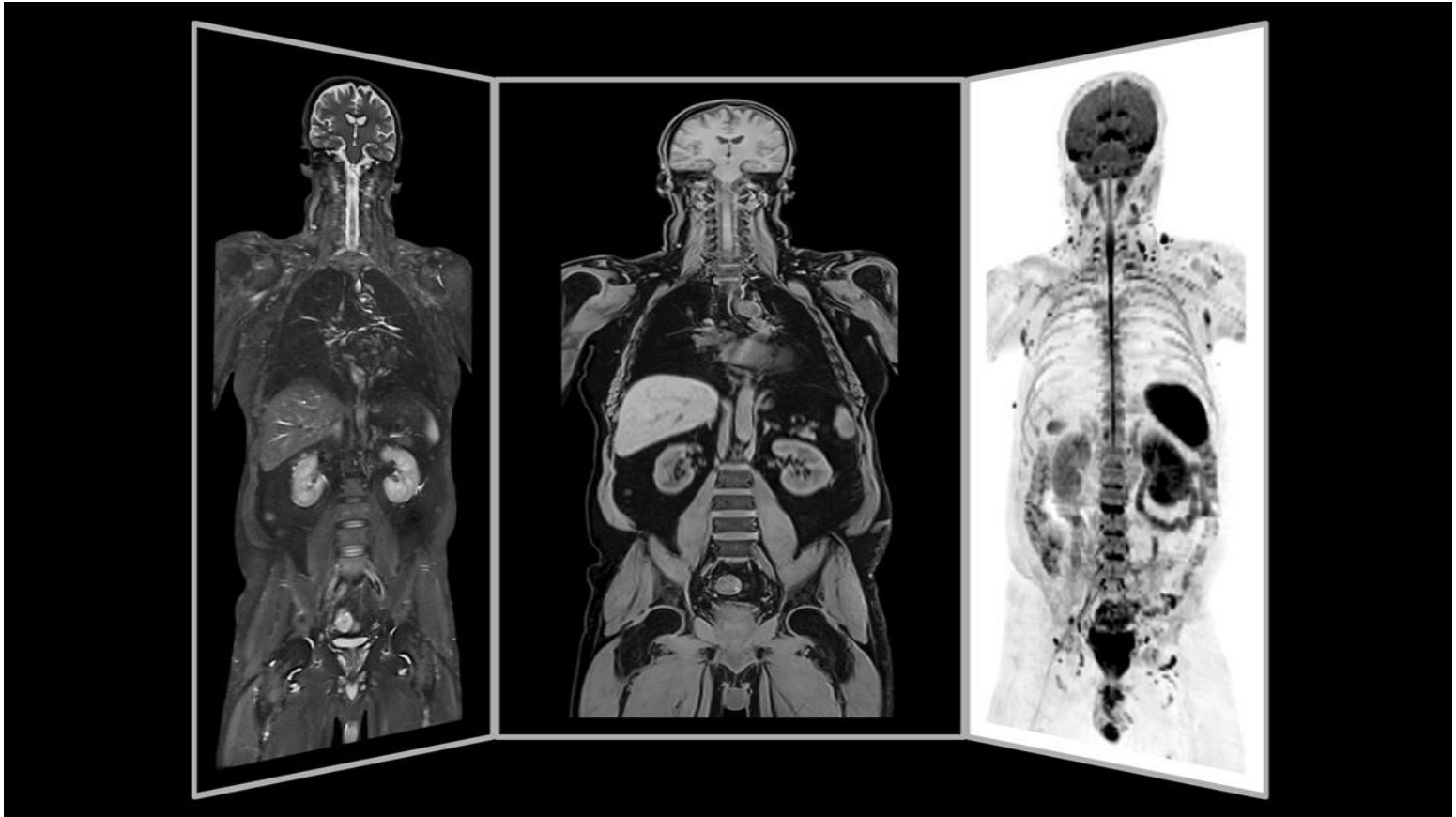

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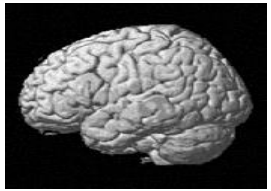
The Basics

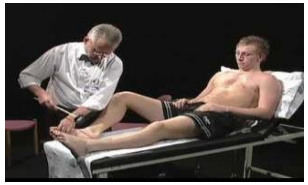
Theory



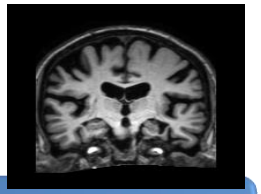
History

Symptoms:
Headache
Dizziness
Tingling
Weakness
Blackout
Confusion…..

Exam



Investigation



Treatment

Differential Diagnosis

Precise Diagnosis

The Basics

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> Different from all other medical specialties, save perhaps psychiatry, the neurologist is heavily dependent on listening to and interpreting what the patient tells us… If you don't know what is happening by the time you get to the feet you are in real trouble

Jerome M Posner, 2013[4]

Why do we image?

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- To confirm a clinical diagnosis
- To rule out something serious
- To aid prognosis or treatment
- Are there any downsides to imaging?

Case 1

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- 42 year old female
- Sudden onset severe occipital headache
- Vomiting, photophobia
- Still present 2 hours post onset

What is the differential diagnosis?

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- Subarachnoid haemorrhage
- Other secondary headache
- Primary headache disorder

What is the next step?

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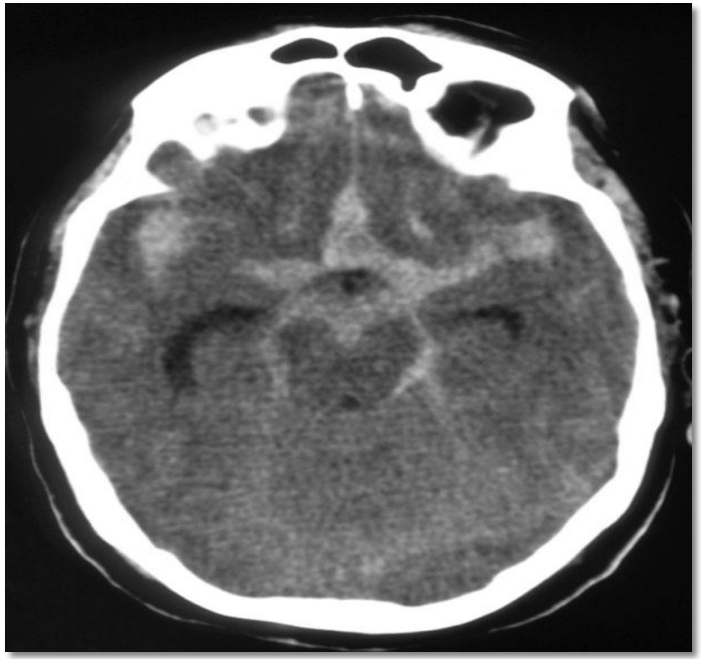

Investigation of suspected SAH

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- Urgent CT brain
  - Sensitivity close to 100% within 6h
  - 50% after 5-7 days
- Confirm diagnosis or alternatives
- Assess for complications
  - ICH, IVH
  - hydrocephalus

Case 2

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- 45 year old male, PMH ulcerative colitis
- 4 day history worsening headache
- Present on waking
- Worse on lying down/coughing/Valsalva
  - Intermittent blurred vision at those times
- Observations normal, GCS 14/15
- Both optic discs swollen
- Neurological examination otherwise normal

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What is the differential diagnosis?

What is the next step?

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- CT brain normal

- Now what?

CT venogram

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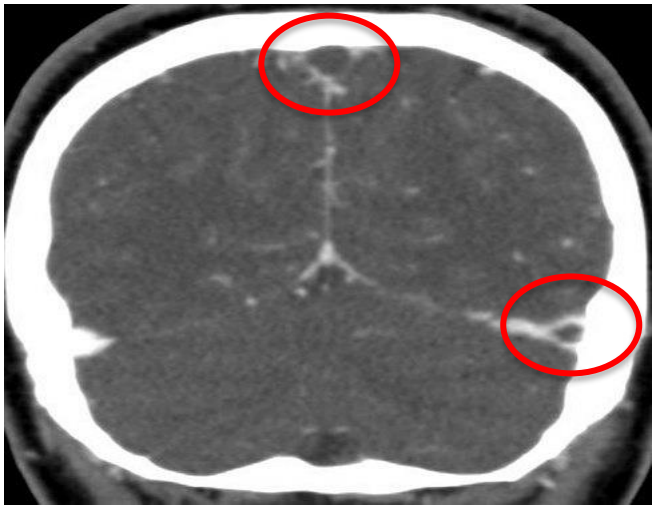

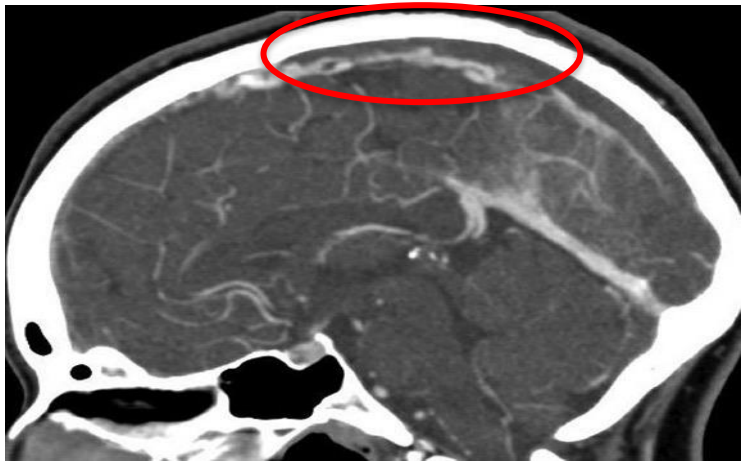

Courtesy of Dr Amit Herwadkar, Consultant Neuroradiologist, SRFT

Cerebral venous sinus thrombosis: aetiology

- Pregnancy/post-partum
- Local infection
  - Mastoiditis, sinusitis
- Dehydration
- Thrombophilia
- Haematological malignancy
- Drugs
  - Oral contraceptives
- Inflammatory conditions
  - **IBD**
  - SLE
  - Behçet's disease
- Head injury
- Recent neurosurgery
- COVID-19 infection
- COVID vaccines

Modailty	Advantages	Disadvantages
Plain CT	Quick, inexpensive	Insensitive
MR venogram	Sensitive to blood Does not require contrast	Artefacts Acquisition time Difficult in acutely unwell patients Contraindications Expensive
CT venogram	Can be added to plain CT Inexpensive Relatively quick Monitoring of critically ill patients	Radiation dose Requires contrast Contraindicated in pregnancy

When to suspect CVST in acute headache

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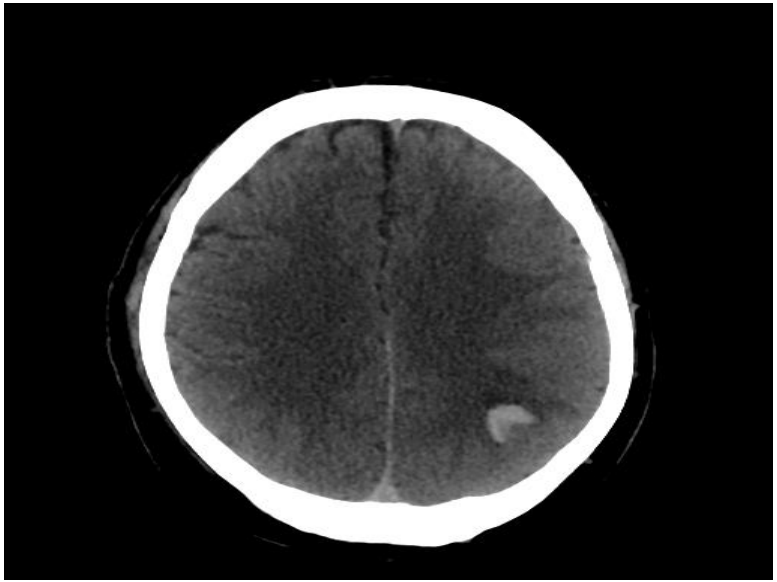
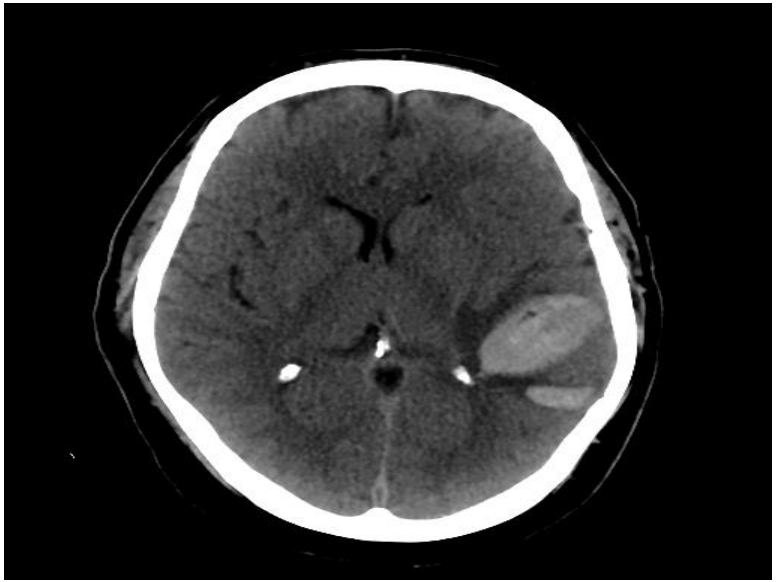
North of England Acute Neurology Update

Ulivi L *et al. Pract Neurol* 2020;20:356-367.

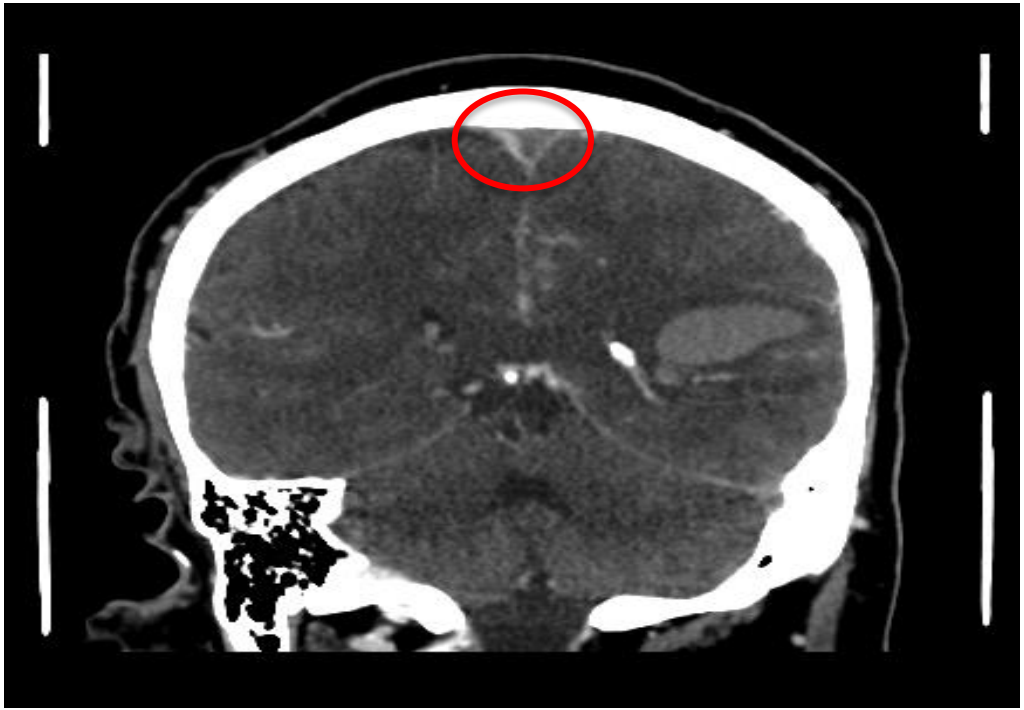
Imaging in CVST





Plain CT often normal

Imaging in CVST



Delta sign Δ

Decisions, decisions…

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CT

MRI

Structural Imaging

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CT

- Quick
- Cheap
- Convenient

- Involves radiation
- Poor quality

Acute Blood

Anything catastrophic?

MRI

- Slow
- Expensive
- Bit more effort…

- No radiation
- High quality

Everything else

A few contraindications

Case 3

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- 23 year old male
- Presents to ED
- Episode of loss of consciousness
  - Preceded by abdominal sensation
  - Tonic phase, then shaking in all 4 limbs for 2 min
  - Confused, combative afterwards

What do you need to know?

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- Normally well, no history of epilepsy
- No medication changes, drug use
- Febrile seizures as a child

- Afebrile, BP 130/80, HR 70
- Capillary blood glucose 5.4
- Neurological exam normal

What is the next step?

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Indications for urgent imaging

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- Focal neurological deficits
- Persistent headache
- Fever
- Cognitive changes
- Recent head trauma
- Immune compromise

- Not a usual seizure in established epilepsy!

Urgent imaging - seizures

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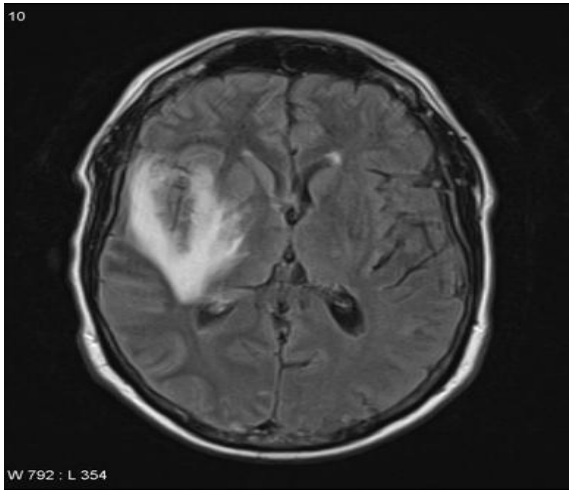
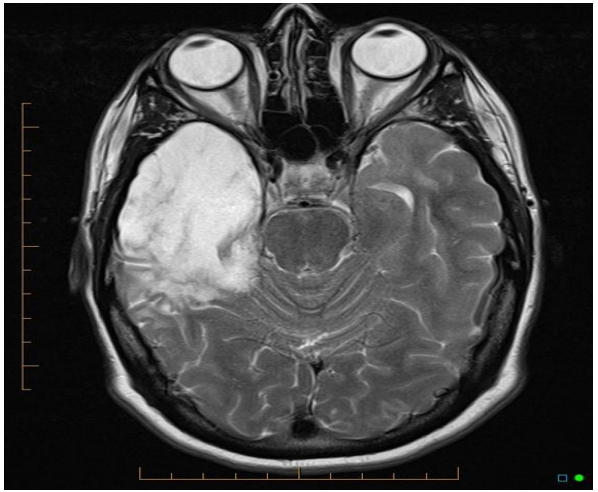
- CT in sick patient, prior to LP

- MRI more sensitive for most lesions
  - Encephalitis
  - Mass lesion
  - Infection in immunocompromised e.g. toxoplasmosis
  - Consider CVST (CT/MR venogram)

- “Any adult with a seizure in the context of febrile illness…must be investigated for possible CNS infection”





Non-urgent imaging

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- Stable patient, no red flags
- CT insensitive for most lesions causing seizures
- Outpatient MR investigation of choice

Limitations of CT imaging in seizures

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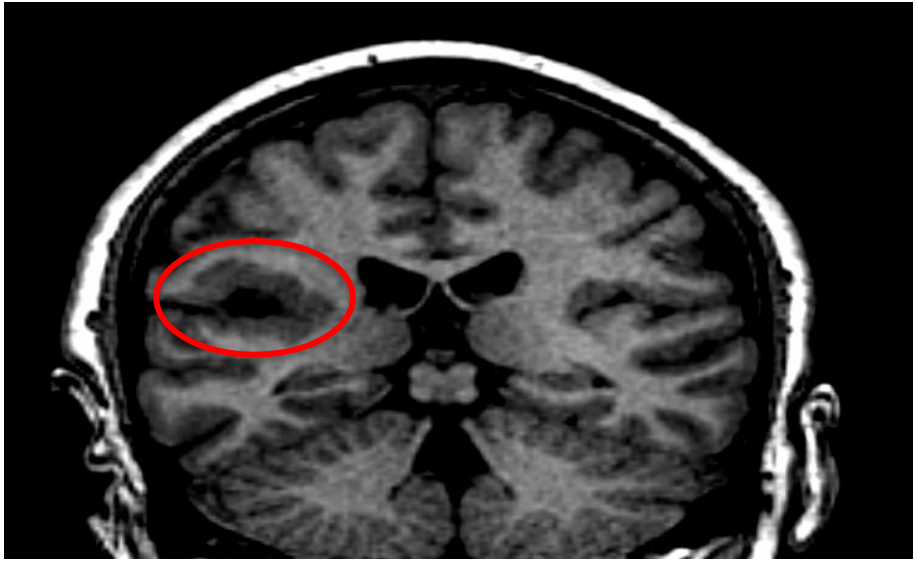
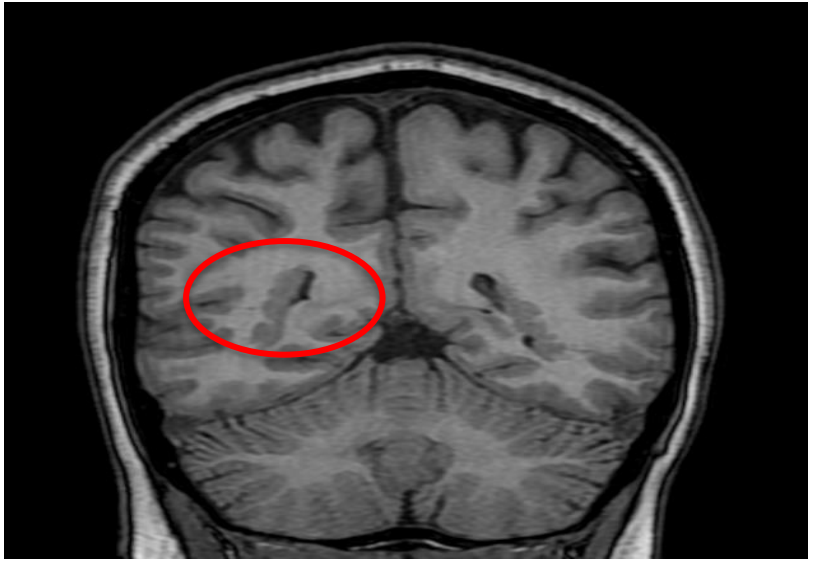


27 year old woman with focal seizures
CT brain unremarkable
Polymicrogyria



34 year old woman
Focal seizures with secondary generalisation
CT brain normal
Grey matter heterotopia

Case 5: On the PTWR…

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35 yr old female
New onset of leg weakness and bladder problems … 2 days…

- Trouble with stairs, fallen at night
- Also has numbness and burning in legs
- Increased urinary frequency and urgency

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Afebrile, obs normal
CN - normal
UL - normal
LL - tone normal, grade 4 weakness b/l, knee and ankle jerks normal, plantars up, patchy pin-prick alteration throughout LL, decreased vibr to waist
Gait – very unsteady, almost falling

Decisions, decisions

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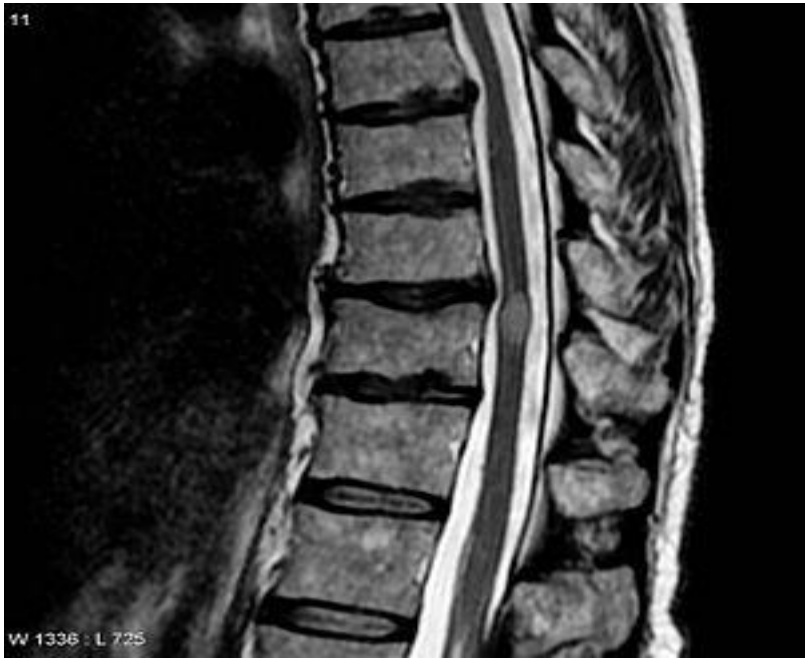
- CT brain
- CT spine
- MRI lumbosacral spine
- MRI cervicothoracic spine
- Lumbar puncture



Worrying Neck Scans

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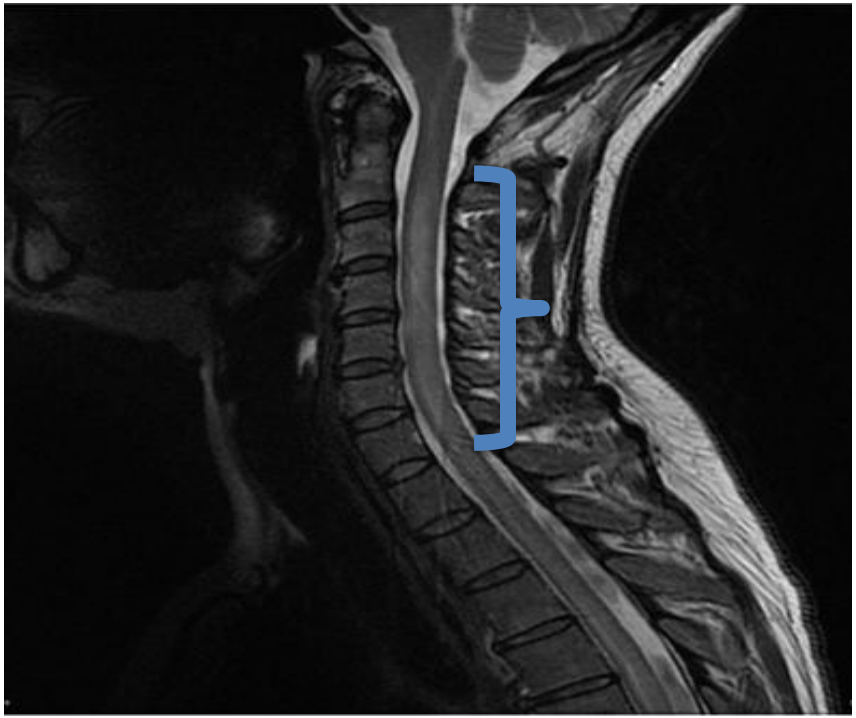

Neuromyelitis Optica (NMO / Devic's)

Posterior columns picked out…

Worrying Scenarios

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- Progressive limb Symptoms
- Sphincteric disturbance
- Increased tone
- Brisk reflexes
- Upgoing plantars
- Sensory levels

Scan Negative Myelopathy

Infarction

Dural AV fistula

B12, Copper, NO

HIV, syphilis, Hep B

Chronic Liver Disease

MS, NMO

Genetic

When not to image

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- Seizures in known epilepsy
- Usual headache in known primary headache disorder e.g. migraine

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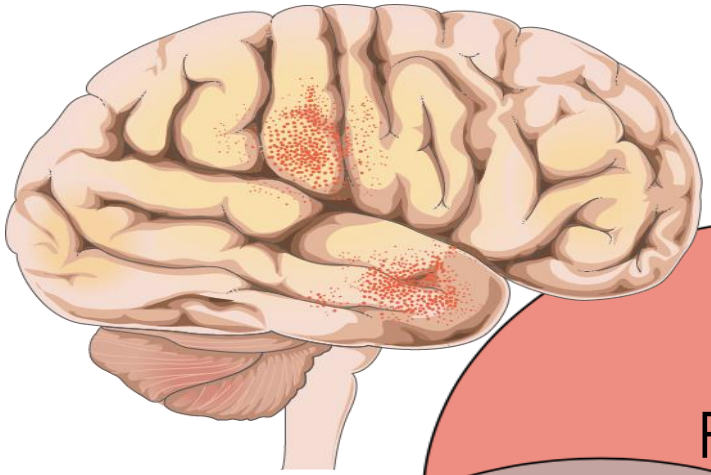
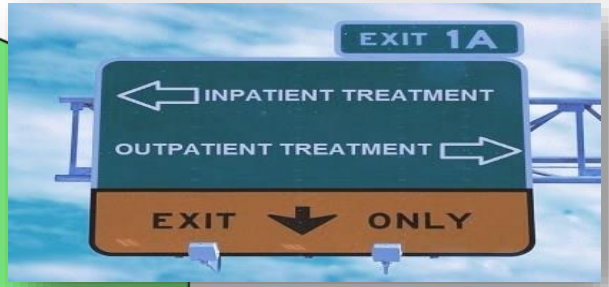


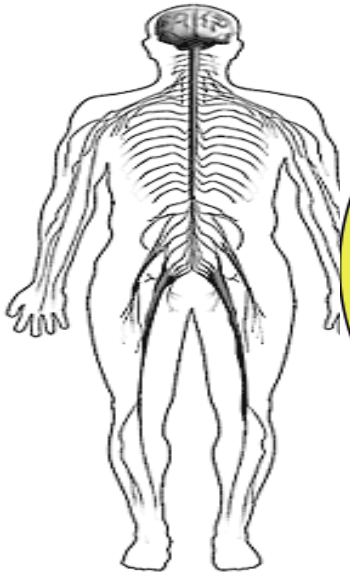
Right Person

Right Place

Right Time

And Right Modality…





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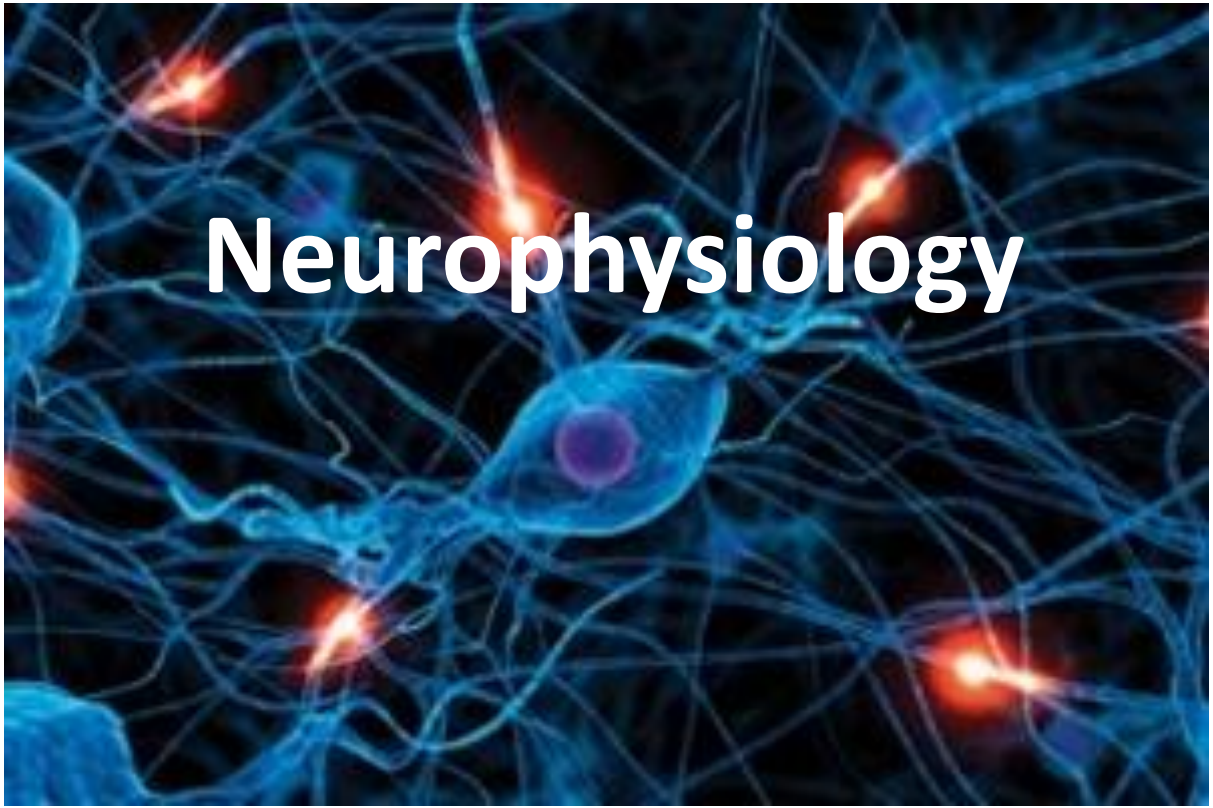

EEG basics

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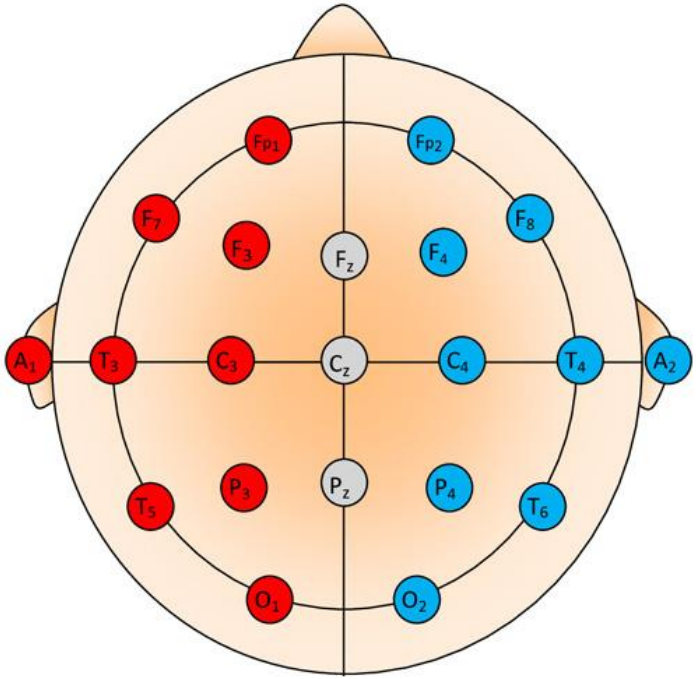
- Recording electrical potentials
- Multiple scalp electrodes and reference



https://www.ebme.co.uk/articles/clinical-engineering/introduction-to-eeg

Case 1

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- 23 year old female
- Presented to ED with unconscious collapse
- Preceding lightheadedness, vision darkened, nausea
- LOC for 20 seconds, shaking in all limbs for 5 s, urinary incontinence
- Rapid recovery, felt nauseated

What now?

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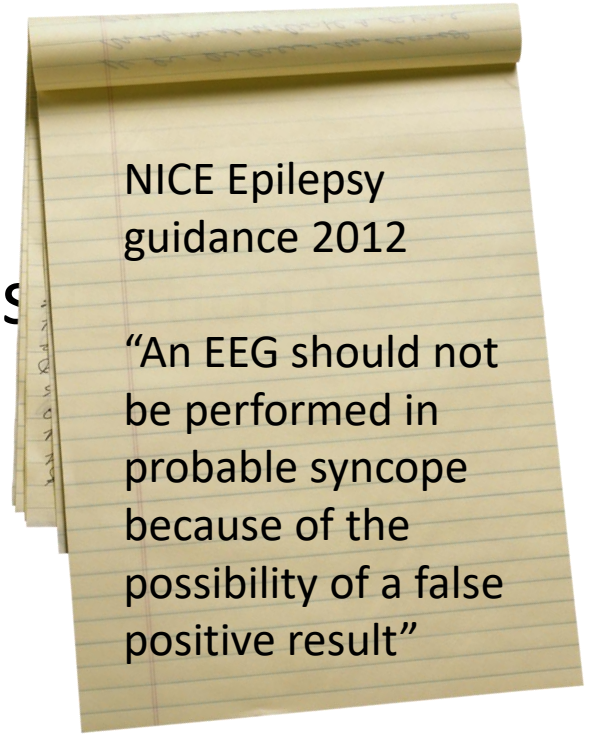
- What is the likely diagnosis?
- What is the highest yield inves
  - EEG
  - ECG
  - MRI brain



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"Routine interictal EEG recording is one of the most abused investigations in clinical medicine and is unquestionably responsible for great human suffering"

David Chadwick, *JNNP* 1994;57:264-277.

Limitations of EEG

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- Low sensitivity for epilepsy diagnosis (up to 50%)
- Up to 10-15% normal population may have nonspecific abnormalities, increasing with age
- Interictal epileptiform discharges in 1-5% normal population

EEG in first fit assessment

- Not recommended to be requested from ED
- Usually requested in selected neurology first fit assessments
  - Look for specific epilepsy syndromes
  - Prognostication re further seizures

Don’t forget the ECG!

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- 12 lead ECG mandatory in all “first fits”
- Discordance between neurologist and cardiologist read in 20% of cases where initial ECG thought normal
- Misdiagnosis of epilepsy
  - Inappropriate use of antiepileptic drugs
  - Missing potentially treatable arrhythmias

Case 2

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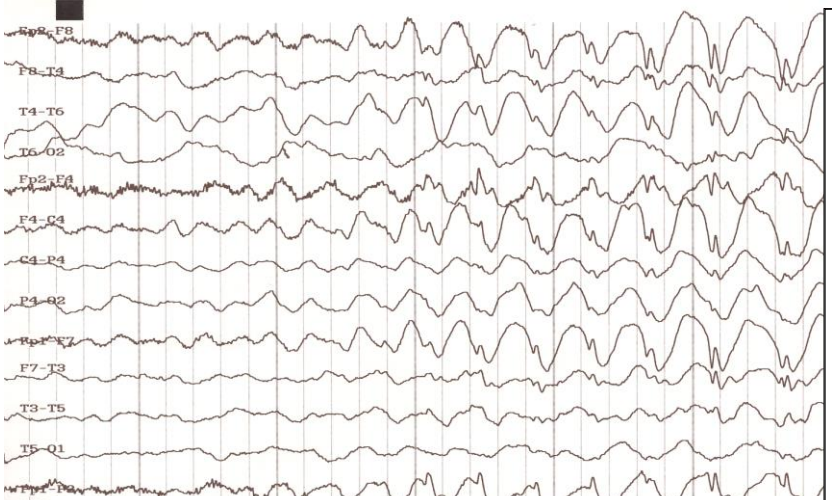
- 23 year old male, GTCS at age 10
  - Absences, ‘twitches’ on waking
  - Diagnosis juvenile myoclonic epilepsy
  - Started valproate, topiramate added
- 3 years later admitted with GTCS
  - Persistent post ictal confusion
  - Inattentive, distractible, MMSE 22/30
  - Neurological examination otherwise normal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T6-O2
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C4-P4
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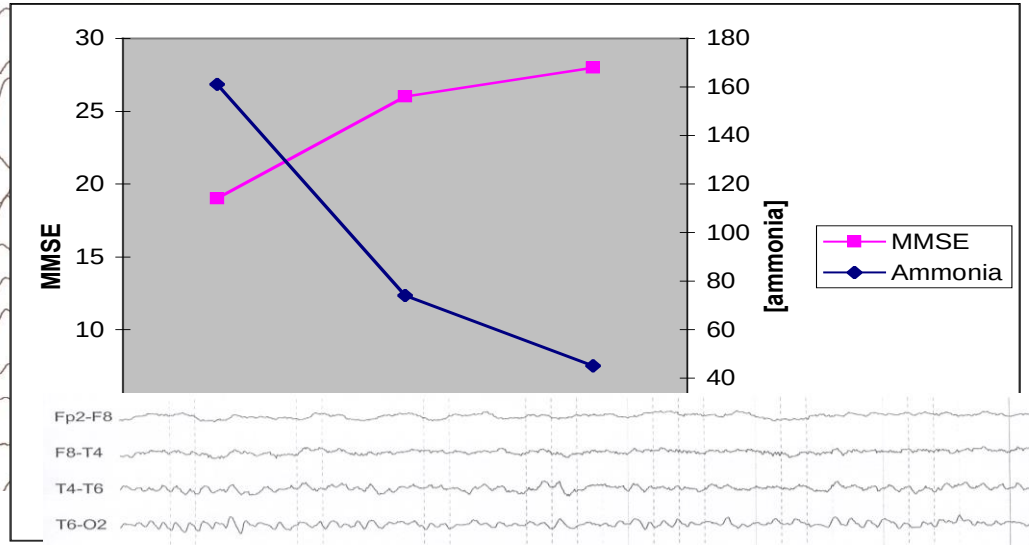
F7-T3
T3-T5
T5-O1
ECG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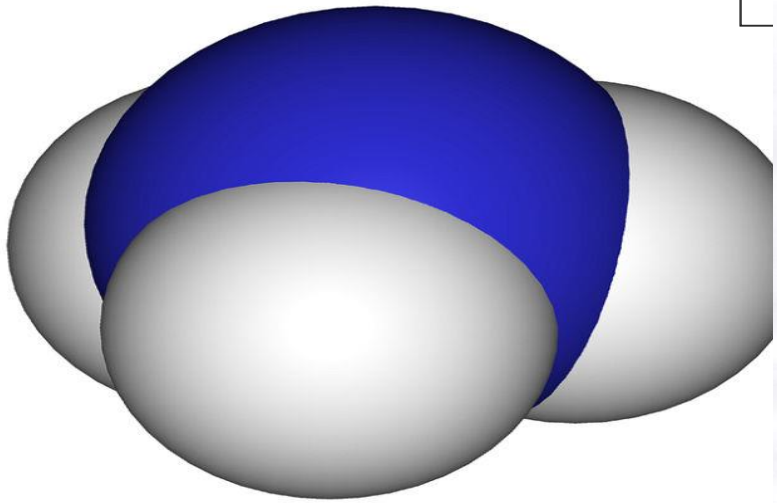
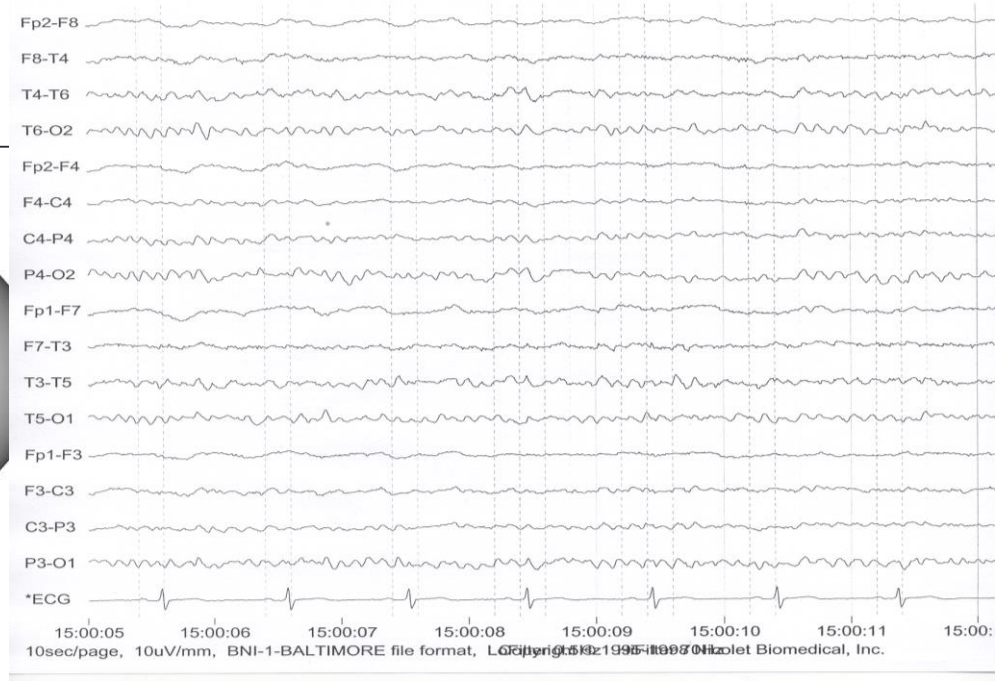
MMSE
Ammonia

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EEG in acute medicine

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Strengths	Weaknesses
Identifying acute seizures or non convulsive status	Findings nonspecific with regard to aetiology
Distinguishing functional seizures	Incidence of pre-existing abnormalities
Predicting outcome in some types of coma	Cannot reliably confirm or exclude epilepsy
Identifying reversible causes of encephalopathy e.g. metabolic	
Identifying specific patterns seen in prion disease	

EEG in prion disease

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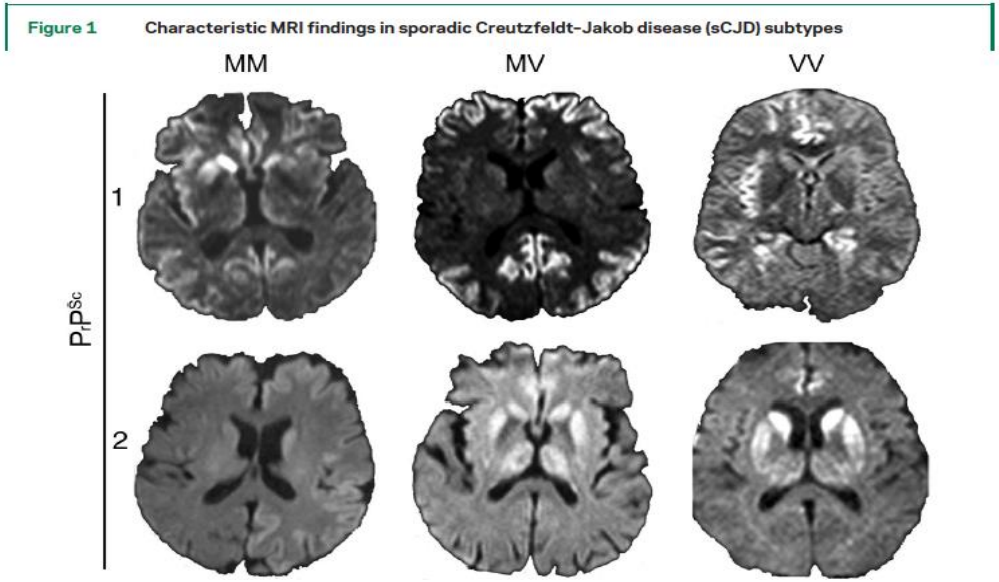

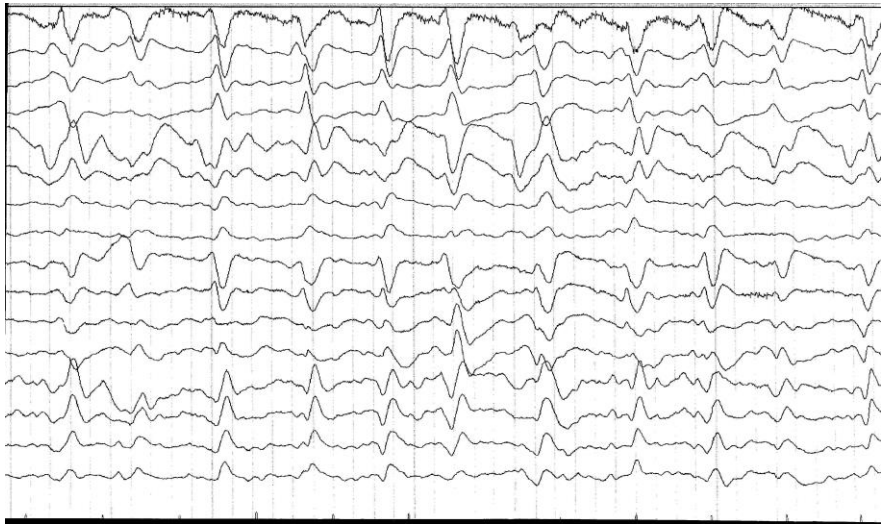

Meissner *et al.* Neurology 2007;72;1994-2001.

www.cjd.ed.ac.uk

Nerve conduction studies in acute weakness

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- NCS are an extension of clinical examination!
- Clinical assessment is key
  - Pattern of weakness (pyramidal, proximal, distal)
  - Reflex loss, plantar responses, sensory deficit
  - Sphincteric involvement
- Remember NCS frequently normal in first 1-2 weeks of GBS presentation

Neurophysiology: summary

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- EEG is more useful for inpatient assessment compared to first fit assessment

- Beware of interpreting EEG when clinical indications not clear

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Update

CSF and Blood Tests

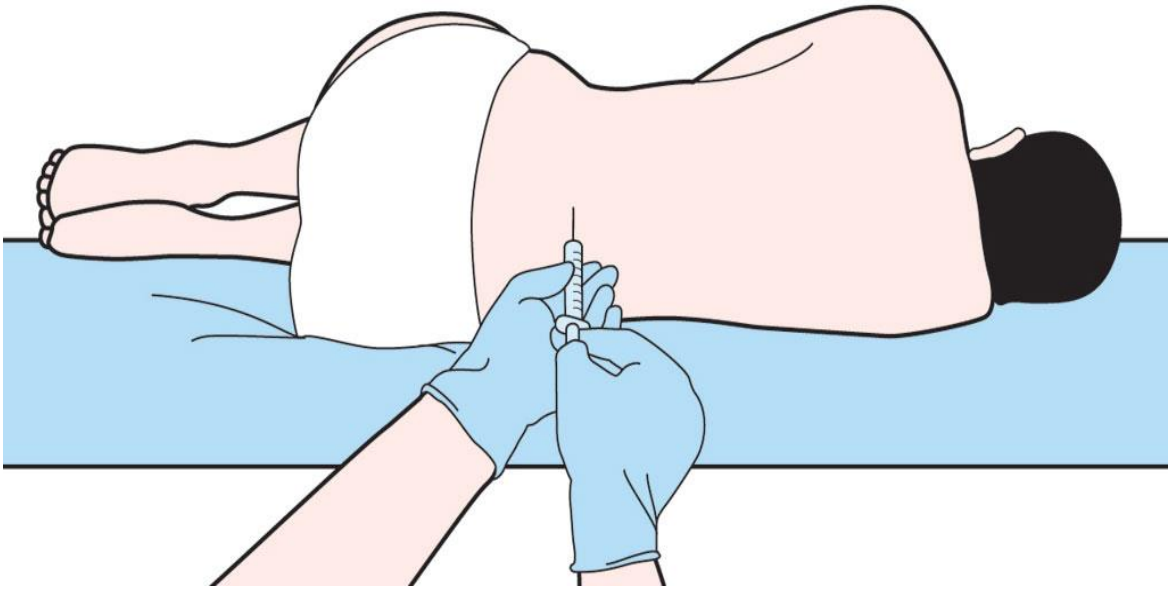
What’s the problem with LPs..?

LP Issues

- Technique variable
- Results non-specific
- Results take too long to come back
- Often contraindicated / delayed by imaging

LP Technique

- Opening Pressure
- Cell count / microscopy
- Protein
- Glucose
- Save sample



LP Technique

- Opening Pressure
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LP Technique

- Opening Pressure
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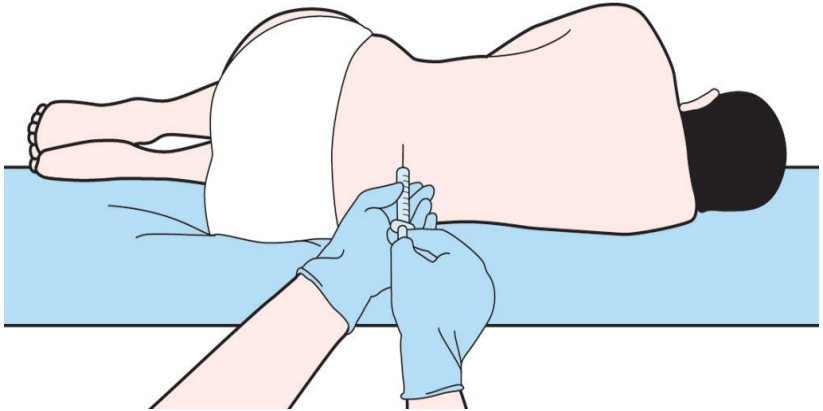

LP Technique

- Opening Pressure
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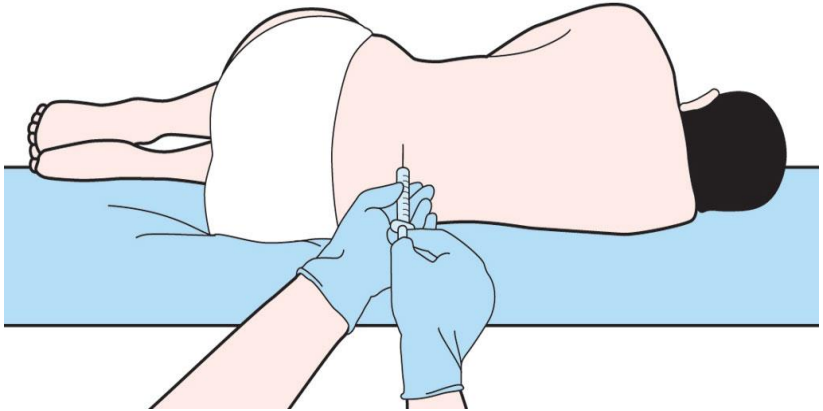

LP Technique

- Opening Pressure
- Cell count / microscopy
- Protein
- Glucose
- Save sample

Minimum data set for CSF analysis

Basic patterns

- **Pressure**
  - High in IIH
  - But also infections, CVST, cancer…
- **Cells**
  - WBC Usually raised in infections, [Neut = bacteria Lymph = viruses]
  - But also high with inflammations and cancers
- **Protein**
  - High in almost anything…
  - But sometimes a bit high in ‘normal’….
- **Glucose**
  - Low in bacterial infections,
  - But lower still in TB/Fungal/Cancer

LP - special tests

~~Special~~…. Hypothesis Driven

- Infection
  - Bacterial
  - Viral
  - Fungal/Other
- Inflammation
  - OCBs
  - Antibodies
- Oncology
  - Microscopy
  - Cytology
  - Flow cytometry
- Stroke(ish)
  - SAH
  - CVST

~~Special~~…. Hypothesis Driven

- Infection
  - Bacterial — MC+S (+/- PCR +/- 16S)
  - Viral — PCR
  - Fungal/Other — specific stains Eg India Ink, Auramine
- Inflammation
  - OCBs
  - Antibodies
- Oncology
  - Microscopy
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  - Flow cytometry
- Stroke(ish)
  - SAH
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Paired serum

LGI1 CASPR2 NMDAr GABA AMPA

CSF >> serum

~~Special~~…. Hypothesis Driven

- Infection
  - Bacterial
  - Viral
  - Fungal/Other
- Inflammation
  - OCBs
  - Antibodies
- Oncology
  - Microscopy
  - Cytology
  - Flow cytometry

} Large Volume 5-10mLs

- Stroke(ish)
  - SAH
  - CVST

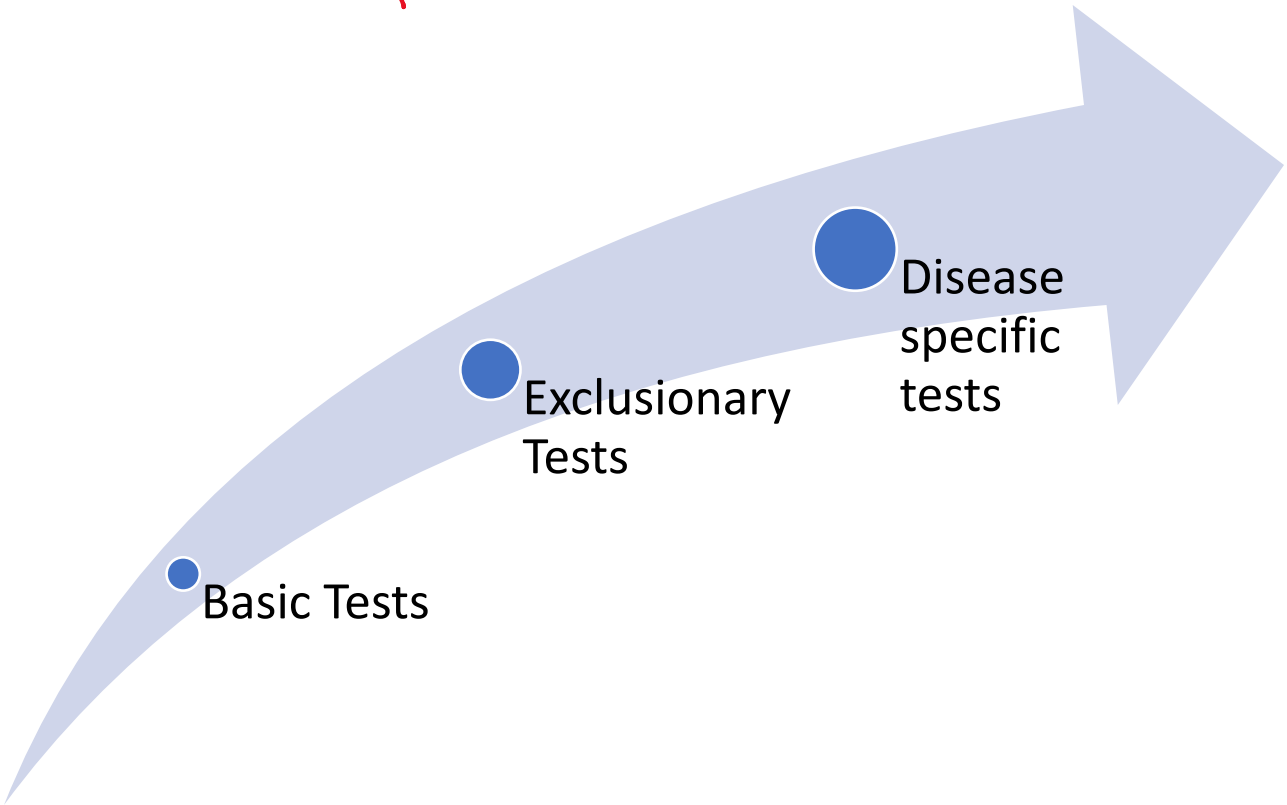
~~Special~~…. Hypothesis Driven

- Infection
  - Bacterial
  - Viral
  - Fungal/Other
- Inflammation
  - OCBs
  - Antibodies
- Oncology
  - Microscopy
  - Cytology
  - Flow cytometry
- Stroke(ish)
  - SAH → Xanthochromia
  - CVST

parainfectious?
pressure = clue?

Results non-specific and take too long..

~~Slow~~, ~~non-specific~~… Patience and hypotheses



Case Example

- 23 yr old female
- 1 month hx anxiety… becoming agitated
- Admitted to hospital… c/o headache, appears paranoid, has self terminating GTCS in ED
- Disorientated, obs normal, physical examination unremarkable, normal basic bloods…

Case Example

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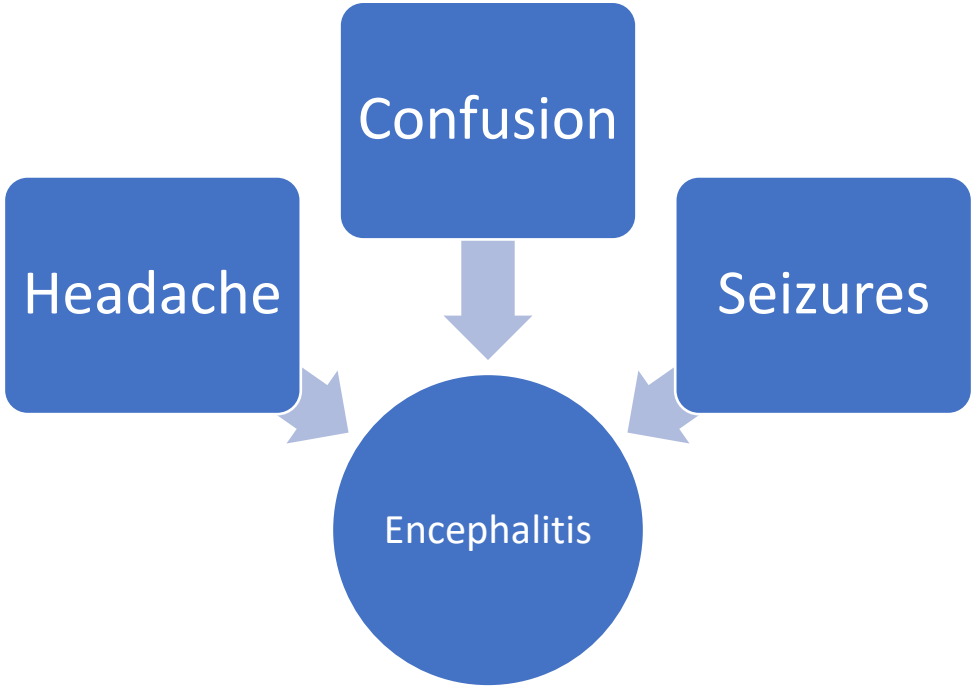

Confusion
Headache
Seizures
Encephalitis

The commonest causes

Viral

Immunocompetent

- Herpes simplex type I
- VZV

Immunocompromised

- HIV
- CMV, JC, other

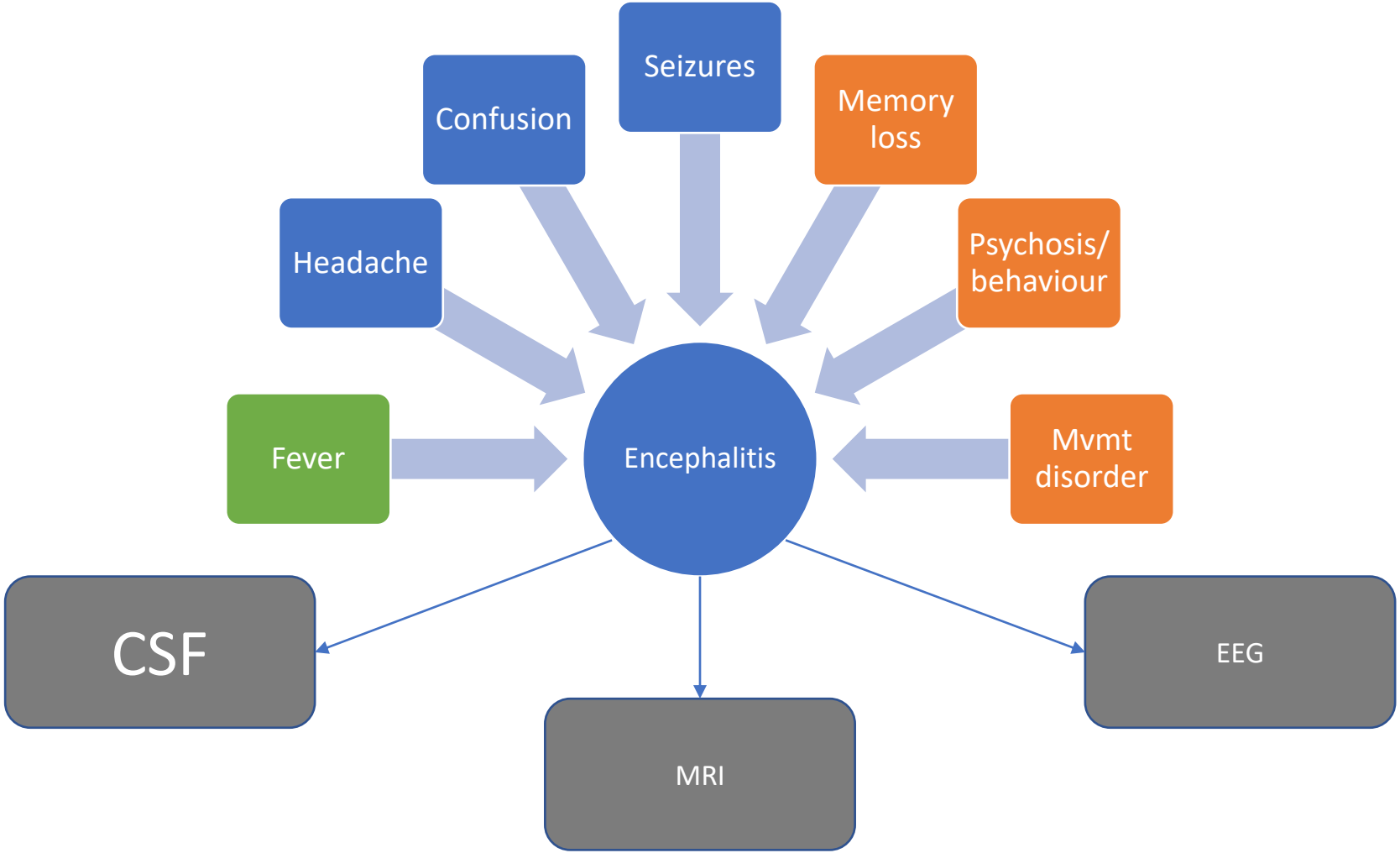
Antibodies

Directed against neuronal surface antigen

- LGI1, CASPR2, NMDA receptor
- GABA, AMPA

Intracellular antigen

- Hu, CV2, Ma1/2,
- GAD


Seizures
Confusion
Memory loss
Headache
Psychosis/ behaviour
Fever
Encephalitis
Mvmt disorder
CSF
MRI
EEG

Case Example

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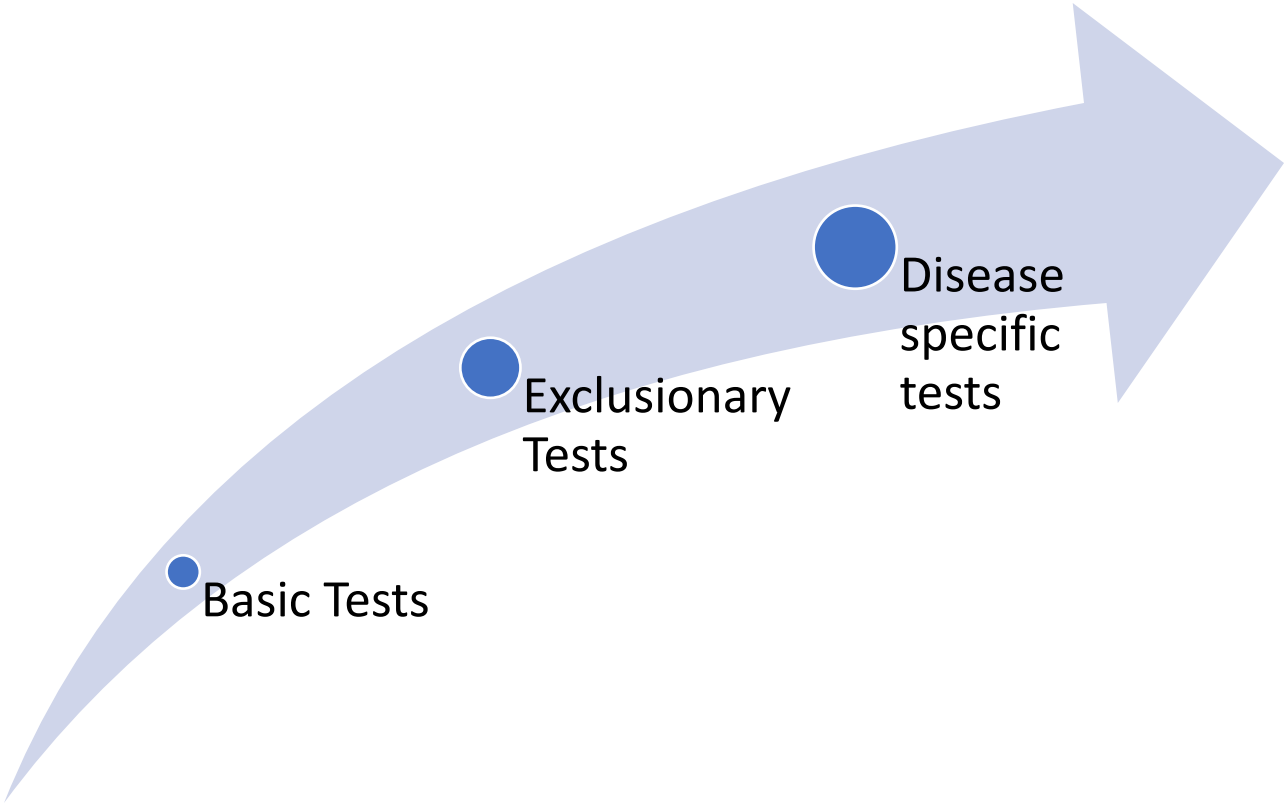
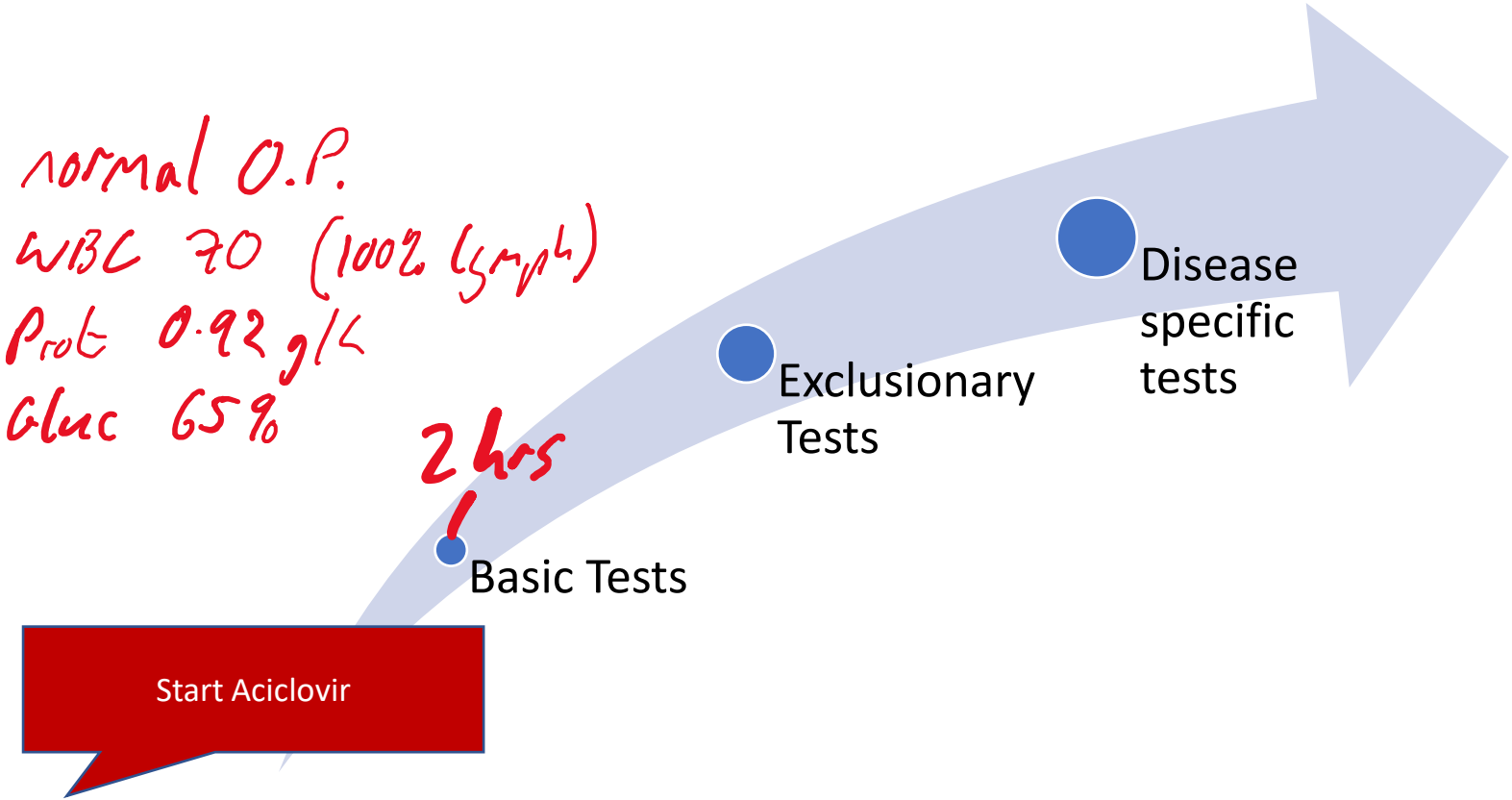
Patience and hypotheses

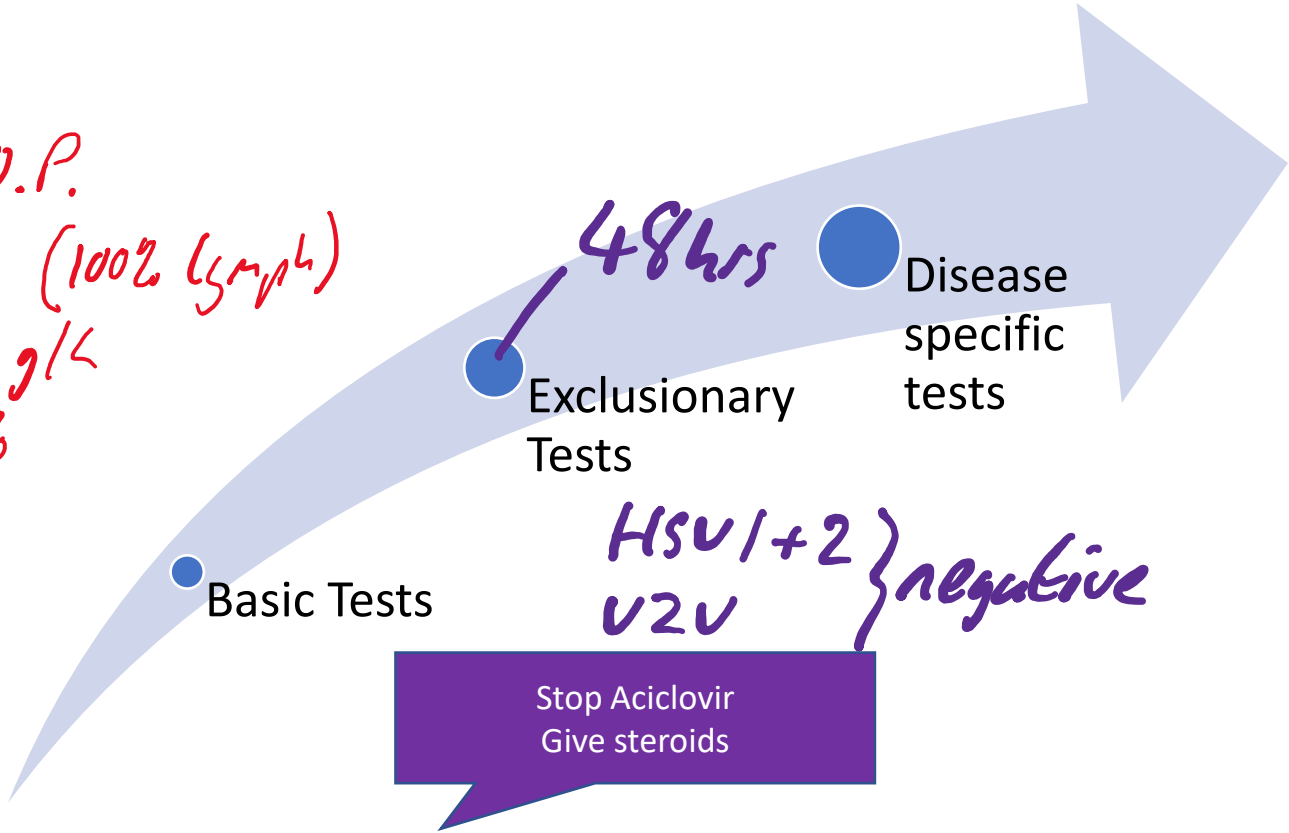


Patience and hypotheses

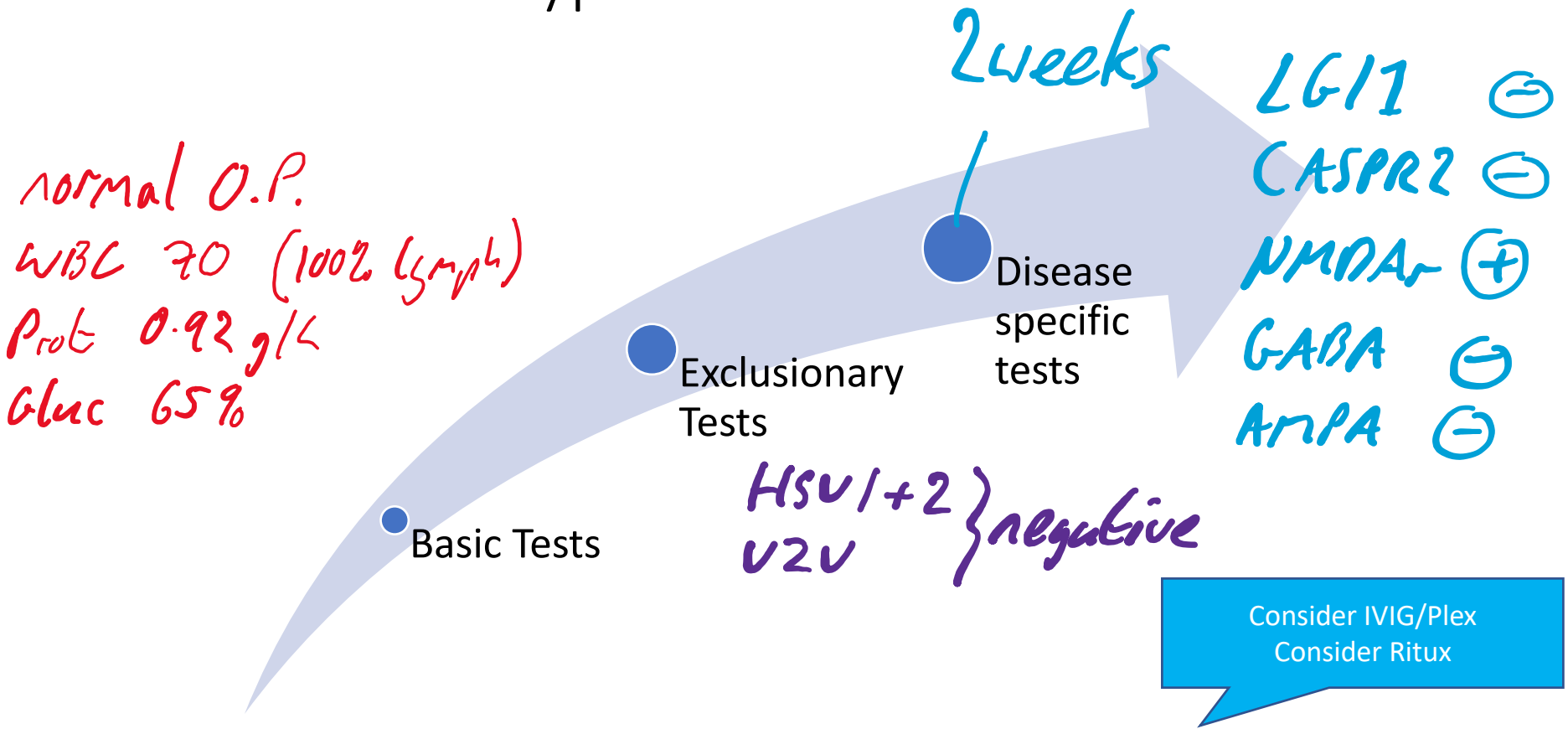


Patience and hypotheses

normal O.P.
WBC 70 (100% lymph)
Prot 0.92 g/L
Gluc 65%



Patience and hypotheses



LP can’t be done…

Do you need imaging before a lumbar puncture?

Usually not…

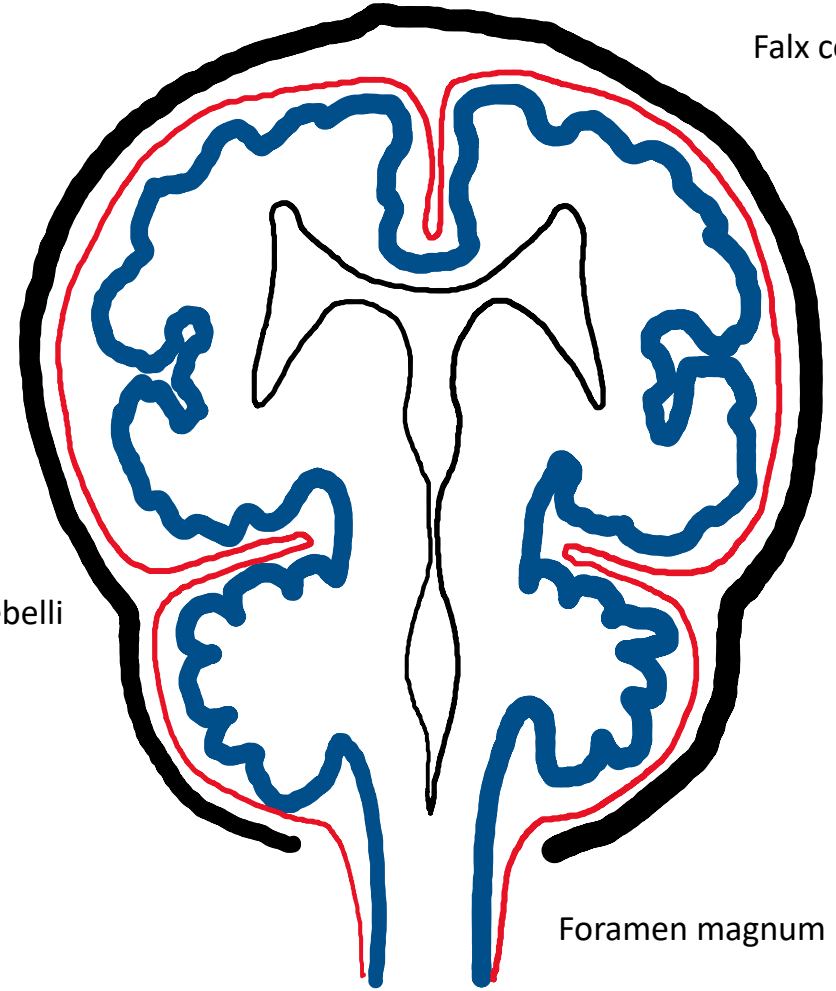
LP first line test

- Meningitis
- Encephalitis

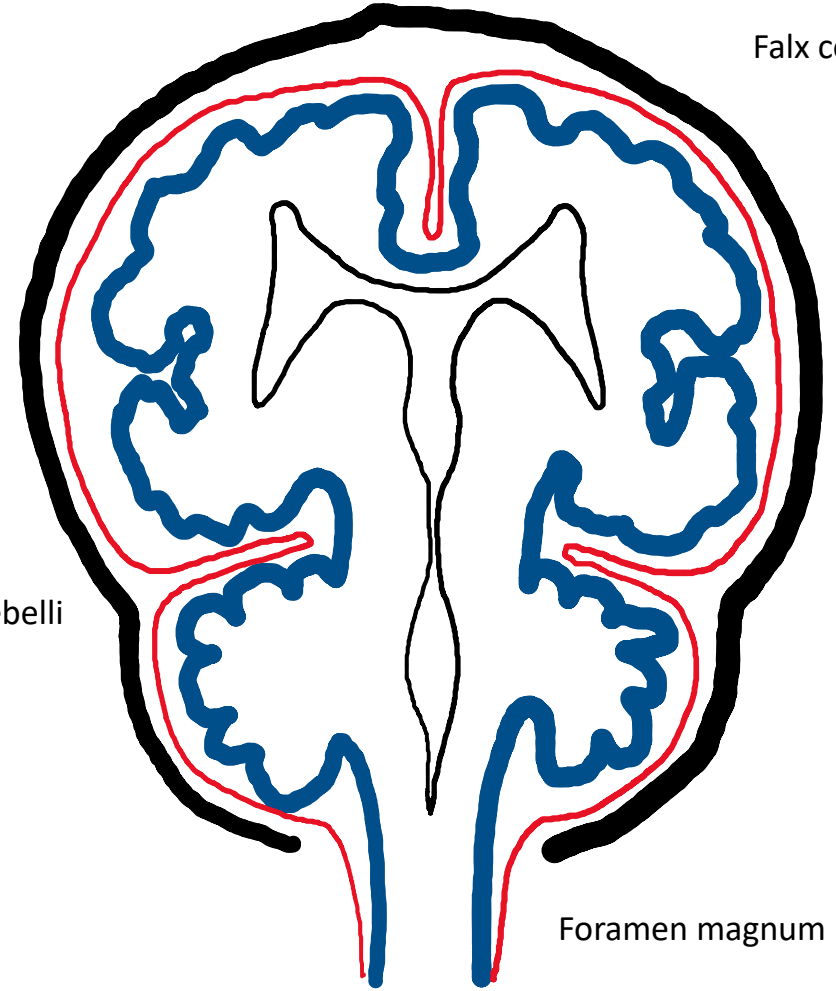
LP not really first line…

- SAH
- Multiple Sclerosis/NMO
- Sarcoid/Lupus/Sjogren’s
- CNS vasculitis

Is raised ICP a contraindication to lumbar puncture?


Falx cerebri
Tentorium cerebelli
Foramen magnum

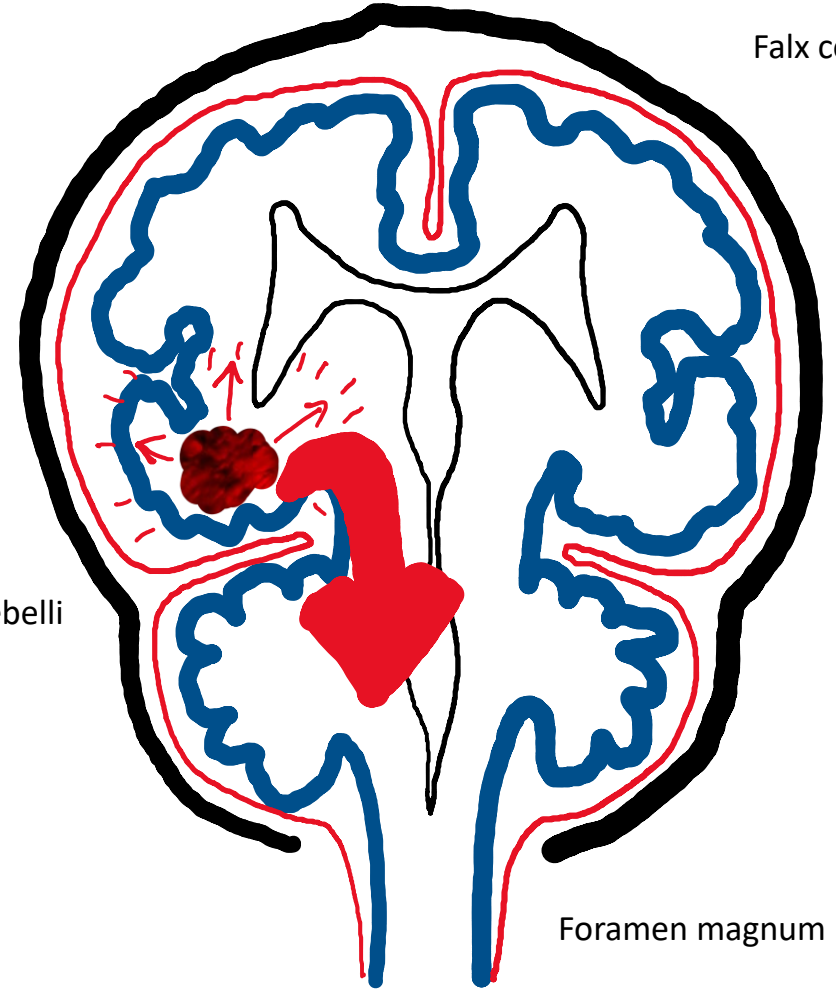
Falx cerebri



Tentorium cerebelli

Foramen magnum

?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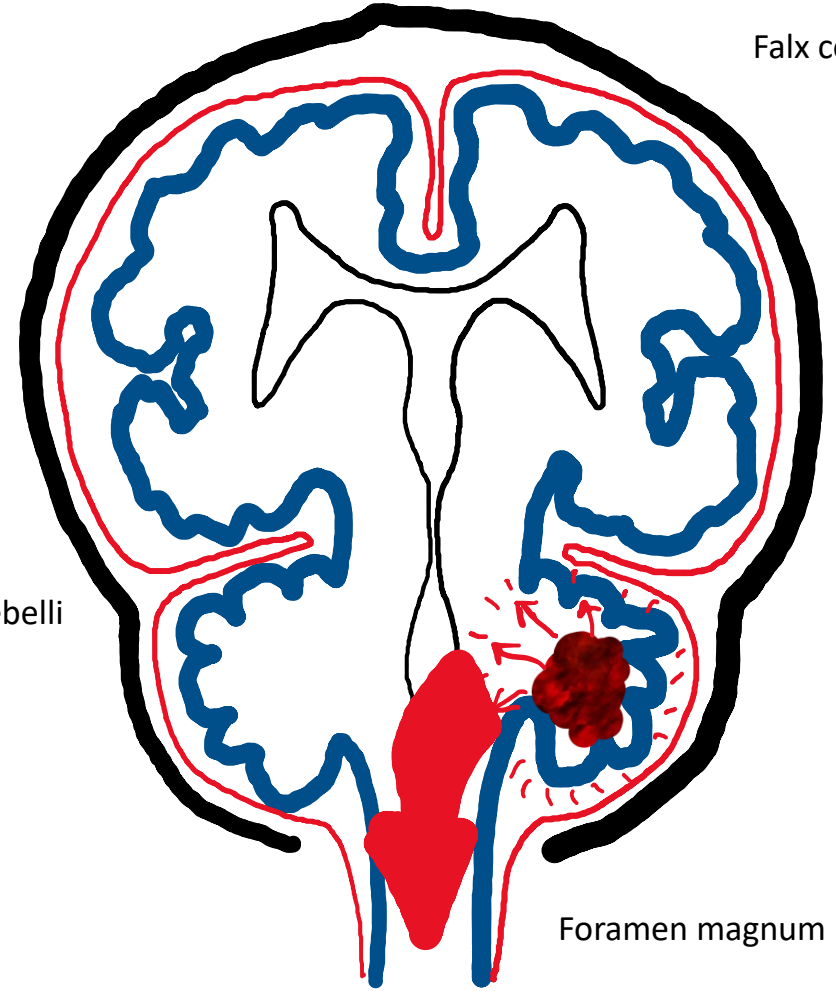
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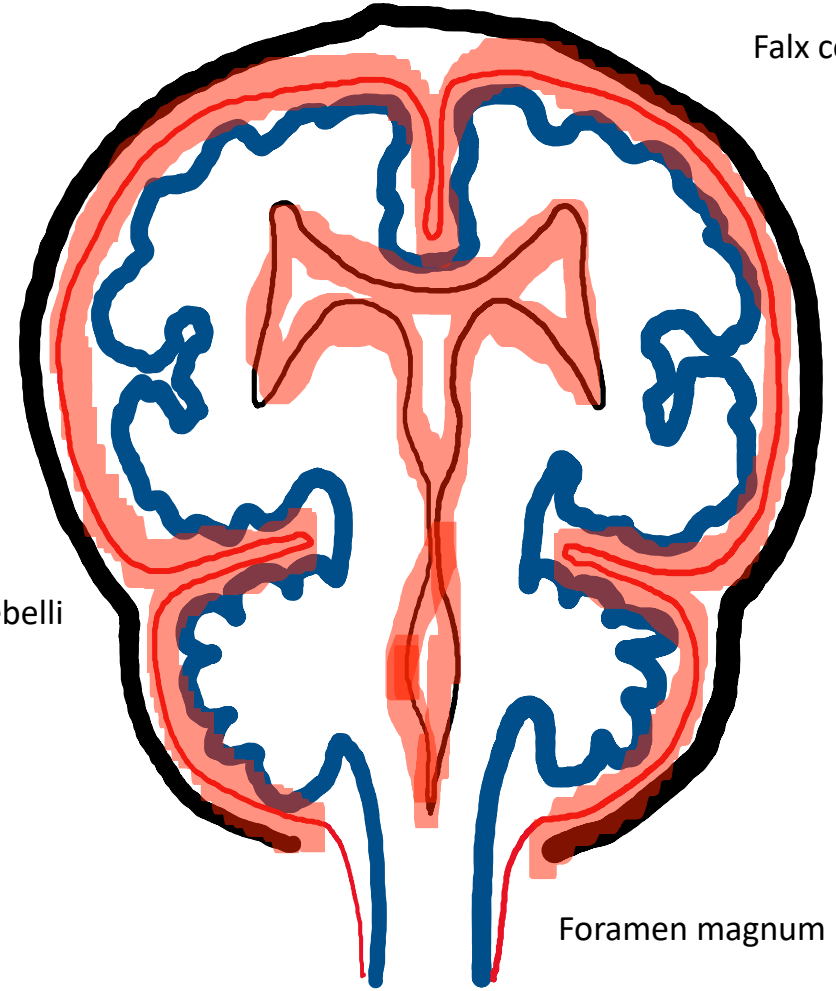
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Foramen magnum

When to delay LP…

Delay LP

if any of the following are present:

- **Signs of severe sepsis or rapidly evolving rash**
- **SEVERE respiratory/ cardiac compromise**
- **Significant bleeding risk**
- **Signs suggesting shift of brain compartments (CT scan before LP is warranted, as long as patient is stable)**
  - **Focal neurological signs**
  - **Presence of papilloedema**
  - **Continuous or uncontrolled seizures**
  - **GCS ≤12**

Dodd et al. Practical Neurology 2018; 0. 1-11

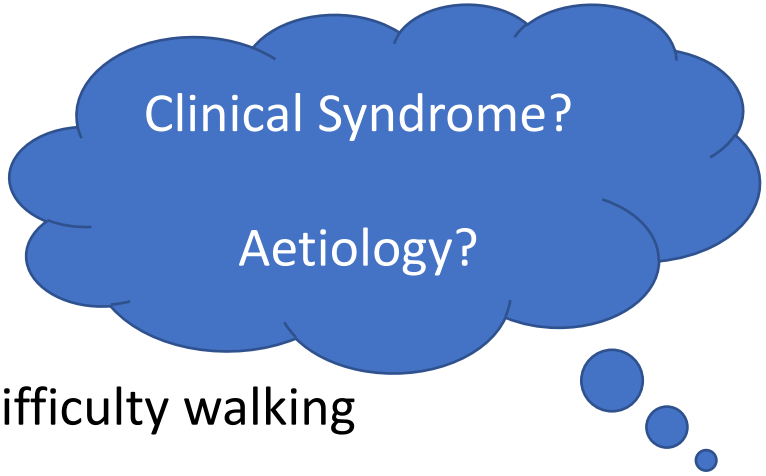
These are the 'risk signs' for raised ICP / brain SOL

The UK Joint Specialist Societies Guideline on the Diagnosis and Management of Acute Meningitis and Meningococcal Sepsis in Immunocompetent Adults.

Another case…

- 43 yr old male admitted with 1 week of difficulty walking
- Legs feel weak, tingling feet, poor balance… fingertips numb today
- O/E
  - normal CN,
  - reduced reflexes in UL,
  - LL: Flaccid tone, weak, areflexic, pl down, stocking PP and vibr loss

Another case…



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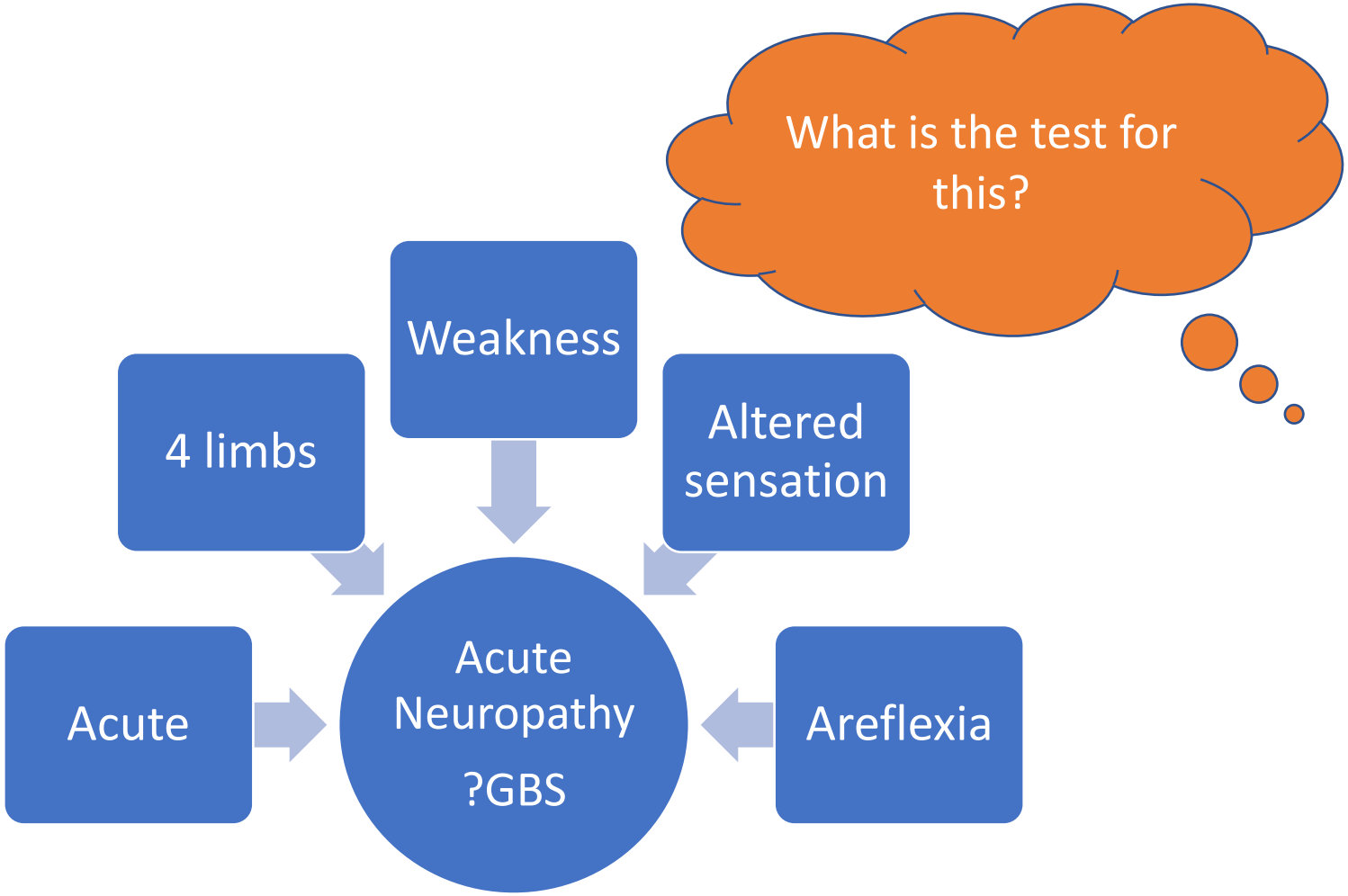

What is the test for this?
Weakness
4 limbs
Altered sensation
Acute
Acute Neuropathy
?GBS
Areflexia

CSF in GBS

The Basics	**The why…?**
• Opening Pressure	• Should be normal
• Cells	• Should be normal
• Protein	• Should be **high**
• Glucose	• Should be normal

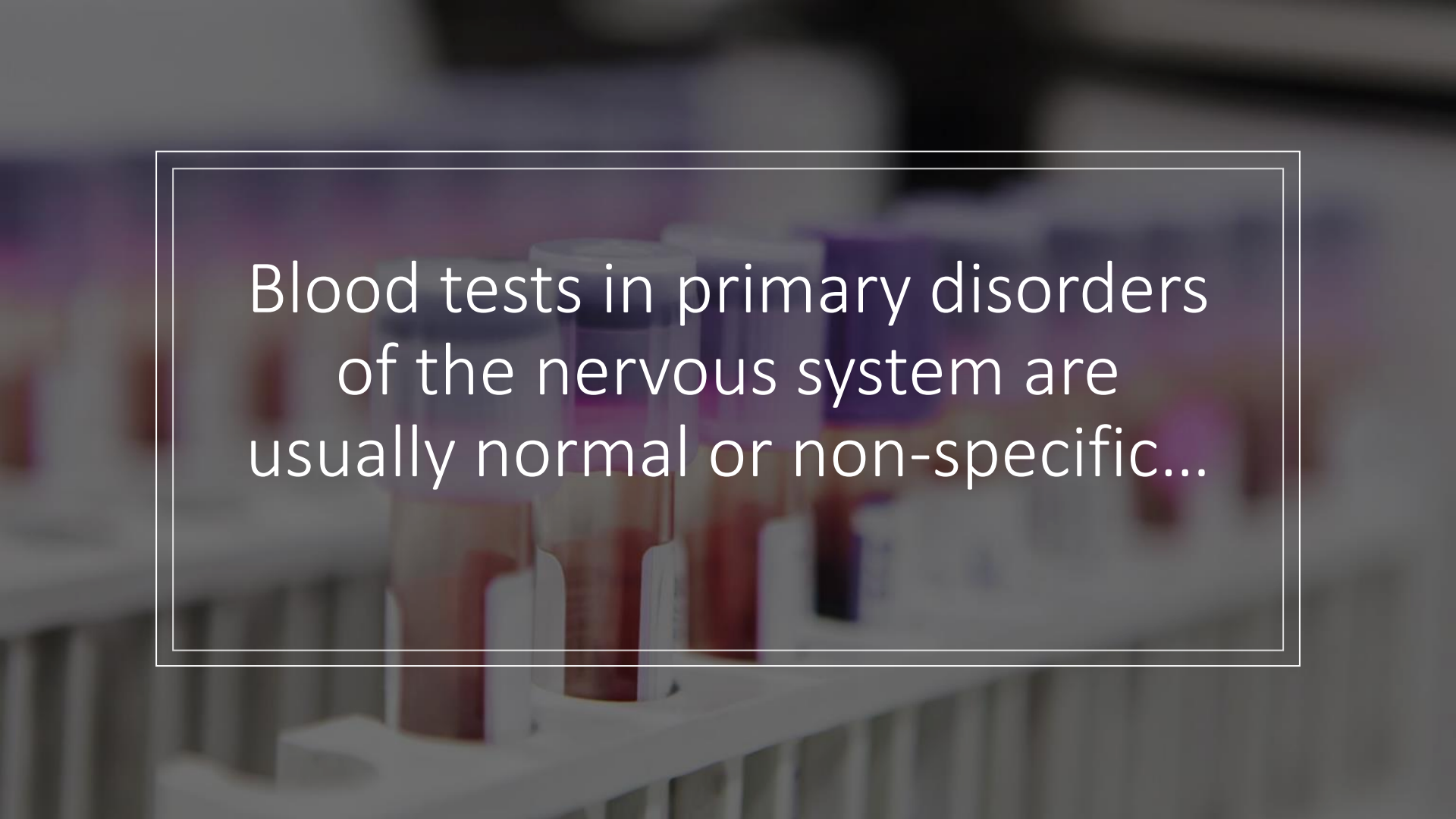
CSF in GBS

The Basics	**The why…?**
• Opening Pressure	• Should be normal
• Cells	• ~~Should be normal~~ WBC 118 80% Lymph
• Protein	• Should be **high**
• Glucose	• Should be normal

CSF in GBS

The Basics	**The why…?**
• Opening Pressure	• Should be normal
• Cells	• Should be normal
• Protein	• Should be ~~high~~ 0·42 g/L
• Glucose	• Should be normal


Blood tests…


Blood tests in primary disorders of the nervous system are usually normal or non-specific…

Notable mentions…

- Patients who are weak
  - CK
- Patients who are confused
  - Ammonia
- Patients with epilepsy
  - Don’t usually need drug levels
- Patients with sensory ataxia
  - B12 and Copper
- Patients with CNS infection
  - Often have normal ESR / CRP
- Patients about to have IVIG/PlEx
  - Need a serum save sample

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Not all ↑CK = muscle

Notable mentions…

- Patients who are weak
  - CK

Not all ↑ Amm = Liver

- Patients who are confused
  - Ammonia

Not all Liver = ↑ Amm

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Phenytoin ** Esp in Status Epilepticus...

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Remember functional B12 def.
Homocysteine + MMA
Same syndrome as B12 def

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- Patients about to have IVIG/PlEx
  - Need a serum save sample [+CSF]

Not

•

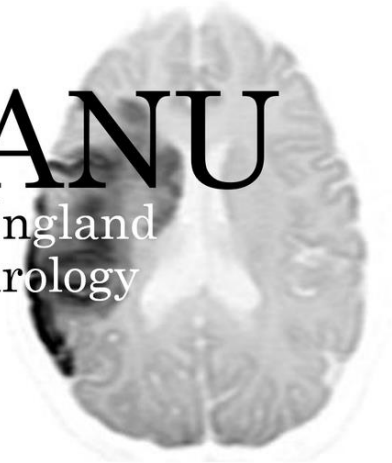
Its almost always worth checking HIV and syphilis…

CNS infection, GBS, Inflamm disease, Encephalopathy

• Pat about to have IVIG/PlEx

• sually need drug leve ed a serum save sample

NEANU
North of England
Acute Neurology
Update



Thanks and Questions?

@chriskobylecki

@NeuroPBL

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The University of Manchester

Manchester Centre for Clinical Neurosciences