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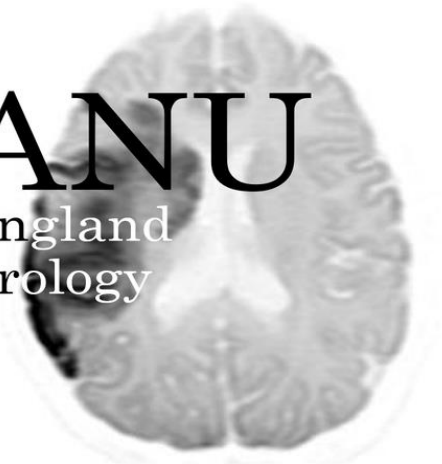
Acute Neurology
Update



Beyond GBS

Dr Tim Lavin

Team Nerve

MANCHESTER 1824
The University of Manchester

Manchester Centre for Clinical Neurosciences

Salford Royal NHS Foundation Trust

Learning Outcomes

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Acute Neurology
Update

- What actually is GBS- Recap
- 3 case vignettes
  - Why is this not GBS?
  - What should our differential be for acute/subacute neuropathies?
  - What are the important treatable disorders not to miss
- Not bore anyone too much with obscure neurophysiology

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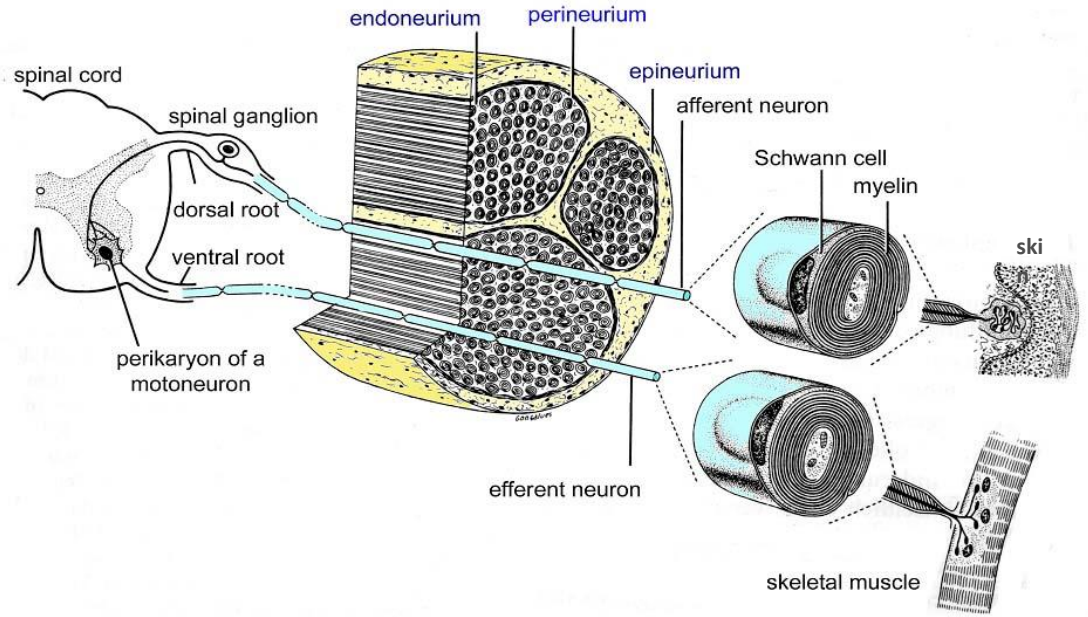
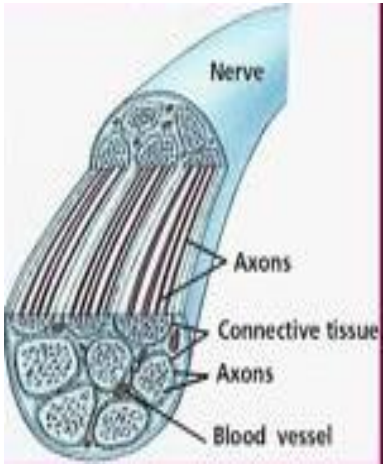
Anatomy of a normal nerve



The peripheral nerve - anatomy

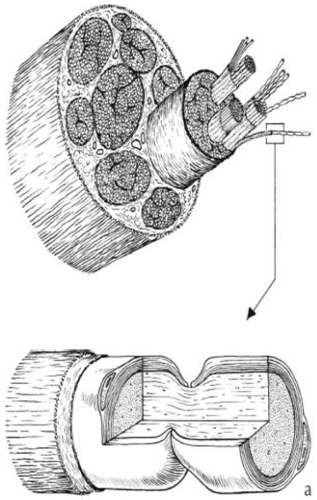


Myelinated axons

Motor
Proprioception

Unmyelinated axons

Pain
Temperature



Case 1- 33yr old

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- Viral illness 2 weeks prior- generally unwell
- Woke 2 days ago with new onset back pain- felt muscular- radiating down her legs, then neck pain
- 1 day ago felt unbalanced- especially in shower, started looking at her feet when walking
- Today- legs buckling when walking
- Clumsy hands, can't use her phone
- Speech feels different
- Normal vision, bowel/bladder function

General: Nil

Cranials: bilateral facial weakness

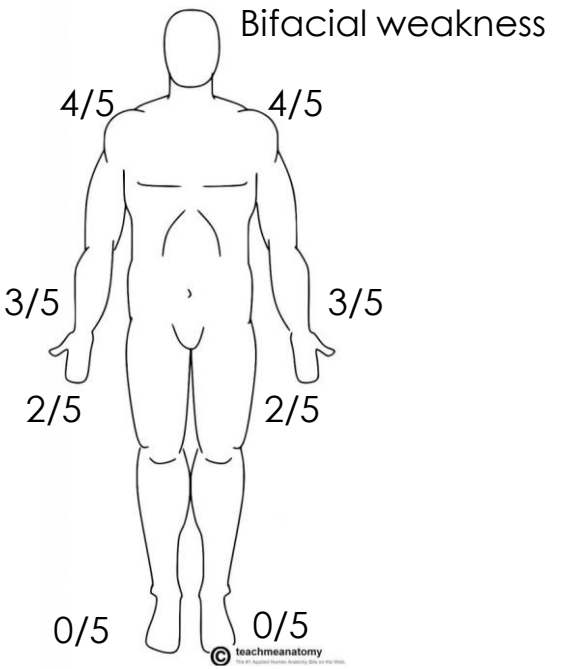
Reflexes: Areflexic

Sensory:

JPS to knee

Vibration to costal margin

PP lost on soles of feet



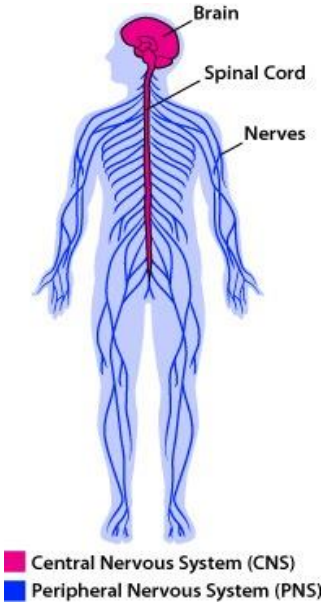
CSF Protein is 1.5g

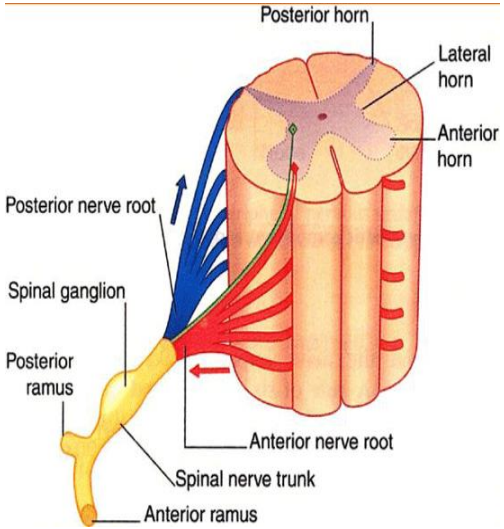
CSF WCC less than 1

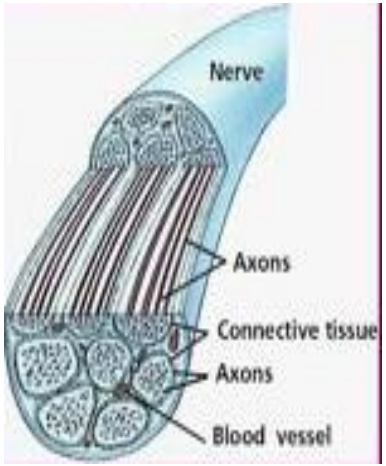
Normal Plasma:CSF Glucose ratio

NCS: performed day 8 – demyelinating neuropathy

Acute Inflammatory Demyelinating Polyradiculoneuropathy







Typical GBS
Acute Demyelinating Polyradiculoneuropathy

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Update

Received: 13 July 2023 | Revised: 25 August 2023 | Accepted: 28 August 2023

DOI: 10.1111/jns.12594

REVIEW

European Academy of Neurology/Peripheral Nerve Society Guideline on diagnosis and treatment of Guillain–Barré syndrome

Typical GBS
Acute Inflammatory Demyelinating Polyradiculoneuropathy

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- **Required**
  - Progressive weakness of arms and legs
  - Absent or decreased deep tendon reflexes in affected limbs
  - Progressive worsening for no more than 4 weeks

- **Supportive**
  - Relative symmetry
  - Relatively mild/absent sensory symptoms and signs
  - Cranial nerve involvement (especially **bilateral facial palsy**)
  - Autonomic dysfunction
  - Respiratory insufficiency (due to muscle weakness)
  - Pain (muscular/radicular in back or limb)
  - Recent history of infection

Typical GBS
Acute Inflammatory Demyelinating Polyradiculoneuropathy

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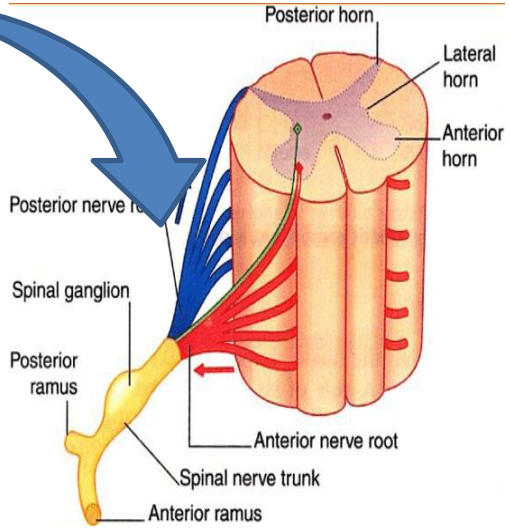
- CSF:
  - Albuminocytological dissociation (high protein)
  - Normal protein does not rule out diagnosis
  - White cells usually <5x10^6/L

High CSF Protein related to proximal disease



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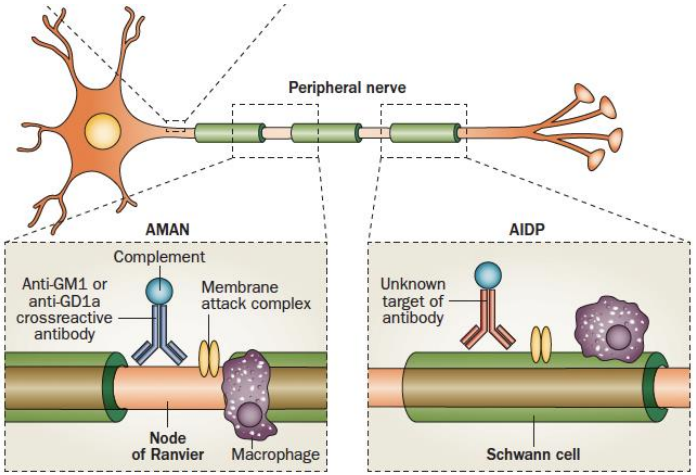


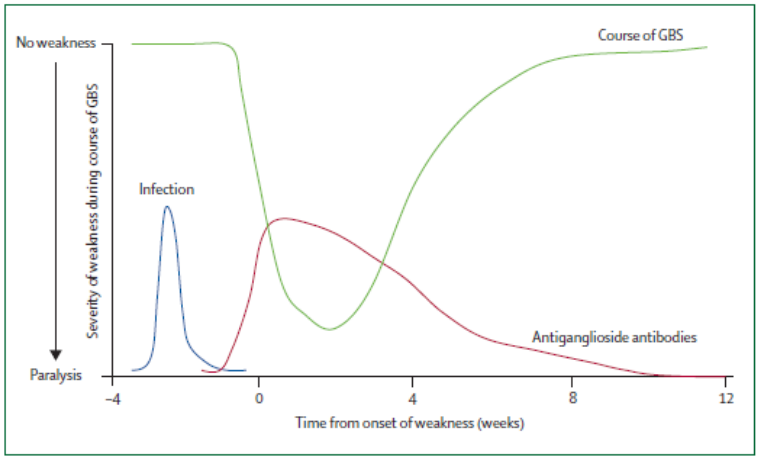
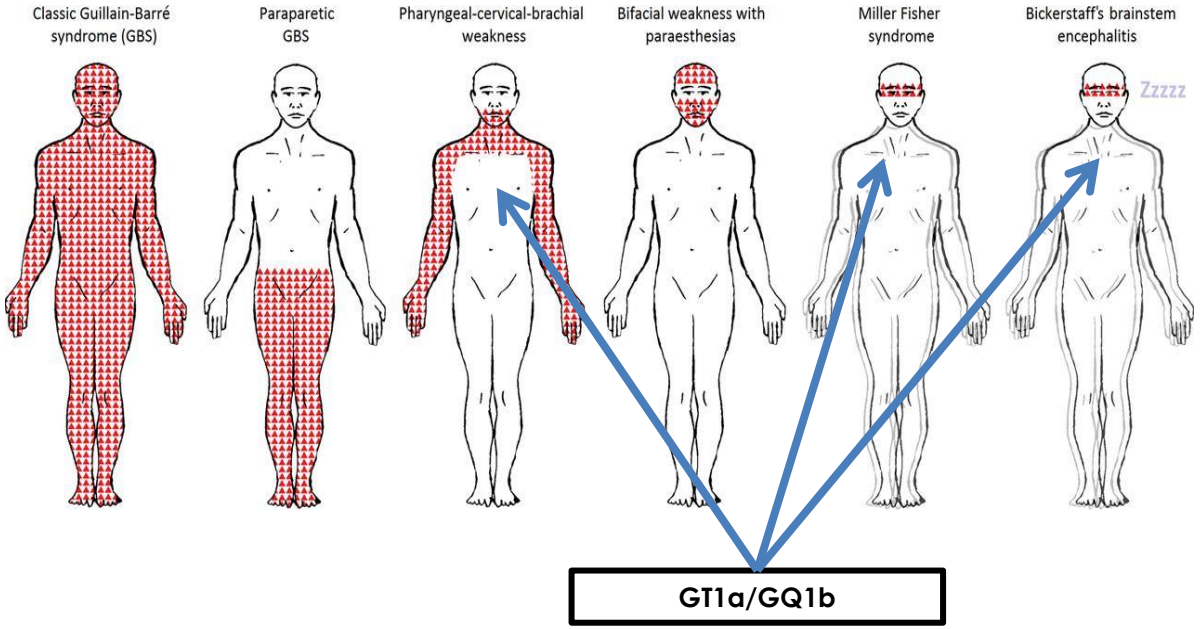


Figure 1: Relation between infections, antiganglioside antibodies, and clinical course of GBS

Post infective, (Probably Ganglioside) antibody mediated, segmental demyelination (internodal)

Patterns of weakness in Guillain-Barré syndrome (GBS) and Miller Fisher syndrome and their subtypes.



Benjamin R Wakerley, and Nobuhiro Yuki Pract Neurol 2015;15:90-99

PN

Store a sample

Lets mix it up

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CSF Protein is 1.5g

CSF WCC 35- predominantly lymphocytes

Normal Glucose ratio

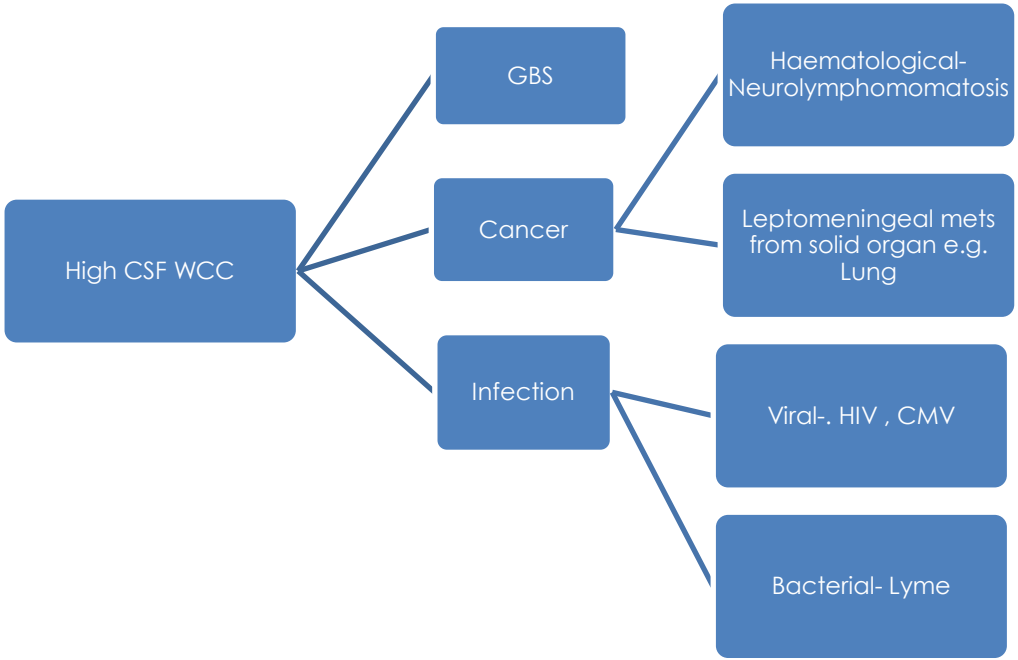
NCS: performed day 8 – demyelinating neuropathy

SO NOT GBS?

Al-Hakem, Helle et al. "CSF Findings in Relation to Clinical Characteristics, Subtype, and Disease Course in Patients With Guillain-Barré Syndrome." Neurology vol. 100,23 (2023)

846 patients with GBS

16% had 5-50 WCC in CSF



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Update

Asymmetric weakness (marked and persistent)
Severe respiratory dysfunction at onset with mild limb weakness
Predominant sensory signs at onset (paraesthesias often occur) with mild weakness
Fever or other prominent systemic features at onset
Sensory level, or extensor plantar responses
Hyperreflexia (initial hyper-reflexia does not exclude GBS)
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Nystagmus
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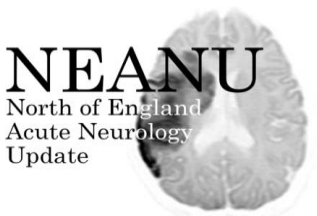

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- Abnormal routine blood tests
  - Significant abnormal inflammatory markers
  - Unexplained renal dysfunction
  - FBC suggestive of Marrow dysfunction/plasma cell dyscrasia

- CSF: >50 x10^6 - less than 1% of GBS cases in IGOS cohort

GBS Insufficiency Score

Retrospective study 377 patients

- Overall 23% ventilated.
  - 20% in the first week
  - Further 3% thereafter

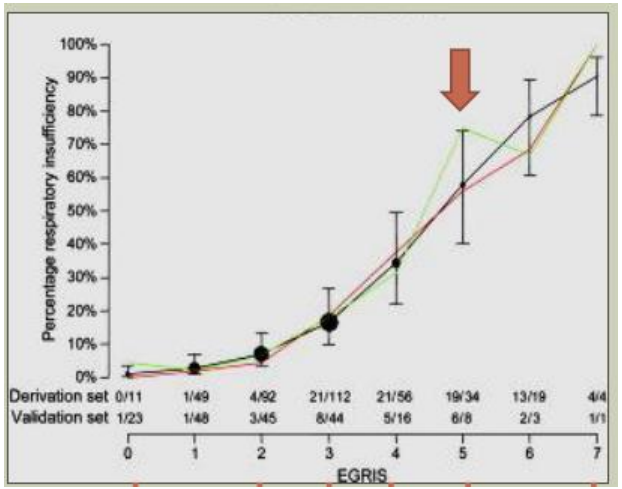
- EGRIS
  - Days between onset of weakness and hospital admission (usually coinciding with loss of ambulation).
  - Facial and or bulbar weakness.
  - MRC sum score

Measure	Categories	Score
Days between onset of weakness and hospital admission	>7 days	0
	4–7 days	1
	≤3 days	2
Facial and/or bulbar weakness at hospital admission	Absence	0
	Presence	1
MRC sum score at hospital admission	60–51	0
	50–41	1
	40–31	2
	30–21	3
	≤20	4
EGRIS		0–7

EGRIS = Erasmus GBS Respiratory Insufficiency Score; MRC = Medical Research Counsel.

GBS RESPIRATORY INSUFFICIENCY SCORE
Walgaard C et al Ann Neurol. 201 Jun;67(6):781-7

EGRIS



- 0-2 low risk- 5%
- 3-5 intermediate risk <33%
- 5-7 high risk 60-90% risk

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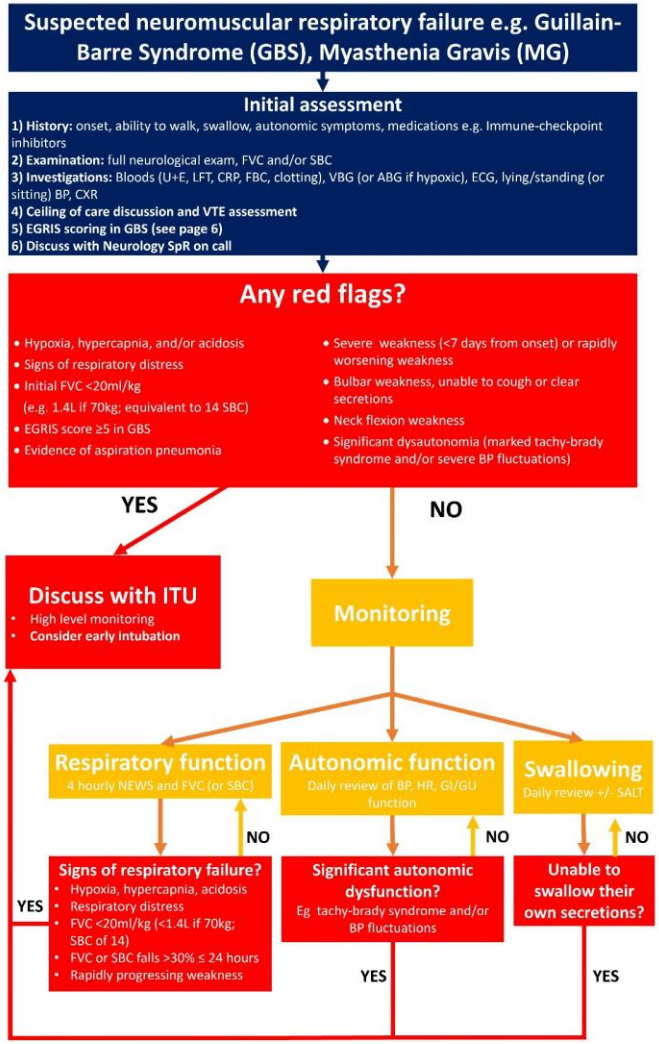

Case 2

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- 3 week hx
  - Severe cramps on R leg and then burning/allodynia pain of the foot
  - 3 days later same symptoms affect the left leg
  - Clumsy left hand, using a fork and key more difficult.
  - Left leg then began buckling beneath him- progressed to being unable to walk
  - Ankle swelling
  - Rash affecting legs
- Denies anorexia or significant weight loss, night sweats
- No visual/sphincter/autonomic/craniobulbar dysfunction

Examination

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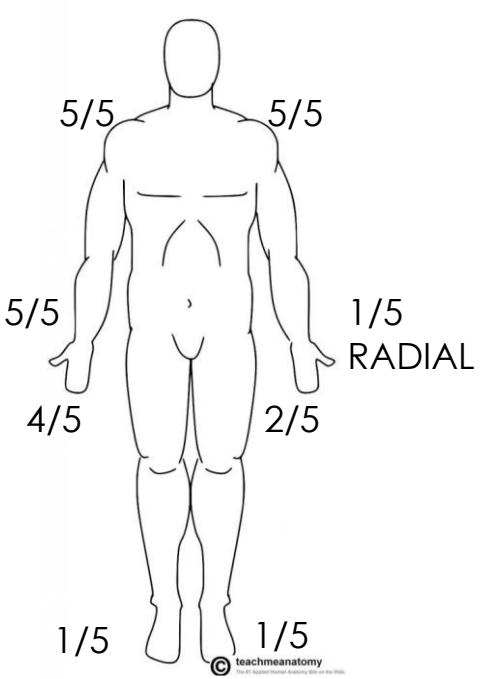
GENERAL: Pedal Oedema

CRANIALS
- Normal

REFLEXES
UL ++
LL reflexes knee +, ankles absent

SENSORY
- PP to ankle bilateral
- Vib to ASIS on left and ankle on R
- JPS to ankle on left and MTP on R



Initial Results

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- CRP 105
- ESR 73

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  - **Significant abnormal inflammatory markers**
  - Unexplained renal dysfunction
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- CSF: >50 x10^6 - less than 1% of GBS cases in IGOS cohort

Further Investigations

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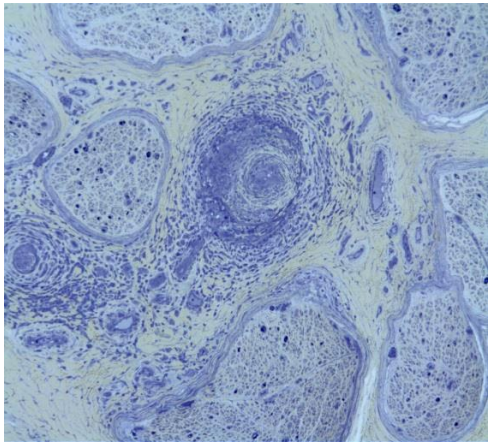
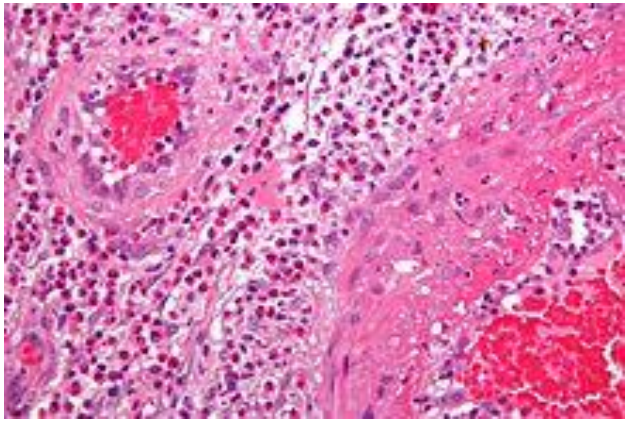
- NCS: Multiple Mononeuropathies
- Nerve Biopsy





Vasculitic Neuropathy

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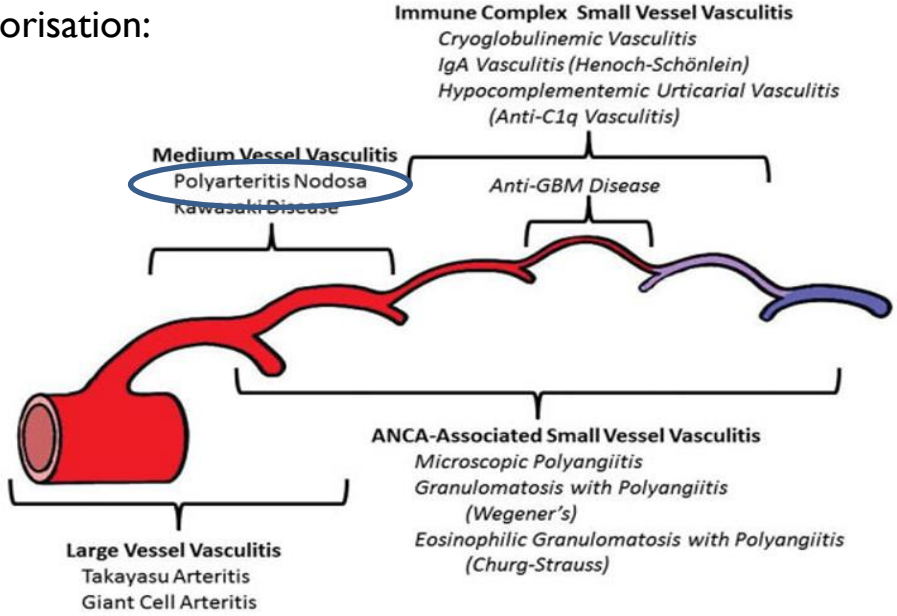
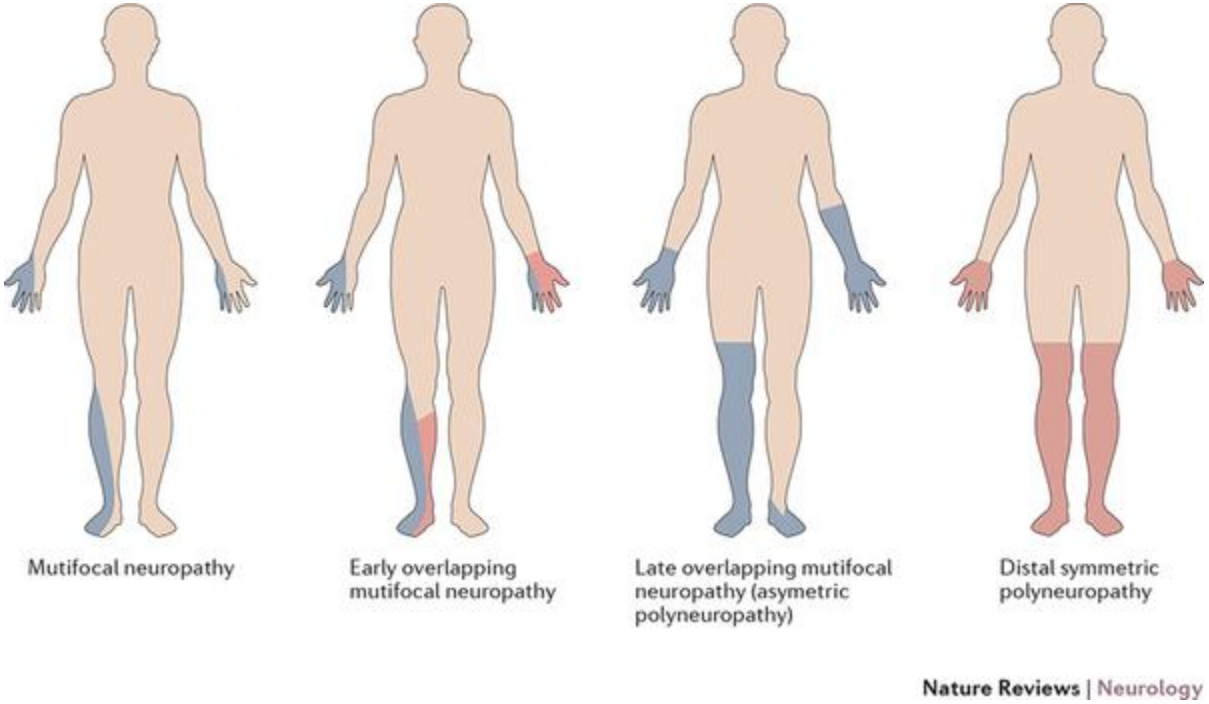
- Definition
- Categorisation:



Vasculitides are a diverse group of conditions with the histopathological signature of blood-vessel centred inflammation that results in vascular damage and ischaemic injury in affected tissues.

Patterns of Nerve Involvement



- Classically presentation is **multiple mononeuropathies**
- Painful (but not always)
- Non localising to entrapment or nerve root

Multisystem Disorder

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- 23 yr old
- Paracetamol OD- acute liver injury and renal dysfunction
- Liver function improved
- Then developed Rash
- Then weakness of her left foot, right hand and then left hand associated with marked pain.
- NCS: multiple mononeuropathies

- Urine Prot-Cr ratio: 315mg/mmol
- Renal Biopsy: IgA Nephropathy

Vasculitic Neuropathy

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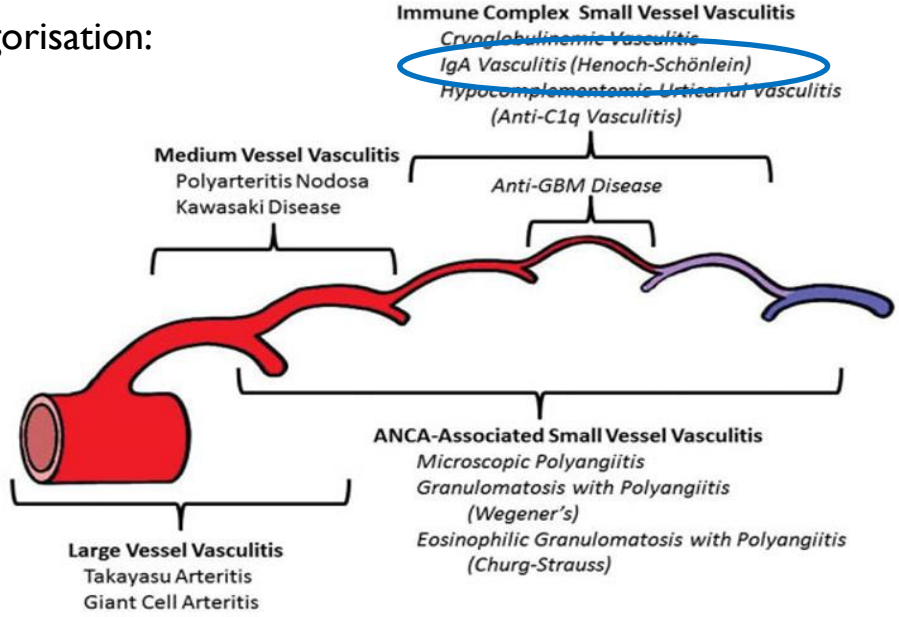
- Categorisation:



Case 3

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- Jan 2018:
  - Left leg weakness over 2 weeks
  - Rapid deterioration over 5 days
  - L arm → R arm → R leg weakness
- Dysphagia
- L eye dropping and diplopia
- Bladder and bowels intact.
- Systemically well

Case 3- Beyond GBS

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Cranials

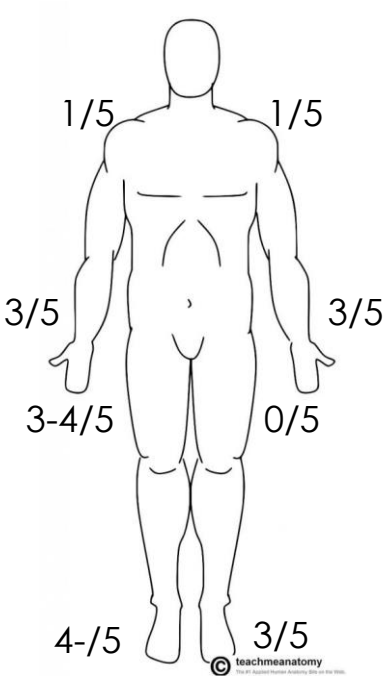
- L partial IIIrd nerve palsy (pupil sparing)
- Bilateral facial weakness
- Normal speech

Reflexes

- Areflexic
- Plantars mute

Sensory

  - ↓ pinprick (patchy) all 4 limbs
  - Vibration to shins
  - Proprioception ↓ L leg.



Initial investigations

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Test	Result
FBC, U&E, LFT, Bone profile, CRP	Normal
TFTs, B12/folate	Normal
ESR	22
HIV, syphilis, Hep B/C	Negative
Lyme serology	Negative
Antiganglioside antibodies	GM1 684 (<500), GM2 718 (<500)
ANA	1:800, Homogenous staining
Paraneoplastic antibodies	Negative
Anti-MAG	Negative
CSF 9/6/18 (day 12 admission)	WCC <1, RBC 4, Prot 0.51, Glu 3.6 (paired 6.1), Cytology NAD
Electrophoresis	Monoclonal IgG λ 4.9 g/L
MR head and spine + contrast	Mild degenerative C4/5 changes. No enhancement.
CT TAP	Pulmonary atelectasis, no lesions. Normal bony structures.

Investigations

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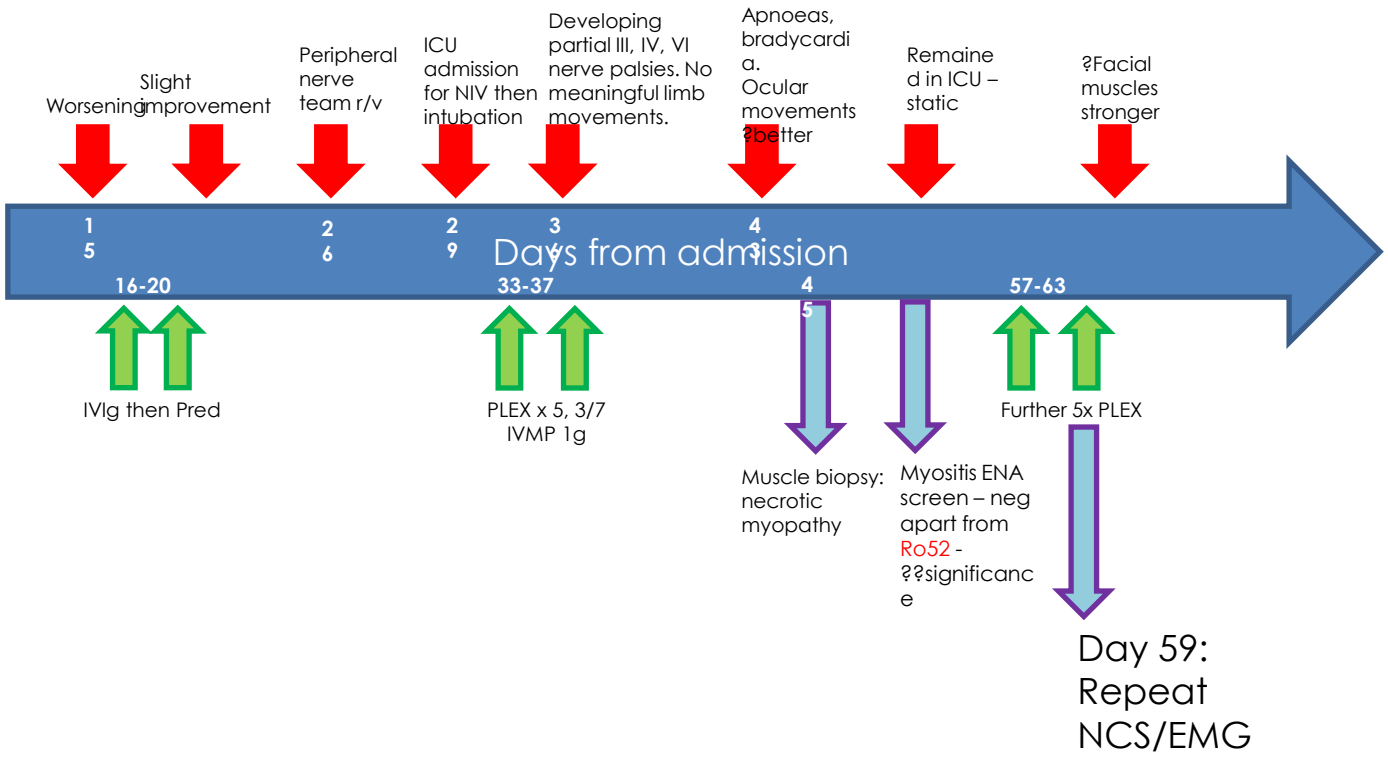
- NCS: Primary Demyelinating- consistent with GBS
- Positive GM abs?

Home and Dry?

Progress and treatment



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Is this GBS

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- No
- Pan-Neurofascin Nodopathy
- OBVS

Nodal/paranodal autoantibodies

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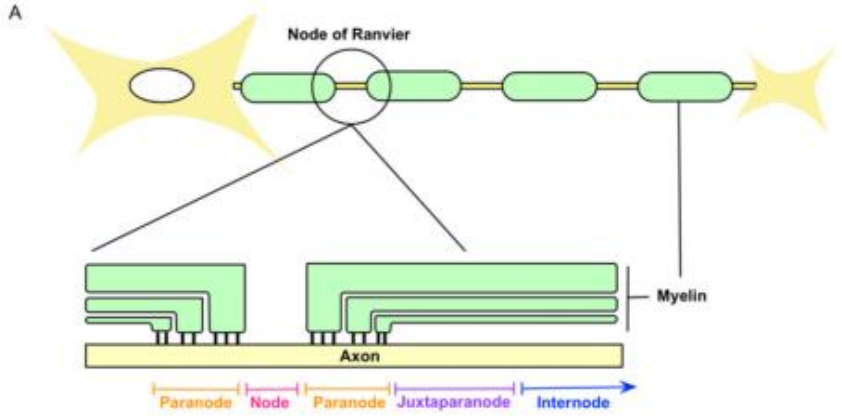
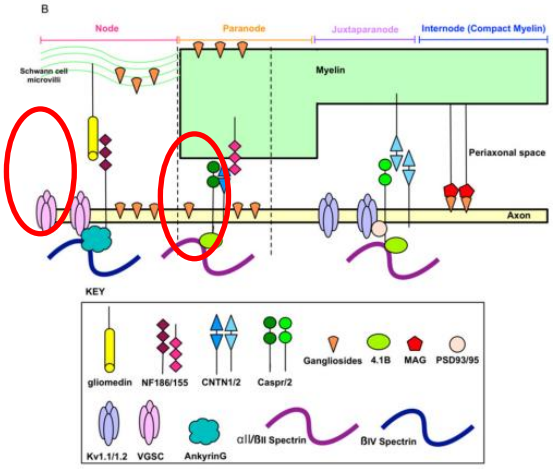
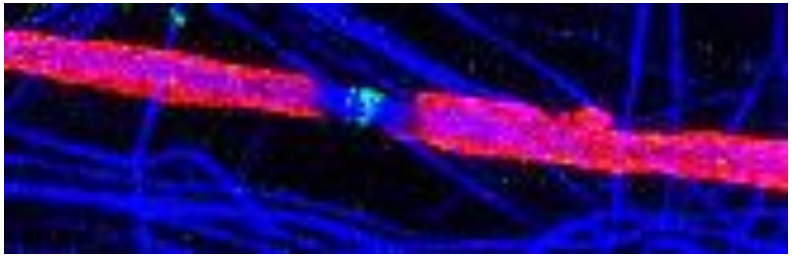






Neuromuscular

OPEN ACCESS

Original research

IgG_1 pan-neurofascin antibodies identify a severe yet treatable neuropathy with a high mortality

Janev Fehmi ,[1] Alexander J Davies,[1] Jon Walters,[2] Timothy Lavin,[3] Ryan Keh,[3] Alexander M Rossor,[4] Tudor Munteanu,[5] Norman Delanty,[5] Rhys Roberts,[6] Dirk Bäumer,[6] Graham Lennox,[7] Simon Rinaldi [1,8]

Anti–pan-neurofascin IgG3 as a marker of fulminant autoimmune neuropathy

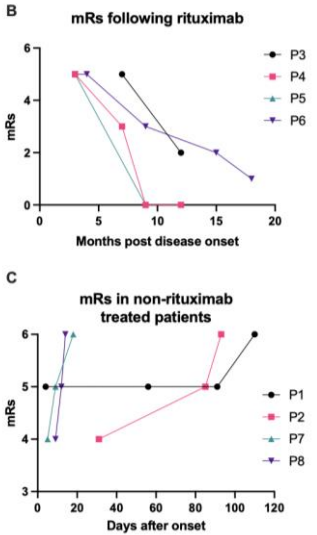
Helena Stengel, Atay Vural, MD, PhD, Anna-Michelle Brunder, Annika Heinius, Luise Appeltshauser, MD, Bianca Fiebig, Florian Giese, MD, Christian Dresel, MD, Aikaterini Papagianni, MD, Frank Birklein, MD, PhD, Joachim Weis, MD, Tessa Huchtemann, MD, Christian Schmidt, MD, Peter Körtvelyessy, MD, Carmen Villmann, PhD, Edgar Meinl, MD, Claudia Sommer, MD, PhD, Frank Leypoldt, MD,* and Kathrin Doppler, MD*

Correspondence
Dr. Doppler
Doppler_K@ukw.de

Neurol Neuroimmunol Neuroinflamm 2019;6:e603. doi:10.1212/NXI.0000000000000603

- **Severe and rapidly progressive**
- Quadriparesis
- Cranial neuropathies
- Autonomic
- Respiratory – ventilatory support
- Nephrotic syndrome and lymphoproliferative disorders
- High mortality
- IgG1 or 3

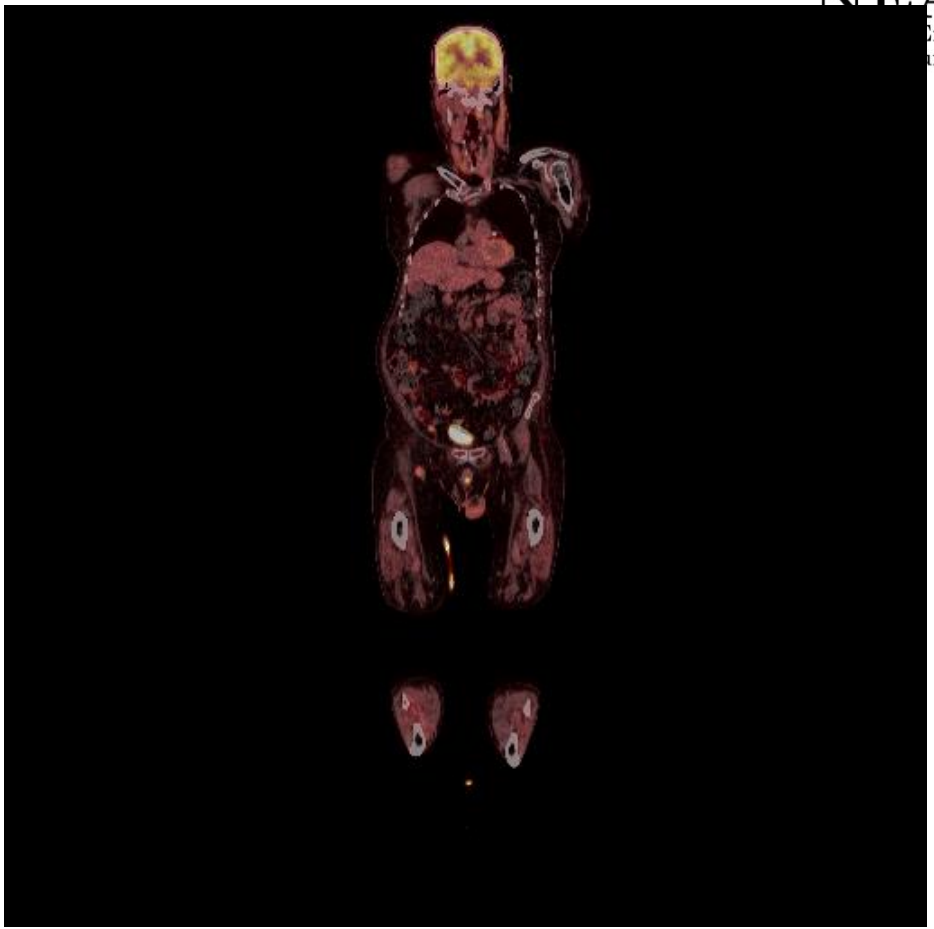
Pan-NF



J Neurol Neurosurg Psychiatry 2021;**0**:1–7. doi:10.1136/jnnp-2021-326343

Palpable lymph node

Confirmed lymphoma



What are the red flags?

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North of England Acute Neurology Update

Asymmetric weakness (marked and persistent)
Severe respiratory dysfunction at onset with mild limb weakness
Predominant sensory signs at onset (paraesthesias often occur) with mild weakness
Fever or other prominent systemic features at onset
Sensory level, or extensor plantar responses
Hyperreflexia (initial hyper-reflexia does not exclude GBS)
Bladder/bowel dysfunction (does not exclude GBS)
Abdominal pain or vomiting
Nystagmus
Alteration of consciousness (except in BBE)
Relatively slow worsening (2–4 weeks) with mild weakness

Continued worsening >4 weeks or ≥3 TRFs (consider A-CIDP)

+ Early Opthalmoplegia

- Abnormal routine blood tests
  - Significant abnormal inflammatory markers
  - Unexplained renal dysfunction
  - FBC suggestive of Marrow dysfunction/plasma cell dyscrasia

- CSF: >50 x10^6 - less than 1% of GBS cases in IGOS cohort

Another Neurologist banging on a weird disease

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- MORE useful to check nodal antibodies than gangliosides- it actually CHANGES management
- PRE-IVIG!
- Respond to Rituximab
- Google – Simon Rinaldi- Oxford- Nodal Antibodies

Many more weird and wonderful

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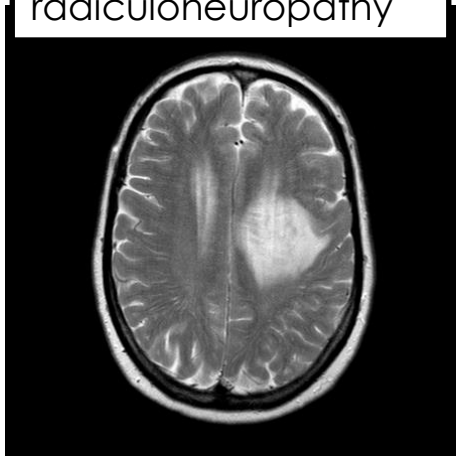
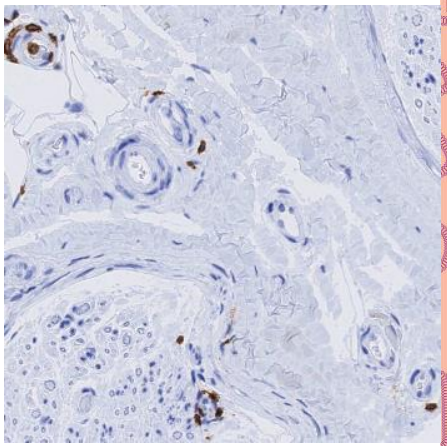
Acute Neurology
Update

Neurolymphomatosis presenting with a demyelinating radiculoneuropathy

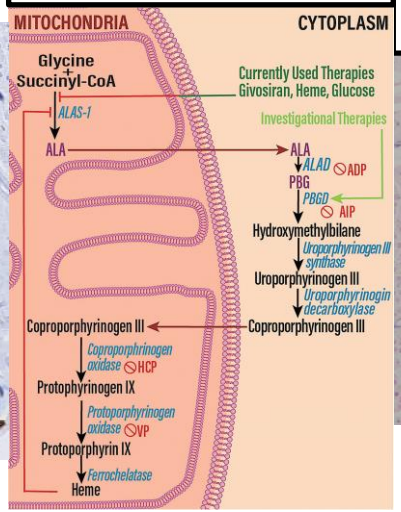


ICI- GBS/Neuritis



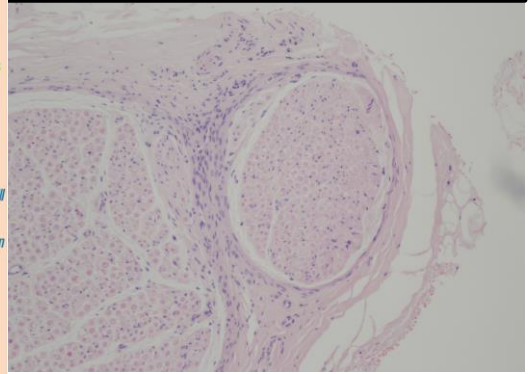
Courtesy of Aisling Carr

Acute Porphyria



Gandhi Mehta, Rachana K et al. "Porphyric neuropathy." *Muscle & nerve* vol. 64,2 (2021): 140-152.

Nitrous Oxide – isolated motor neuropathy with perineuritis



Neuropathies mimicking GBS

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North of England
Acute Neurology
Update

- Nutritional – B1, B2, B6,
- Toxic – NO, chemo (Velcade)
- Infective- HIV, Lyme
- Inherited Metabolic- MNGIE, Porphyria
- Paraneoplastic- POEMS
- Infiltrative Malignant Polyradiculopathy – Lung, Breast
- Inflammatory - Vasculitis

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Acute Neurology
Update

Take home messages

- Identify atypical features on hx, exam and bloods

- Store a sample for immunology!

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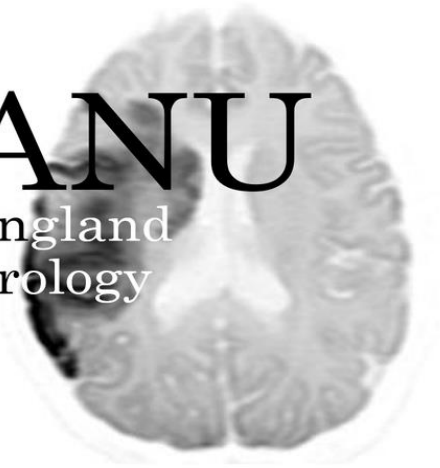
North of England
Acute Neurology
Update



CNS/PNS cases... Beyond the normal

Matt Jones and Tim Lavin

MANCHESTER 1824
The University of Manchester

Manchester Centre for
Clinical Neurosciences

Disclosures

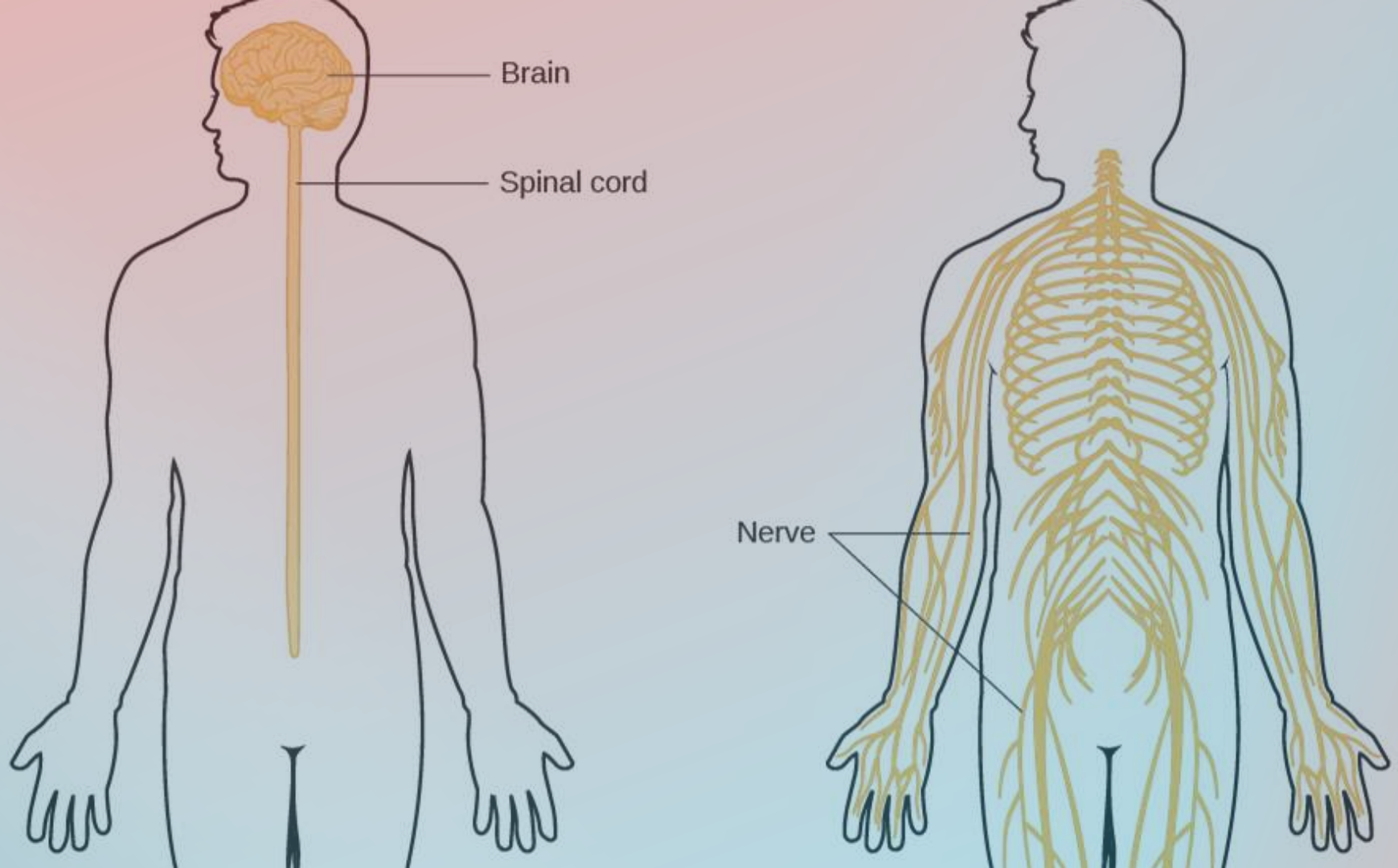
NEANU
North of England Acute Neurology Update

Matt Jones

- Expert Advisor BMJ Best Practice
- Honoraria for talks; Biogen, Eisai
- Assoc British Neurologists Education Committee chair

Tim Lavin

- Honoraria from Alnylam


Brain
Spinal cord
Nerve

Case 1

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Acute Neurology
Update

- Admitted in ‘confusional state’
- Preceding 1 month of altered behavior and poor memory
- No witnessed seizures
- CT on admission NAD

60 yr old female
No PMH
No meds
Lives alone
Non smoker, moderate alcohol
No rec drugs

Admitted to med HDU

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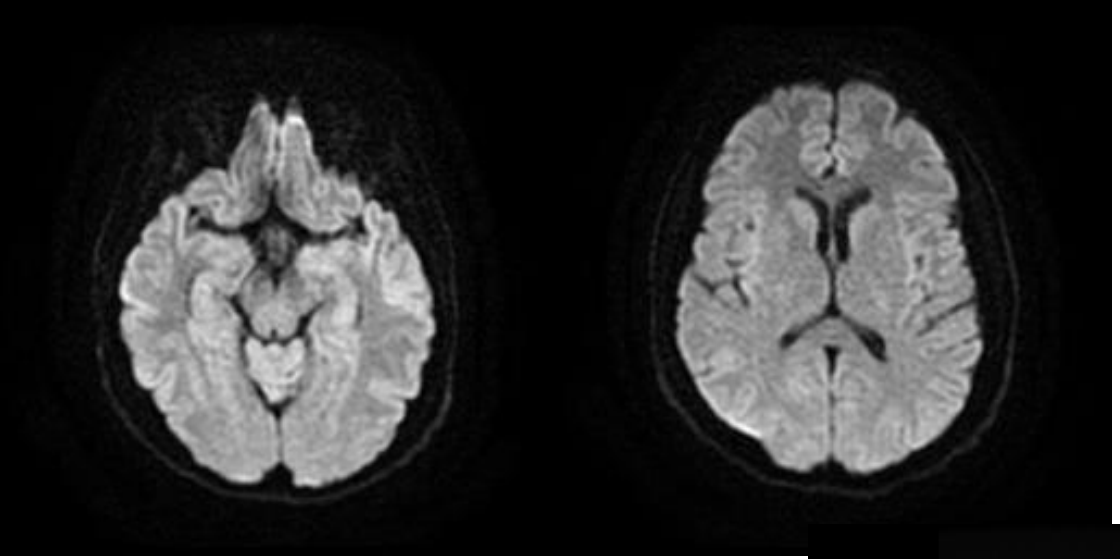
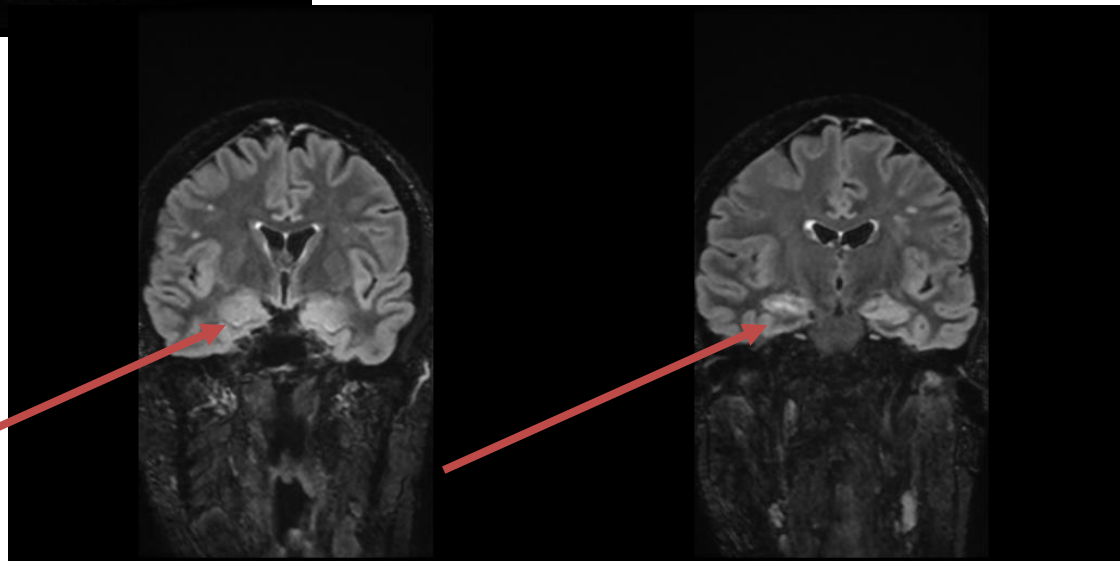
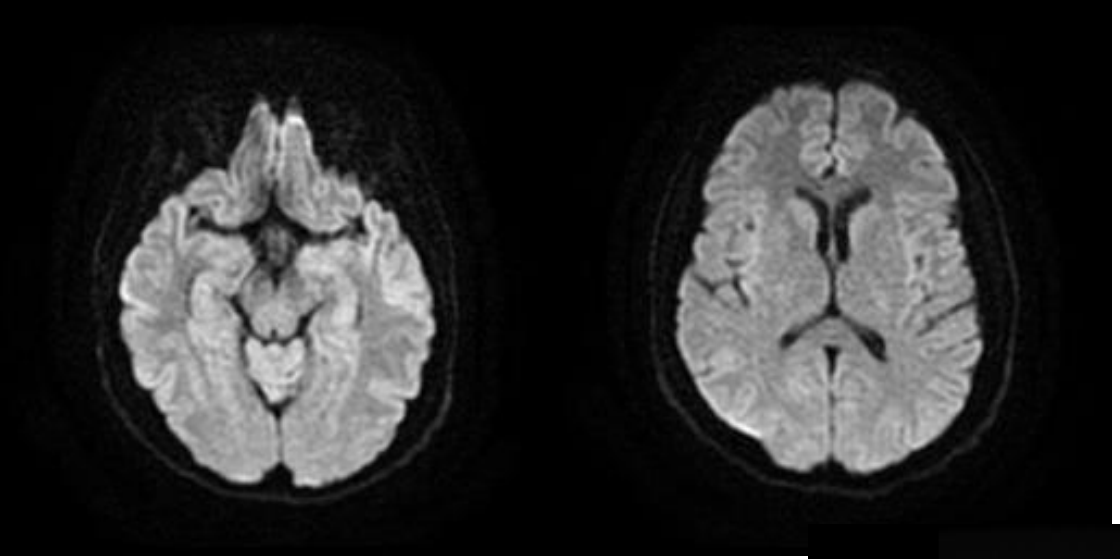
North of England
Acute Neurology
Update

- Gen unwell, hypotensive, hyponatraemic, afebrile
- Systems exam otherwise NAD
- Other basic bloods - normal range

- Plan?

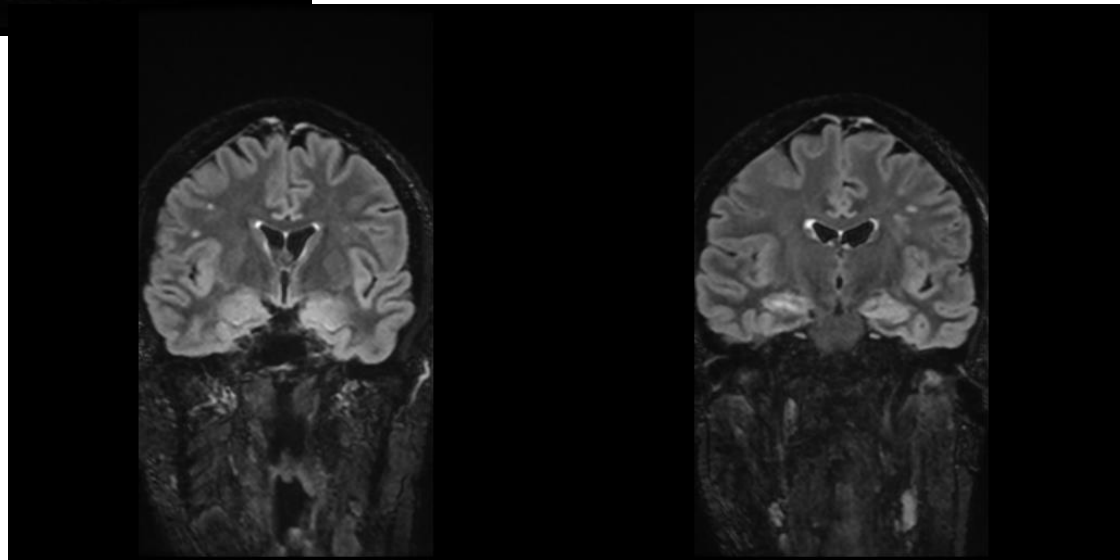


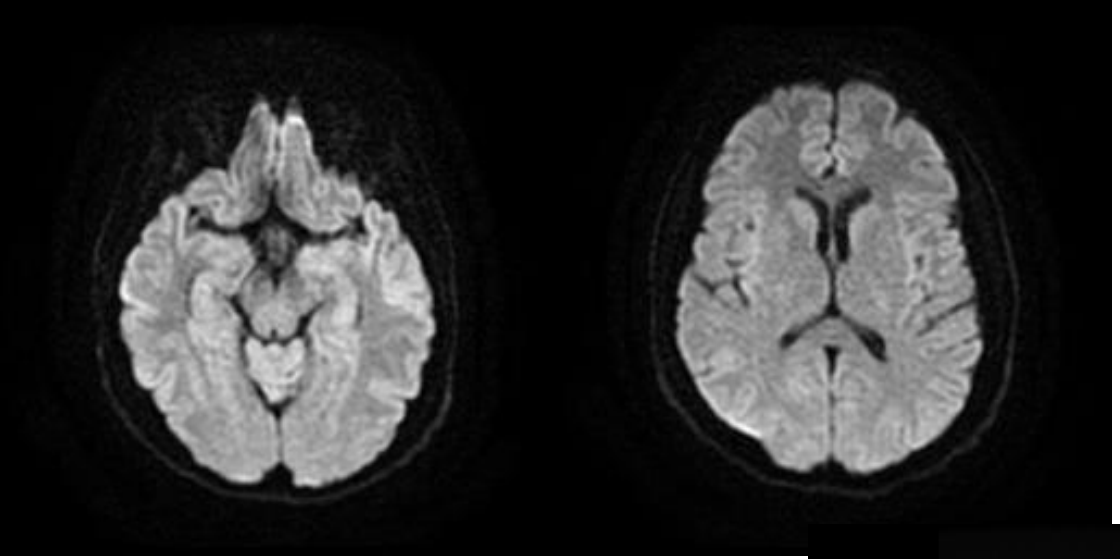




CSF

8 WBC
Normal protein & glucose

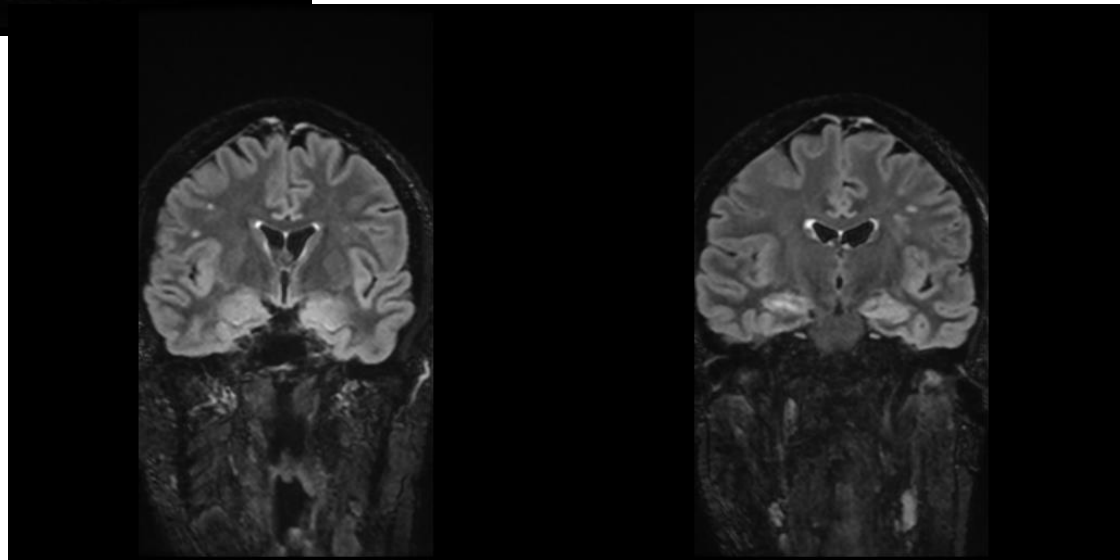


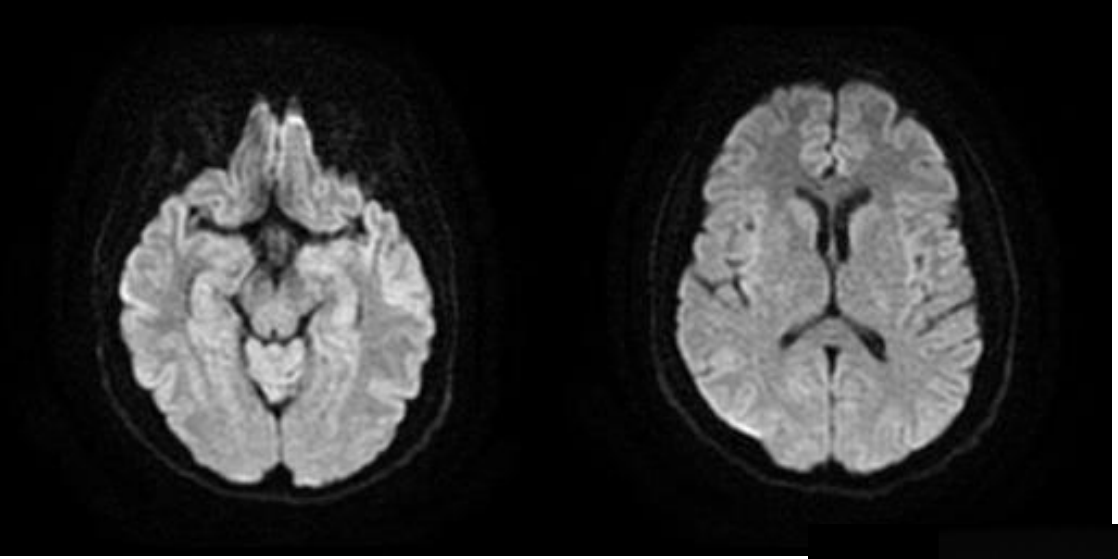


CSF

8 WBC
Normal protein & glucose

Plan?



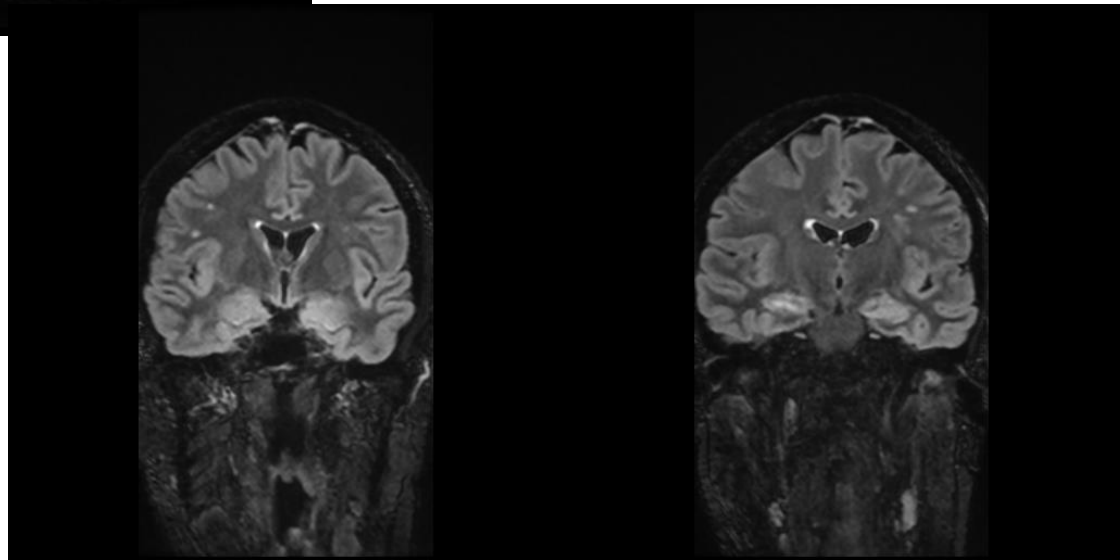


CSF

8 WBC
Normal protein & glucose

HSV 1+2 –ve
VZV, enterovirus,
parechovirus also –ve

Blood: IgG HSV1 +ve
IgG HSV2 –ve
IgG VZV +ve



Progress...

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Acute Neurology
Update

- Continued IV acyclovir for 2/52
- Gradual improvement
- Discharged home (minor support) after 4/52

But... Readmitted 3/12 later

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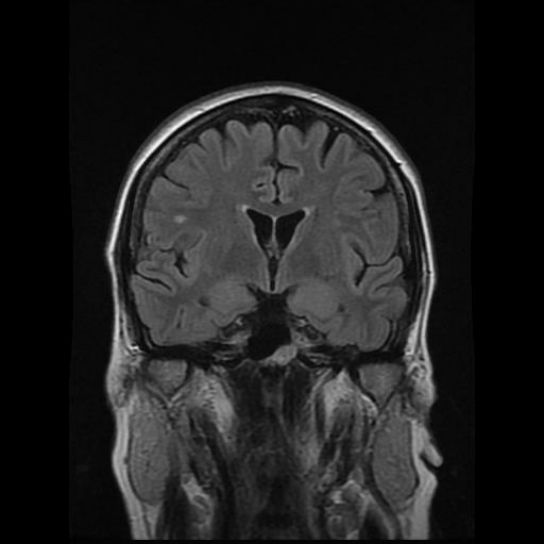
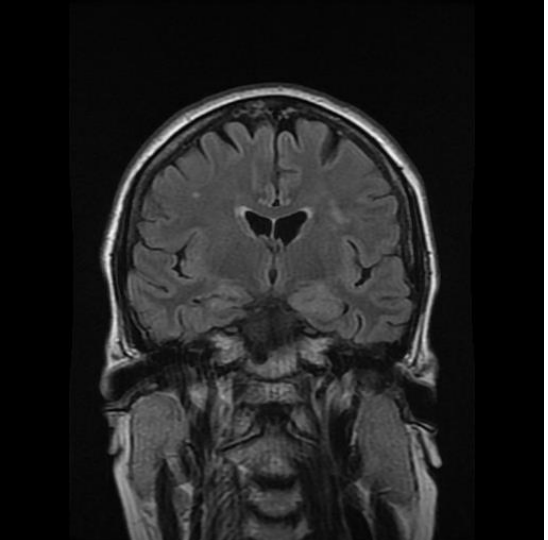
North of England
Acute Neurology
Update

- Struggling living alone
- Imperfect memory – varies day-to-day. Slightly ‘giggly’
- Paroxysmal attacks
  - ‘overwhelming feeling’ at onset, then no recollection from patient
  - Witness: she develops uncomfortable feeling in R arm, may scratch at leg, some posturing R arm. Couple of minutes, fatigued and upset afterwards.
  - Variable frequency – probably daily





Tests this time…

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CSF

0 WBC
Normal protein & glucose
All viral PCRs -ve

EEG

Normal background rhythm

1 attack captured – no correlate on EEG

What's going on now?

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North of England Acute Neurology Update

- Patient still not normal (?waxing and waning)
  - Focal seizures prominent
- MRI still probably abnormal

- CSF now looks normal

What now?

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North of England Acute Neurology Update

- HIV, Trep –ve
- Paraneoplastic Ab panel –ve
- NMDA, AMPA, GABA, CASPR –ve

- LGI1 +ve

Autoimmune limbic encephalitis

Improved with steroids, ASMs and olanzapine

Case 2

NEANU
North of England
Acute Neurology
Update

- Admitted in ‘confusional state’
- Preceded by 2x GTCS in last 24 hrs
- URTI sx and fever for 1/52

- Exam normal
- Basic bloods ok
- Given Keppra

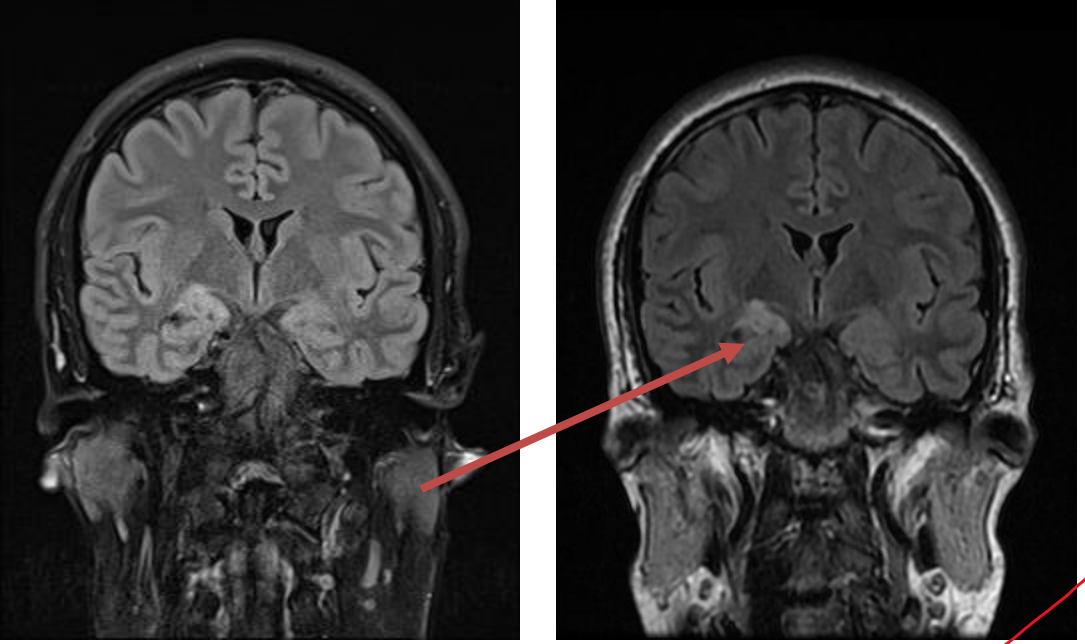
39 yr old male
No PMH except anxiety
No meds
Lives with partner
Non smoker, no alcohol
No rec drugs

Admitted to EAU

NEANU
North of England
Acute Neurology
Update

- No further GTCS
- Patchy memory (not amnesic), c/o odd smells and déjà vu
- Plan?

What do these symptoms mean?



CSF

0 WBC
Normal protein & glucose

Given acyclovir

HSV 1+2 –ve
VZV, enterovirus, parechovirus also –ve

But still having focal seizures....

Acyclovir stopped, steroids given

Transferred to ANU

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North of England
Acute Neurology
Update

No convincing evidence of AIE

Steroids stopped

ASMs optimized for discharge

So, what's going on?

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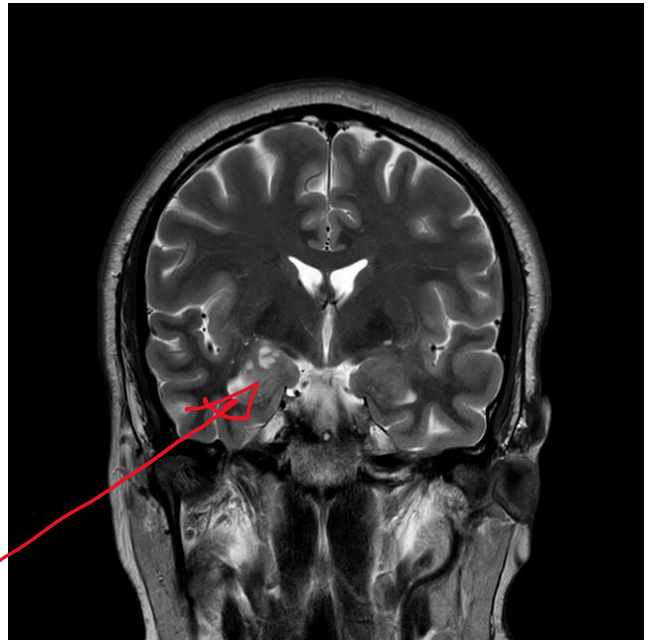
North of England Acute Neurology Update

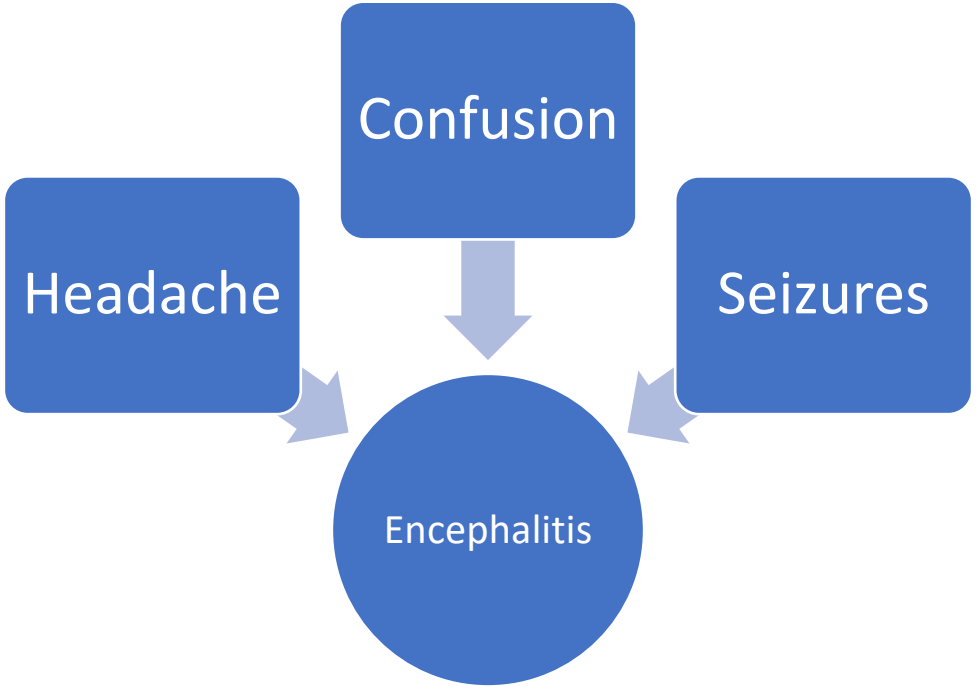
LGI1, CASPR, NMDAr, GABA, AMPA all –ve

Paraneoplastic and GAD Ab also all –ve

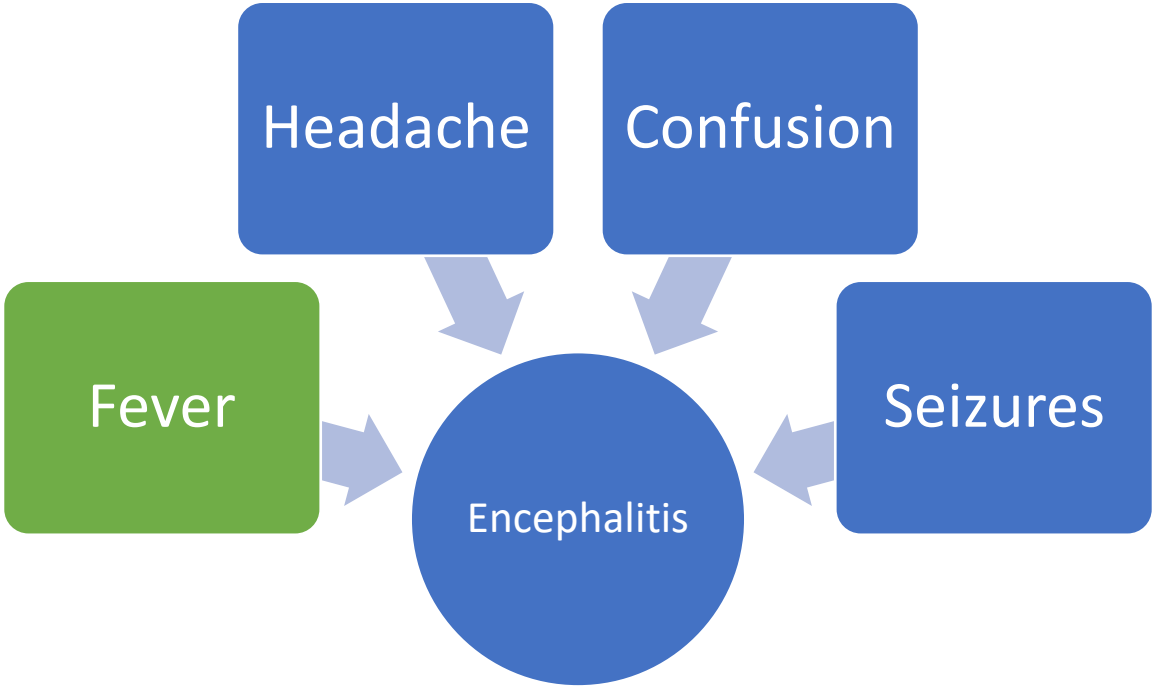


When is it encephalitis?

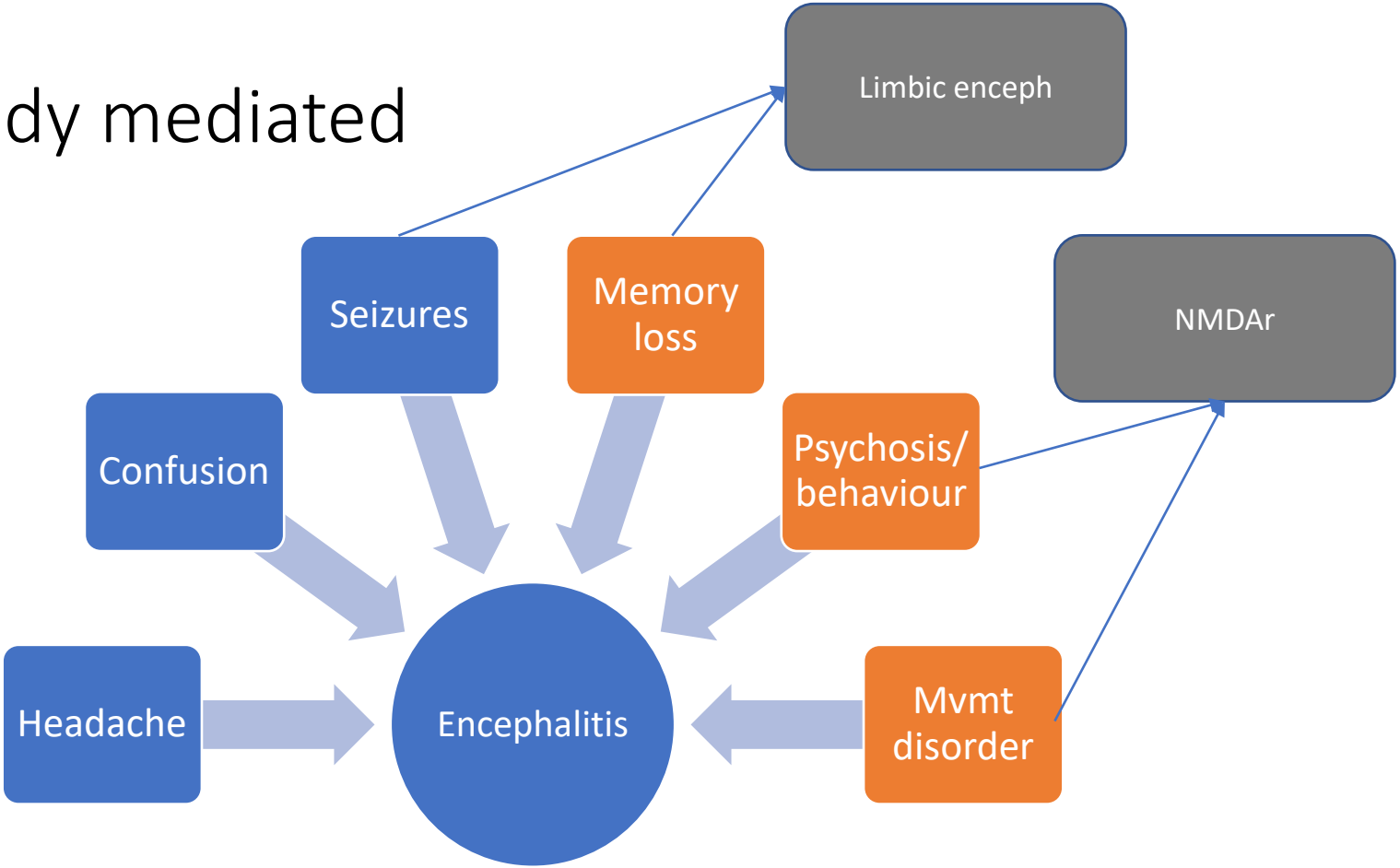
Encephalitis – the rough guide…

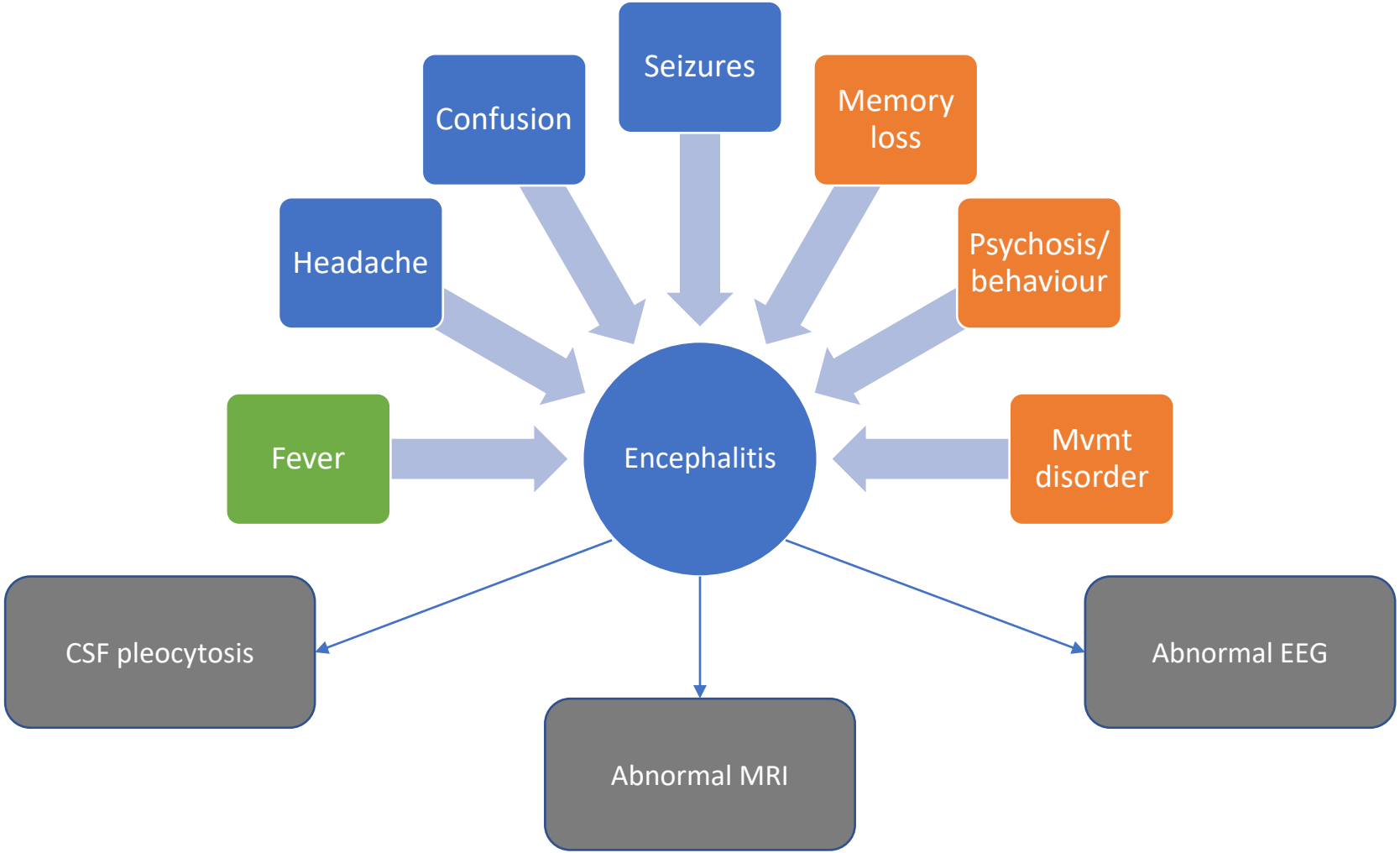


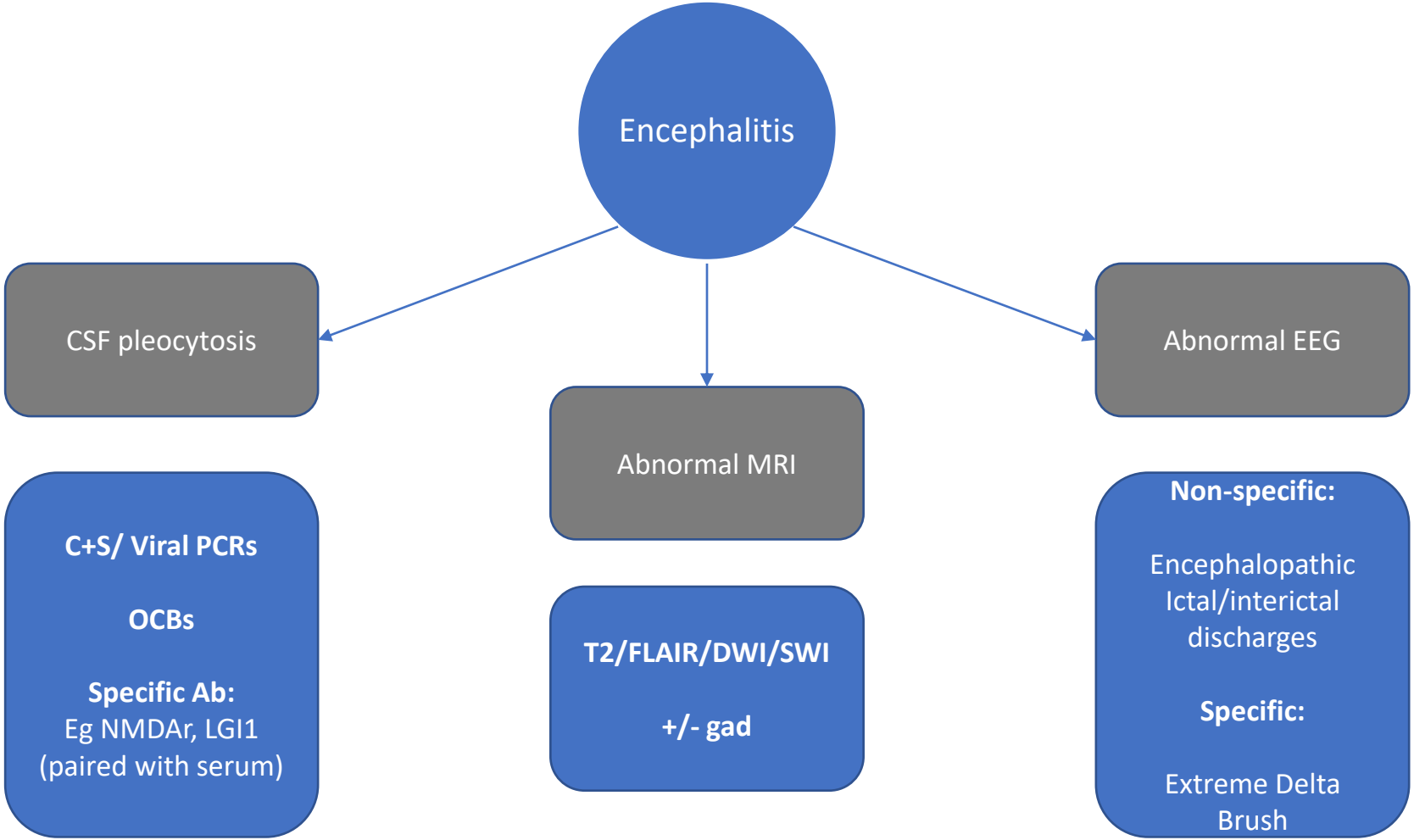
Infective



Antibody mediated




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


Encephalitis
CSF pleocytosis
Abnormal MRI
Abnormal EEG
C+S/ Viral PCRs
OCBs
Specific Ab:
Eg NMDAr, LGI1
(paired with serum)
T2/FLAIR/DWI/SWI
+/- gad
Non-specific:
Encephalopathic
Ictal/interictal
discharges
Specific:
Extreme Delta
Brush

Define the syndrome

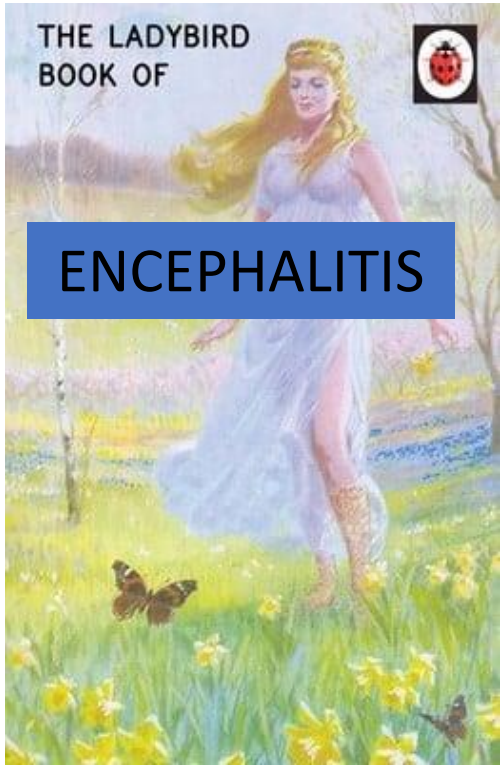
- Hx, exam, (EEG)

Biomarkers of inflammation

- MRI, CSF

Rule in/out infections

- CSF WBC/ culture/ viral PCR



Encephalitis… a less rough guide…

Major Criterion (required):
Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting ≥24 h with no alternative cause identified.
Minor Criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed[a] encephalitis):
Documented fever ≥38° C (100.4°F) within the 72 h before or after presentation[b]
Generalized or partial seizures not fully attributable to a preexisting seizure disorder[c]
New onset of focal neurologic findings
CSF WBC count ≥5/cubic mm[d]
Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset[e]
Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.[f]

Consensus Document on Encephalitis • **CID 2013:57 (15 October)**

Table 2. Diagnostic Algorithm for Initial Evaluation of Encephalitis in Adults[a]

ROUTINE STUDIES
CSF
Collect at least 20 cc fluid, if possible; freeze at least 5–10 cc fluid, if possible
✓ Opening pressure, WBC count with differential, RBC count, protein, glucose
✓ Gram stain and bacterial culture
✓ HSV-1/2 PCR (if test available, consider HSV CSF IgG and IgM in addition)
✓ VZV PCR (sensitivity may be low; if test available, consider VZV CSF IgG and IgM in addition)
✓ Enterovirus PCR
Cryptococcal antigen and/or India Ink staining
Oligoclonal bands and IgG index
VDRL
SERUM
Routine blood cultures
HIV serology (consider RNA)
Treponemal testing (RPR, specific treponemal test)
Hold acute serum and collect convalescent serum 10–14 d later for paired antibody testing

The commonest causes

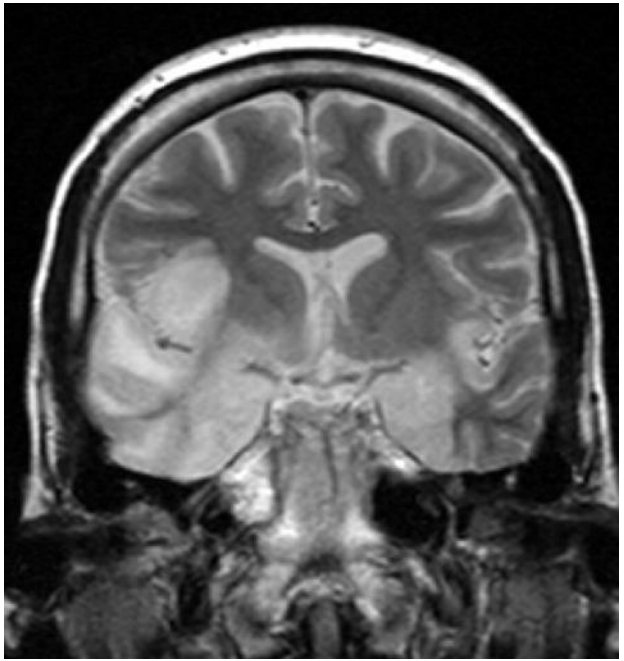
Viral

Immunocompetent

- Herpes simplex type I
- VZV

Immunocompromised

- HIV
- CMV, JC, HHV6, toxo, other



The commonest causes

Viral

Immunocompetent

- Herpes simplex type I
- VZV

Immunocompromised

- HIV
- CMV, JC, HHV6, toxo, other

Mediterranean / Europe

Toscana
Tick borne encephalitis

Asia

Japanese encephalitis

USA

West Nile virus

Basically, if they've been on their hols ring ID…

Treatment

Viral

Acyclovir

ASMs

Steroids?

Intensive care

What if its not viral..?

Possible Autoimmune Encephalitis

The basics…

- Need to exclude:
  - Septic encephalopathy
  - Metabolic encephalopathy
  - Infective encephalitis
  - CJD
  - DLB
  - Epilepsy
  - Neoplasia
- Not so basic:
  - Vasculitis /vasculopathy
  - Mitochondrial
  - Inborn errors metabolism
  - Multisystem AI disease (Eg sarcoid, lupus)

Therefore, everyone will need:

Detailed collateral hx
Proper physical exam
Routine bloods
MRI
CSF
EEG

The commonest causes

Antibodies

Directed against neuronal surface antigen

- LGI1, CASPR2, NMDA receptor
- GABA, AMPA

Intracellular antigen

- Hu, CV2, Ma1/2,
- GAD

Treatment

Antibodies

Steroids

Plasma exchange / IVIG

Rituximab / cyclophos

ASMs

Antipsychotics

Intensive care

But the Ab are all negative…

Ab –ve AI Encephalitis

1) Rapid progression (less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms

2) Exclusion of well-defined syndromes of autoimmune encephalitis (eg, typical limbic encephalitis, Bickerstaff's brainstem encephalitis, acute disseminated encephalomyelitis)

3) Absence of well characterised autoantibodies in serum and CSF, and at least two of the following criteria:

- MRI abnormalities suggestive of autoimmune encephalitis
- CSF pleocytosis, CSF-specific oligoclonal bands or elevated CSF IgG index, or both
- Brain biopsy showing inflammatory infiltrates and excluding other disorders (eg, tumour)

4) Reasonable exclusion of alternative causes

Research

JAMA Neurology | Original Investigation

Autoimmune Encephalitis Misdiagnosis in Adults

Eoin P. Flanagan, MD; Michael D. Geschwind, MD, PhD; A. Sebastian Lopez-Chiriboga, MD; Kyle M. Blackburn, MD; Sanchit Turaga, MD; Sophie Binks, MD; Jennifer Zitser, MD; Jeffrey M. Gelfand, MD; Gregory S. Day, MD; S. Richard Dunham, MD; Stefanie J. Rodenbeck, MD; Stacey L. Clardy, MD, PhD; Andrew J. Solomon, MD; Sean J. Pittock, MD; Andrew McKeon, MD; Divyanshu Dubey, MD; Anastasia Zekeridou, MD, PhD; Michel Toledano, MD; Lindsey E. Turner; Steven Vernino, MD, PhD; Sarosh R. Irani, MD, DPhil

Table 1. Alternative Final Diagnoses in Those Initially Misdiagnosed as Autoimmune Encephalitis

Alternative diagnosis	No. (%)	
	Individuals with initial diagnosis (n = 107)	Individuals who fulfilled possible autoimmune encephalitis criteria (n = 30)
Functional neurologic disorder	27 (25)	6 (22)
Neurodegenerative dementia	22 (20.5)	5 (23)
Alzheimer disease[a]	6	0
Dementia with Lewy bodies[b]	4	1
Behavioral variant frontotemporal dementia	4	2
Creutzfeldt-Jakob disease	2	1
Vascular cognitive impairment	1	0
Other[c]	5	1[c]
Psychiatric disease	19 (18)	2 (11)
Depression[d]	7	2
Anxiety	3	0
Schizophrenia	2	0
Bipolar	2	0
Other[e]	5	0
Nonspecific cognitive syndrome in the setting of ≥1 of fibromyalgia, chronic fatigue, sleep disorder, medication adverse reaction, or other comorbidity[f]	11 (10)	1 (9)[f]
Neoplasm	10 (9.5)	7 (70)
Glioma (glioblastoma, astrocytoma, or not otherwise specified)[g]	7	5
Primary central nervous system lymphoma	2	2
Cerebellar medulloblastoma with cerebellar cognitive syndrome	1	0
Seizure disorder, nonimmune-mediated[h]	5 (4.5)	3 (60)
Infectious	3 (2.5)	1 (33)

Diagnostic criteria for autoimmune encephalitis: utility and pitfalls for antibody-negative disease

Josep Dalmau, Francesc Graus

Increased awareness of autoimmune encephalitis has led to two unintended consequences: a high frequency of misdiagnoses and the inappropriate use of diagnostic criteria for antibody-negative disease. Misdiagnoses typically occur for three reasons: first, non-adherence to reported clinical requirements for considering a disorder as possible autoimmune encephalitis; second, inadequate assessment of inflammatory changes in brain MRI and CSF; and third, absent or limited use of brain tissue assays along with use of cell-based assays that include only a narrow range of antigens. For diagnosis of possible autoimmune encephalitis and probable antibody-negative autoimmune encephalitis, clinicians should adhere to published criteria for adults and children, focusing particularly on exclusion of alternative disorders. Moreover, for diagnosis of probable antibody-negative autoimmune encephalitis, the absence of neural antibodies in CSF and serum should be well substantiated. Neural antibody testing should use tissue assays along with cell-based assays that include a broad range of antigens. Live neuronal studies in specialised centres can assist in resolving inconsistencies with respect to syndrome-antibody associations. Accurate diagnosis of probable antibody-negative autoimmune encephalitis will identify patients with similar syndromes and biomarkers, which will provide homogeneous populations for future assessments of treatment response and outcome.

Is there a rough guide for this bit..?

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- Apply the criteria rigorously
- Take ‘reasonable exclusion of other causes’ seriously
- Optimise Ab testing
  - Serum and CSF – every time… yes, really… plus OCBs…
- It’s a team sport
  - Gen Med, Neurology, ID, micro, CrCU, local and national MDT

Use criteria

Define the syndrome

- Hx, exam, (EEG)

Biomarkers of inflammation

- MRI, CSF

"save sample" check OCBs

Rule in/out infections

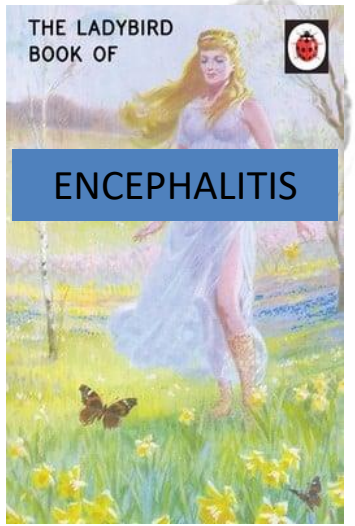
- CSF WBC/ culture/ viral PCR

Give steroids if "possible AIE"

Give Acyclovir

Check Antibodies

- CSF and Serum



Just one headache...

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- Whilst exercising, sudden head and neck discomfort
- Went to bed for 1hr, felt better... But then got up and felt much worse and had to attend hospital
- CT 4.5hrs post onset NAD
- Discharged home

47 yr old female
Usually well
No meds, no FH

Next few weeks...

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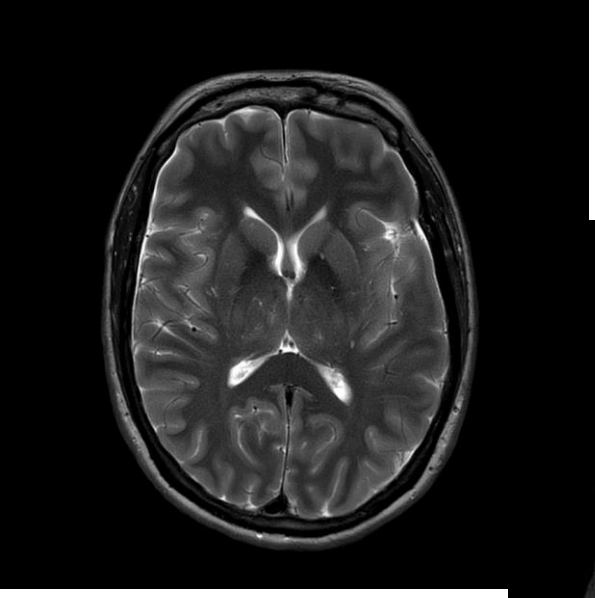
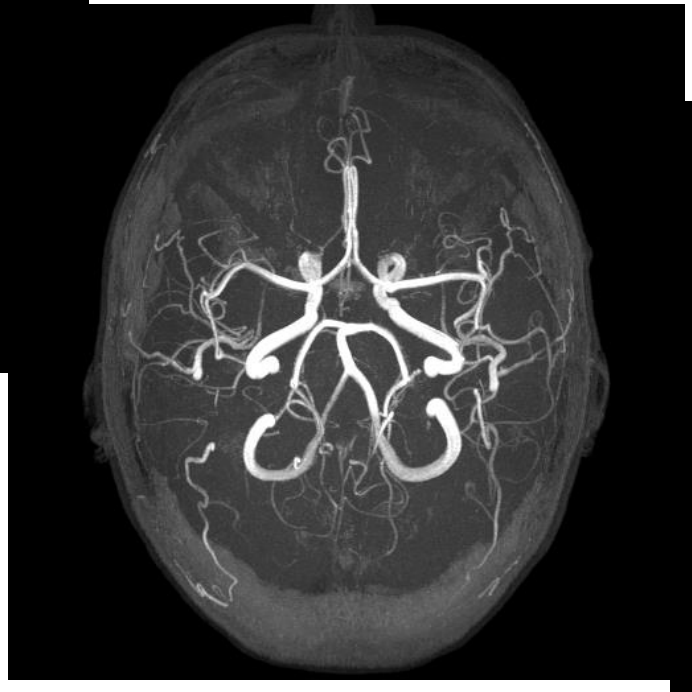
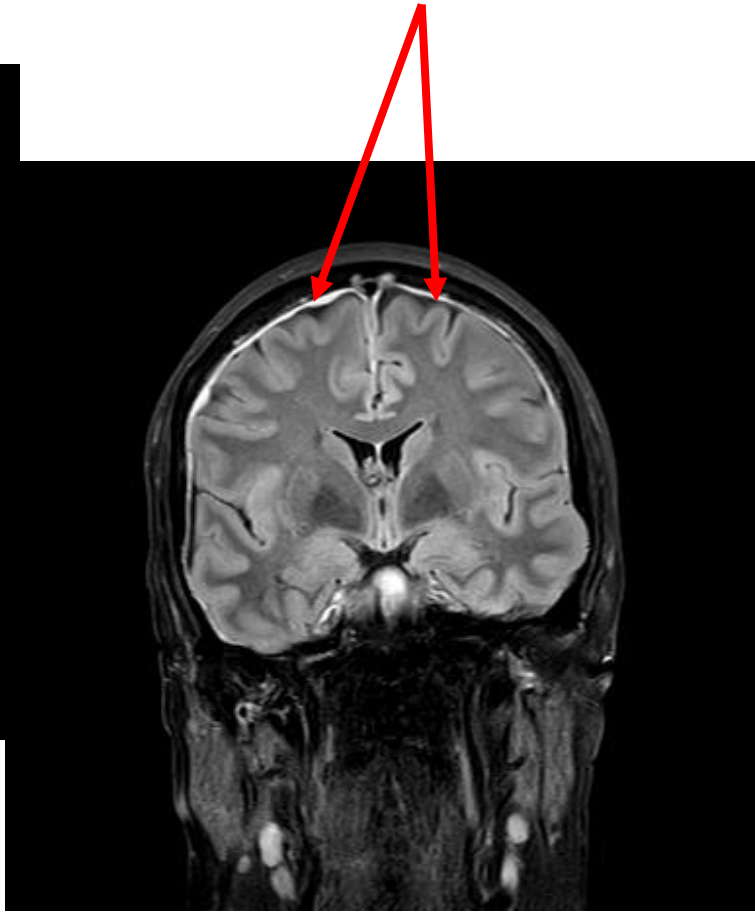
- Had to stay in bed for 1 week
- After that more active, but ongoing head and neck pain, tinnitus and muffled hearing

- Private MRI scan:







If you had only one Q...?

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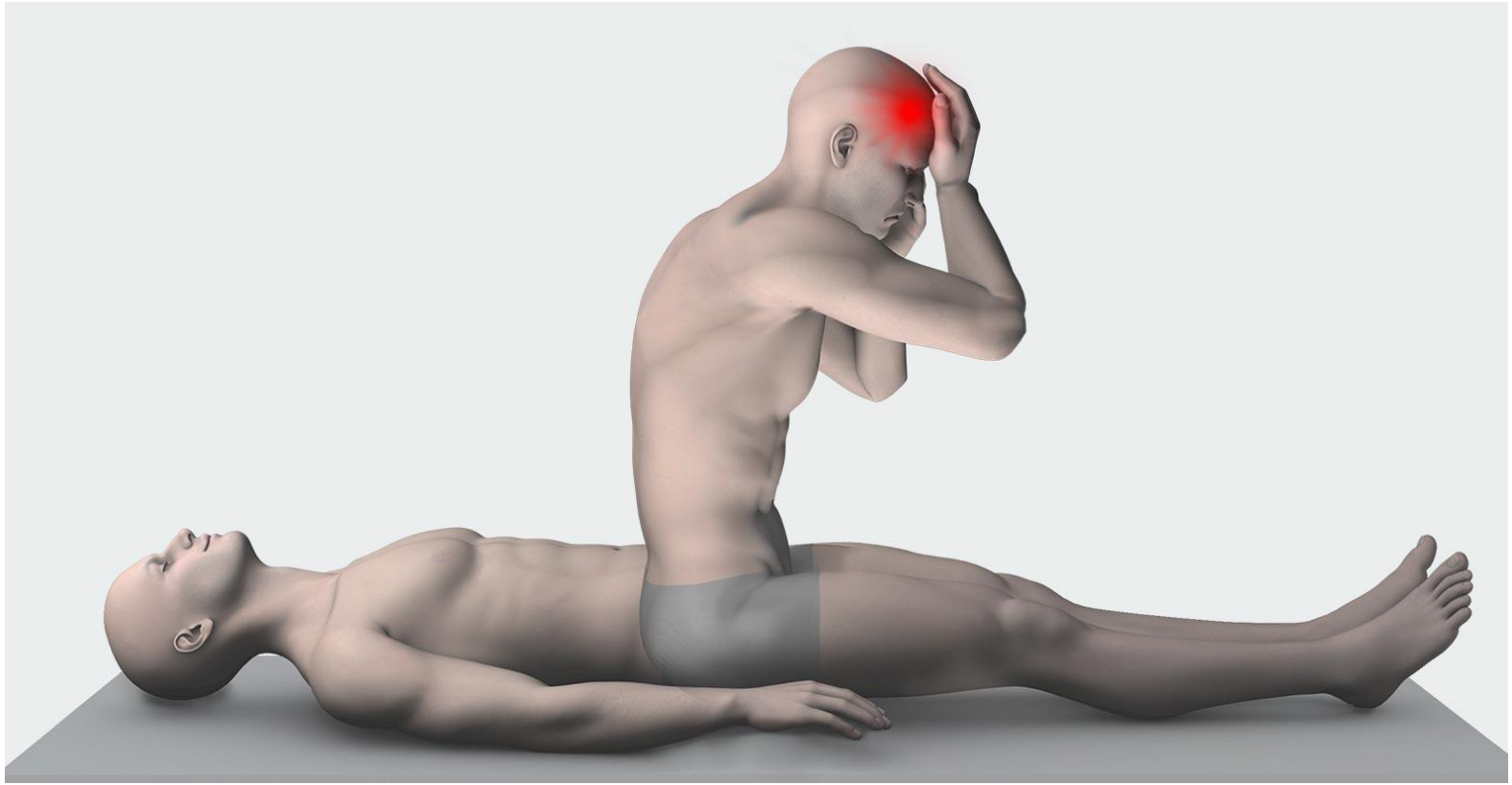


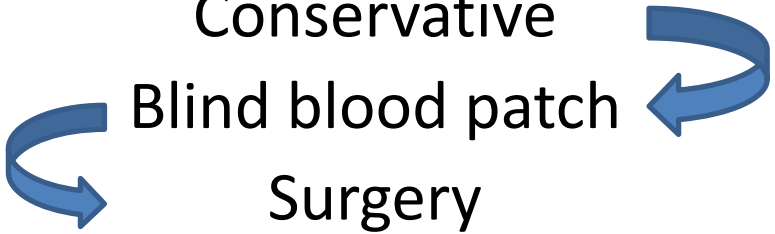
Spontaneous intracranial hypotension

Due to CSF leak

Conservative

Blind blood patch

Surgery



General neurology

Original research

Multidisciplinary consensus guideline for the diagnosis and management of spontaneous intracranial hypotension

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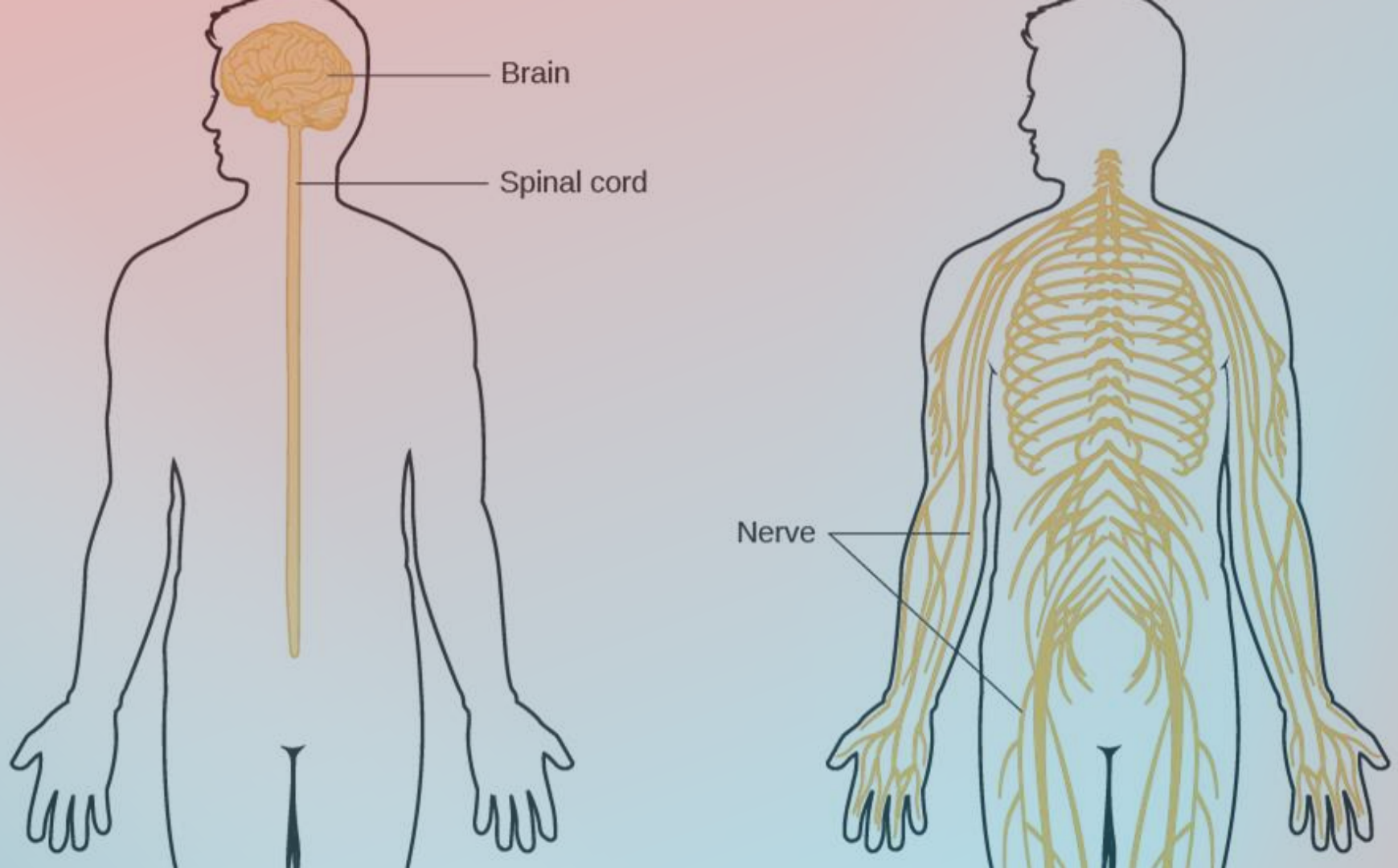
Thunderclaps...

- SAH
- Reversible Cerebral Vasoconstriction Syndrome
- Cerebral Venous Sinus Thrombosis
- Intracerebral Haemorrhage
- Spontaneous Intracranial Hypotension
- Neck vessel dissection
- Meningitis
- Idiopathic


Brain
Spinal cord
Nerve