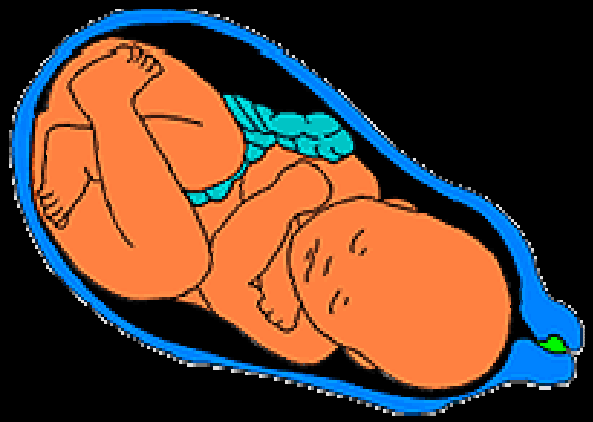
Pregnancy and Neurological Disorders



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United Kingdom

Outline

- Why is it important?
- Specific conditions
  - Eclampsia
  - Cerebrovascular disease
  - Epilepsy
  - Idiopathic intracranial hypertension
- Imaging in pregnancy

Why is it important?

- The neurological disease may impact on:

  Pregnancy, labour or delivery

- ‘It often requires balancing conflicting interests and supporting the patient and her partner in making potentially far-reaching decisions, sometimes based on insufficient evidence.’

  Marsh, Nashef, and Brex in ‘*Neurology and Pregnancy*’

Physiological changes in Pregnancy

- Allow mother to:
  - Tolerate the genetically distinct foetoplacental unit
  - Nourish and support a rapidly growing foetus
  - Prepare for the hazards of delivery

- Consequences
  - Insulin resistance
  - Thrombophilic
  - Relatively immunosuppressed
  - Hypervolaemic

Maternal Death

- Gradual improvement in direct obstetric related deaths in UK but relative increase in indirect causes (other conditions associated)

  - Neurological conditions third commonest cause of maternal deaths (direct and indirect combined)
    - Epilepsy (status, trauma)
    - SAH
    - Cerebral Haemorrhage
    - Cerebral venous thrombosis

Case 1

- 24 year old woman
- First pregnancy, uncomplicated
- Spontaneous labour at 40 weeks 3 days
- BP on admission 132/70 mmHg… No urinalysis done
- Baby delivered at midnight (vaginal delivery)
- Persistent vomiting an hour and a half after delivery associated with a severe headache ... BP 194/112 mmHg
- 90 minutes later – generalised tonic clonic seizure

Case 1

- Given Magnesium bolus
- Bloods; Hb 10.3, platelets 40, LDH 3300, ALT 2917, creatinine 79

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- Bloods; Hb 10.3, platelets 40, LDH 3300, ALT 2917, creatinine 79

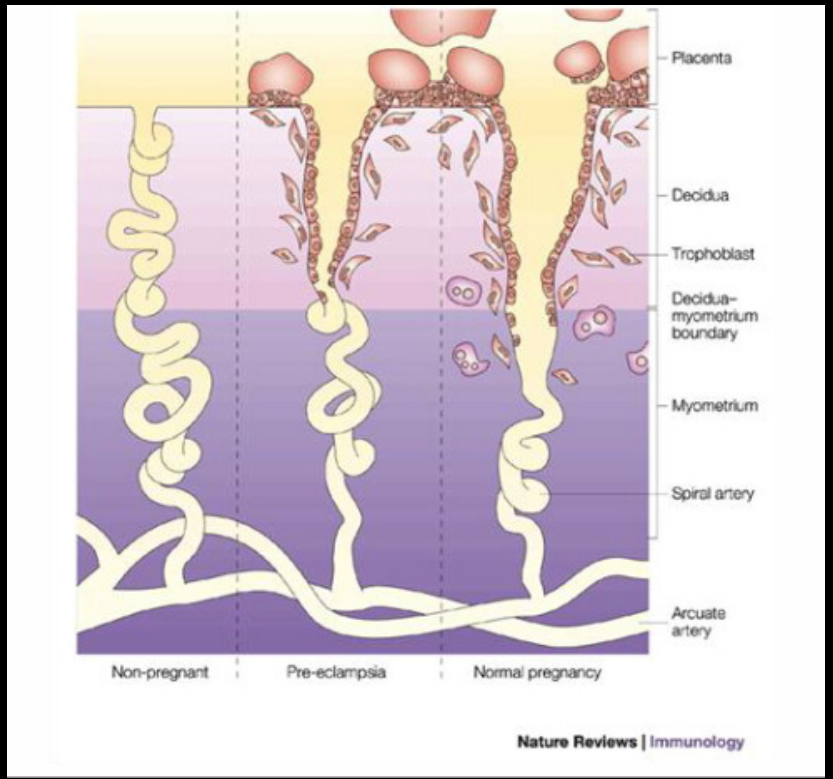
- ... What is the diagnosis?

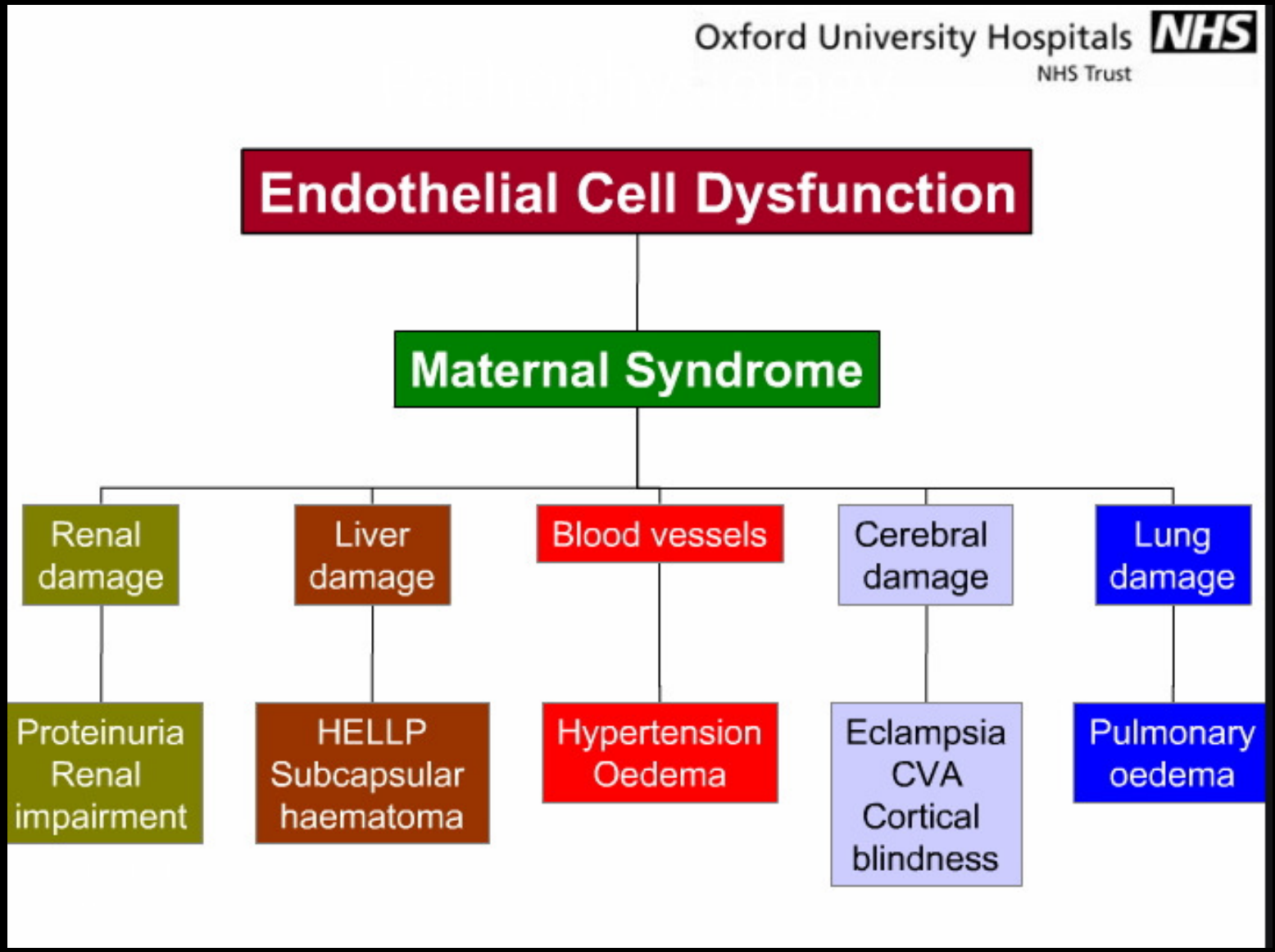
Differential Diagnosis of Seizures in Pregnancy

- Eclampsia
- Epilepsy
- Cerebral Venous Thrombosis
- Stroke (cerebral haemorrhage, SAH)
- Space occupying lesion
- Thrombotic thrombocytopenic purpura
- Infection – meningitis, encephalitis
- Drug / alcohol related
- Metabolic (hypoglycaemia, hypercalcaemia)

Eclampsia

- Placental problem
- In pre-eclampsia – oxidatively stressed placenta, systemic inflammation and dysfunctional maternal endothelium
- Endothelial dysfunction and vasospasm




Oxford University Hospitals
NHS
NHS Trust
Endothelial Cell Dysfunction
Maternal Syndrome
Renal damage
Liver damage
Blood vessels
Cerebral damage
Lung damage
Proteinuria
Renal impairment
HELLP
Subcapsular haematoma
Hypertension
Oedema
Eclampsia
CVA
Cortical blindness
Pulmonary oedema

Eclampsia

- In around 30% seizure precedes hypertension / proteinuria
- Up to 50% postnatal
- Prevent and treat with Magnesium Sulphate
  - 58% lower risk of eclampsia, and non-significant reduction in maternal mortality (Duley MAGPIE *Lancet* 2002; 359: 1877-90)
- Stablise patient and deliver the baby

Seizure prevention and control

Prevention:

- Magnesium sulphate
- IV 4g loading dose over 5 min
- IV infusion 1g per hour
- 2-4 g for recurrent seizures
- Monitor Mg level if
  - Oliguric
  - Renal dysfunction
  - Signs of toxicity
  - Low BMI

Seizure:

- Lorazepam 2mg IV
- Magnesium sulphate bolus

Case 2

- 30 year old woman, first pregnancy, uncomplicated so far
- 18 weeks pregnant
- Presents at 3 am to A+E
  - Husband woken an hour earlier by loud grunting noises
  - Describes seeing his wife foaming at the mouth, violent bilateral jerking of her limbs, eyes open
  - Lasted 2 minutes, and she was then unresponsive, breathing heavily and only opened her eyes and responded 10 minutes later, but remains drowsy and slightly confused
  - Bitten her tongue, no incontinence

Case 2

- On examination:
  - GCS 15, normal temperature and observations
  - No headache
  - No focal neurological signs
- Blood glucose – normal
- BP 100 / 70 mmHg
- FBC, U+E, LFT all normal

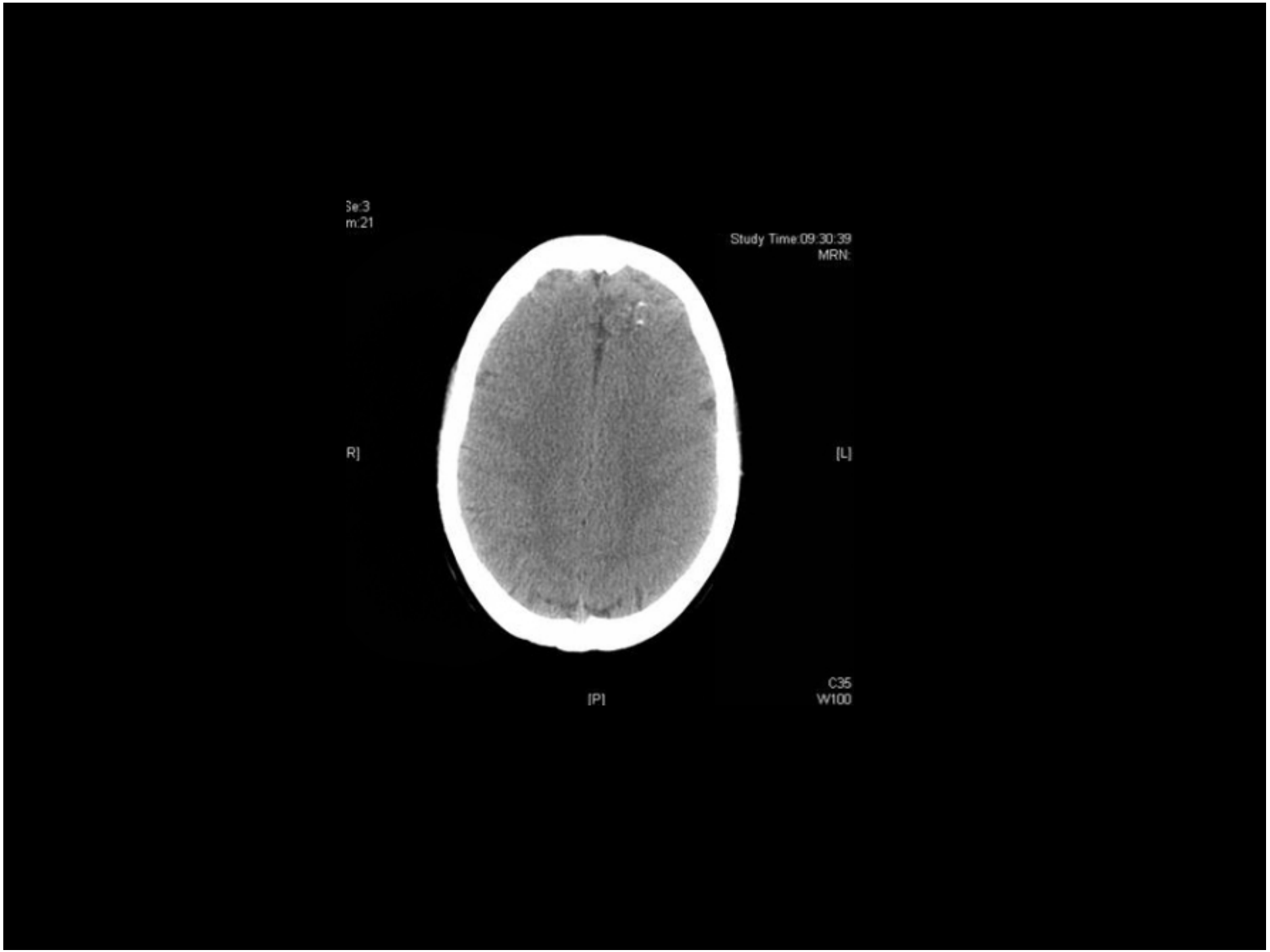
Case 2

- What now?

Imaging in Pregnancy

- Background radiation to the foetus during pregnancy is around 1mGy
- CT head is <0.1mGy
- Iodinated contrast and Gadolinium is ideally avoided
- MRI is generally avoided in the first trimester
- Wedge useful to prevent aortocaval compression


Se:3
Im:17
[A]
Study Time:09:30:39
MRN:
[R]
[L]
[P]
C35
W100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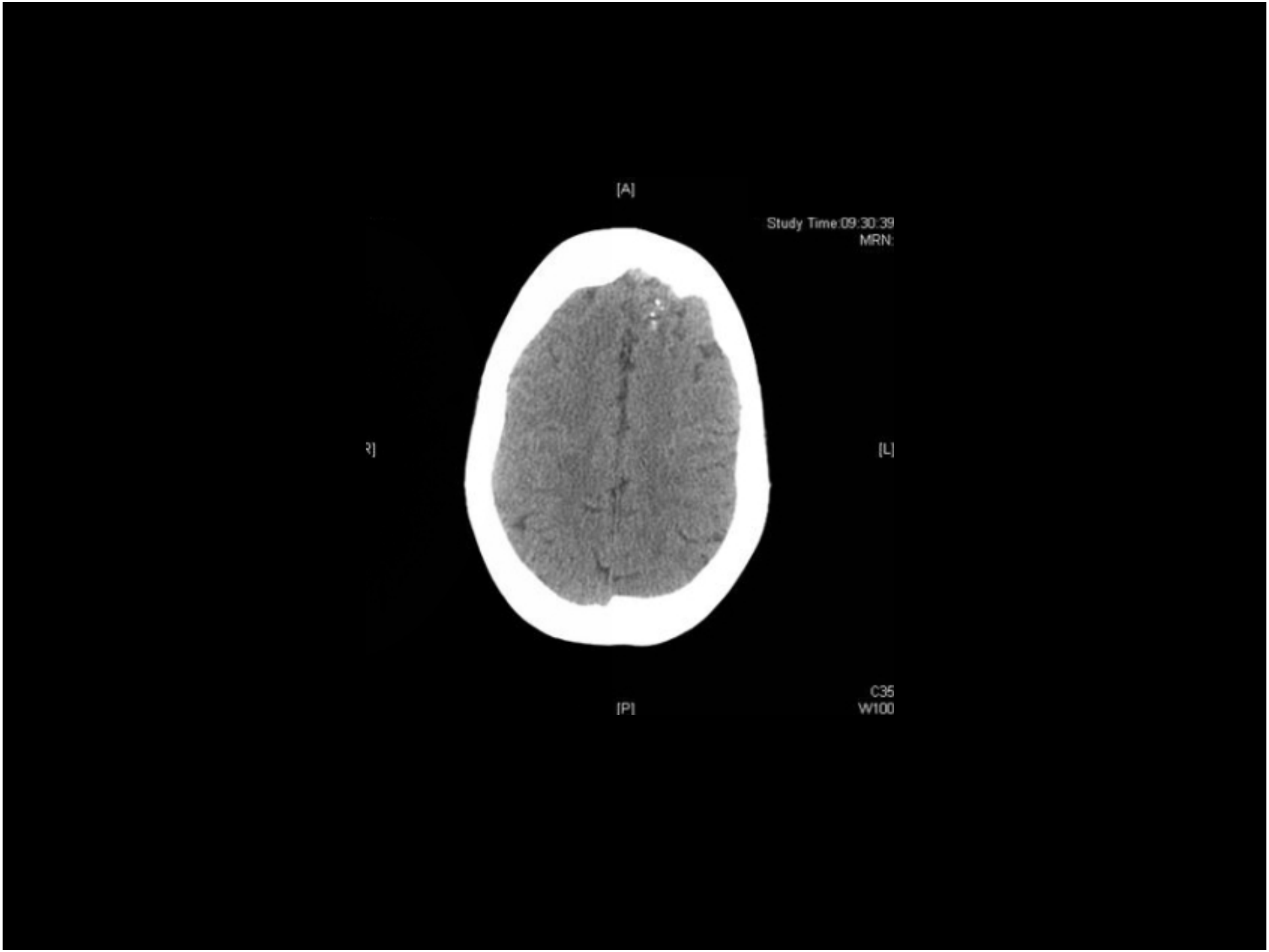
W100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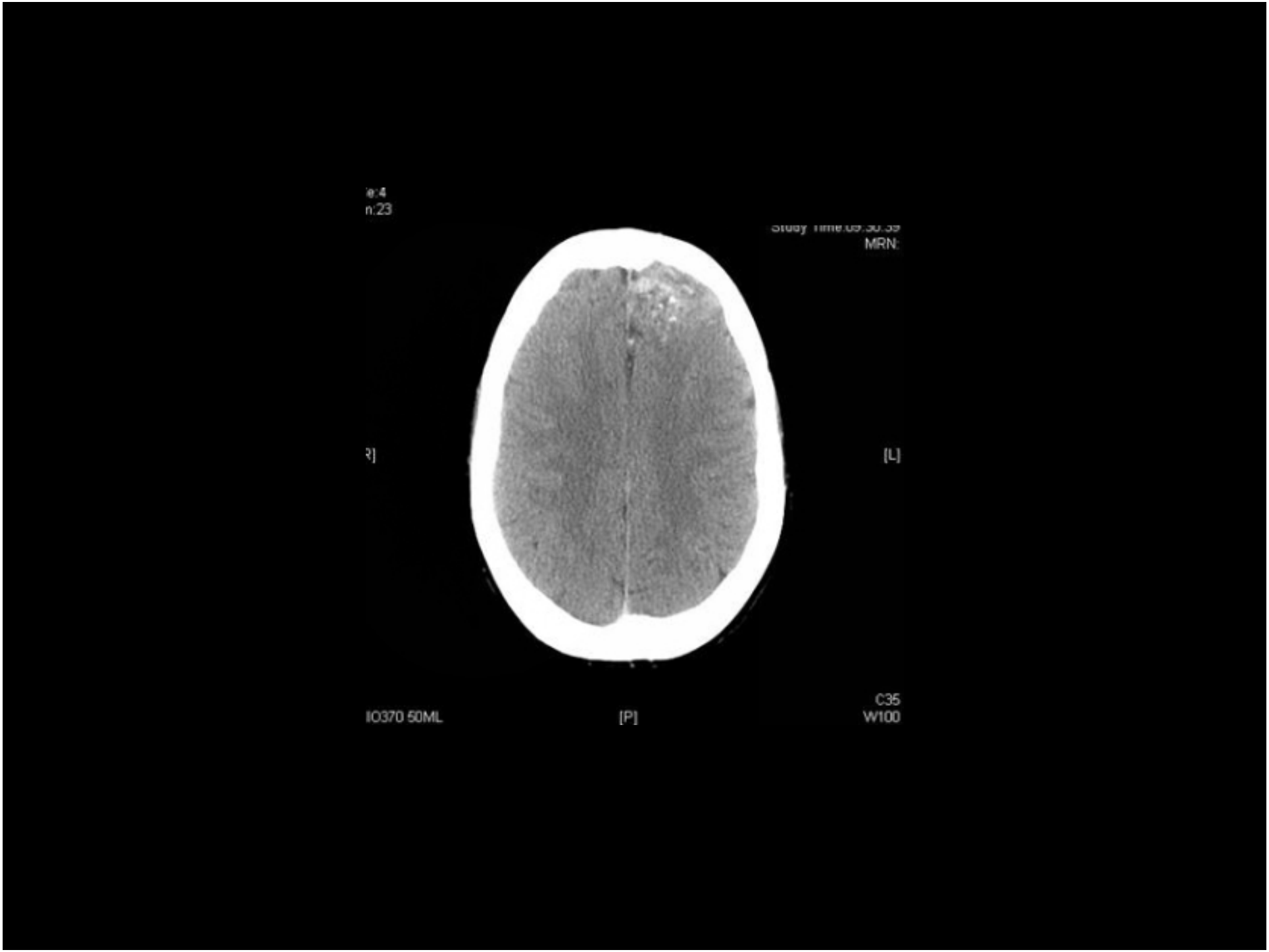
C35
W100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n:23
MRN:
R]
[L]
IO370 50ML
[P]
C35
W100


[A]
Study Time:09:30:39
MRN:
[R]
[L]
NIO370 50ML
[P]
C35
W100

Case 2

- And the diagnosis is...?

Case 2

- Left frontal arteriovenous malformation – no haemorrhage

- Key issues:
  - Risk of bleeding
  - Risk of further seizure
  - Implication for delivery
  - Issues related to seizure: safety, driving etc.

Case 2

- Started on Carbamazepine
- No further seizures prior to delivery by C/S with regional anaesthesia at 39 weeks.
- Two further seizures post-delivery
- CT head no new findings
- Discharged Day 4 on CBZ

- .... Further management

Epilepsy

- Pre-conceptual counselling is imperative
- Involvement of neurologist during pregnancy
- Key questions
  - Are antiepileptic drugs necessary?
  - Which drugs?
  - ? Increase in dose of Lamotrigine
  - Implication for labour
- Post-delivery: caring for a new baby

Finding the balance

- Seizures are associated with:
  - Preterm delivery
  - Small for gestational age
  - Low birth weight
  - Poor cognitive performance in childhood
  - Death
- Antiepileptic drugs area associated with:
  - Congenital malformations
  - Spontaneous abortions
  - Intrauterine growth restriction
  - Low birth weight
  - Poor cognitive performance

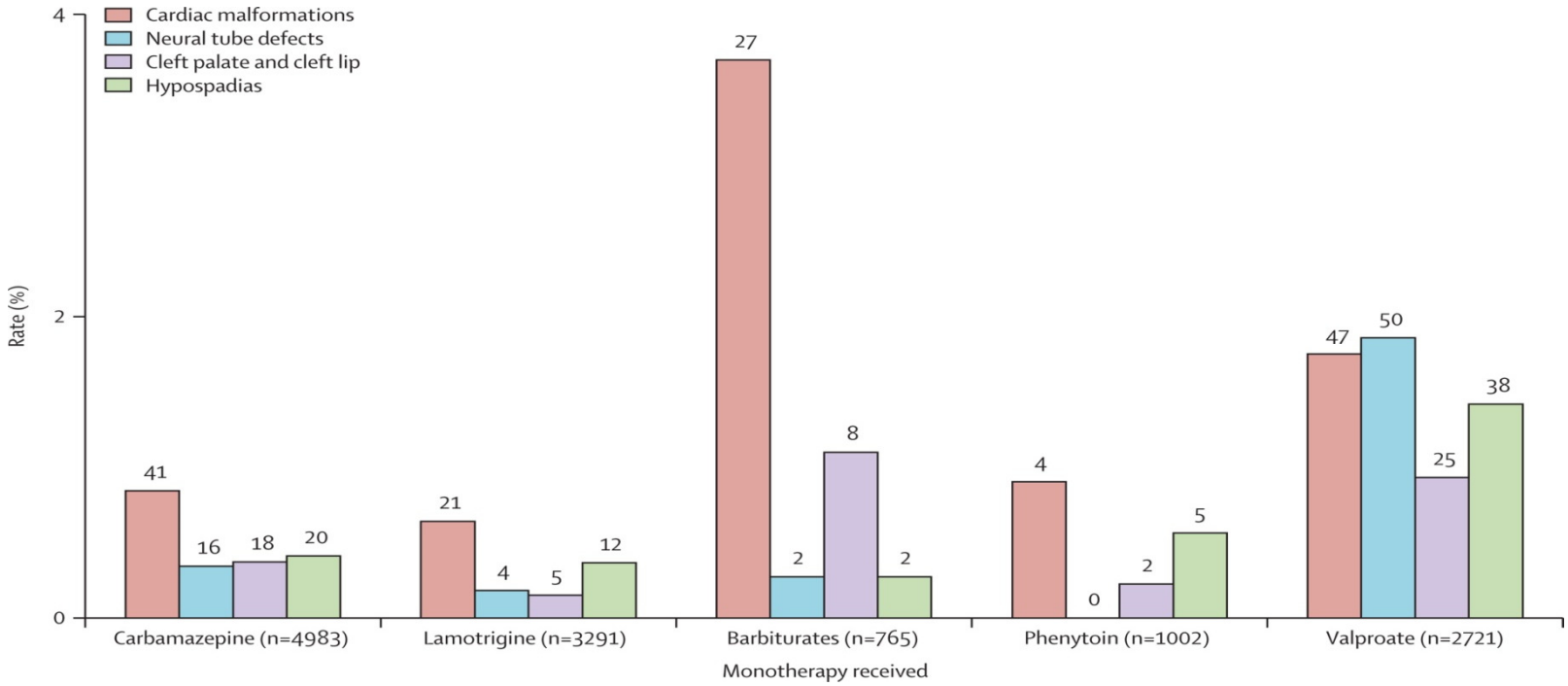
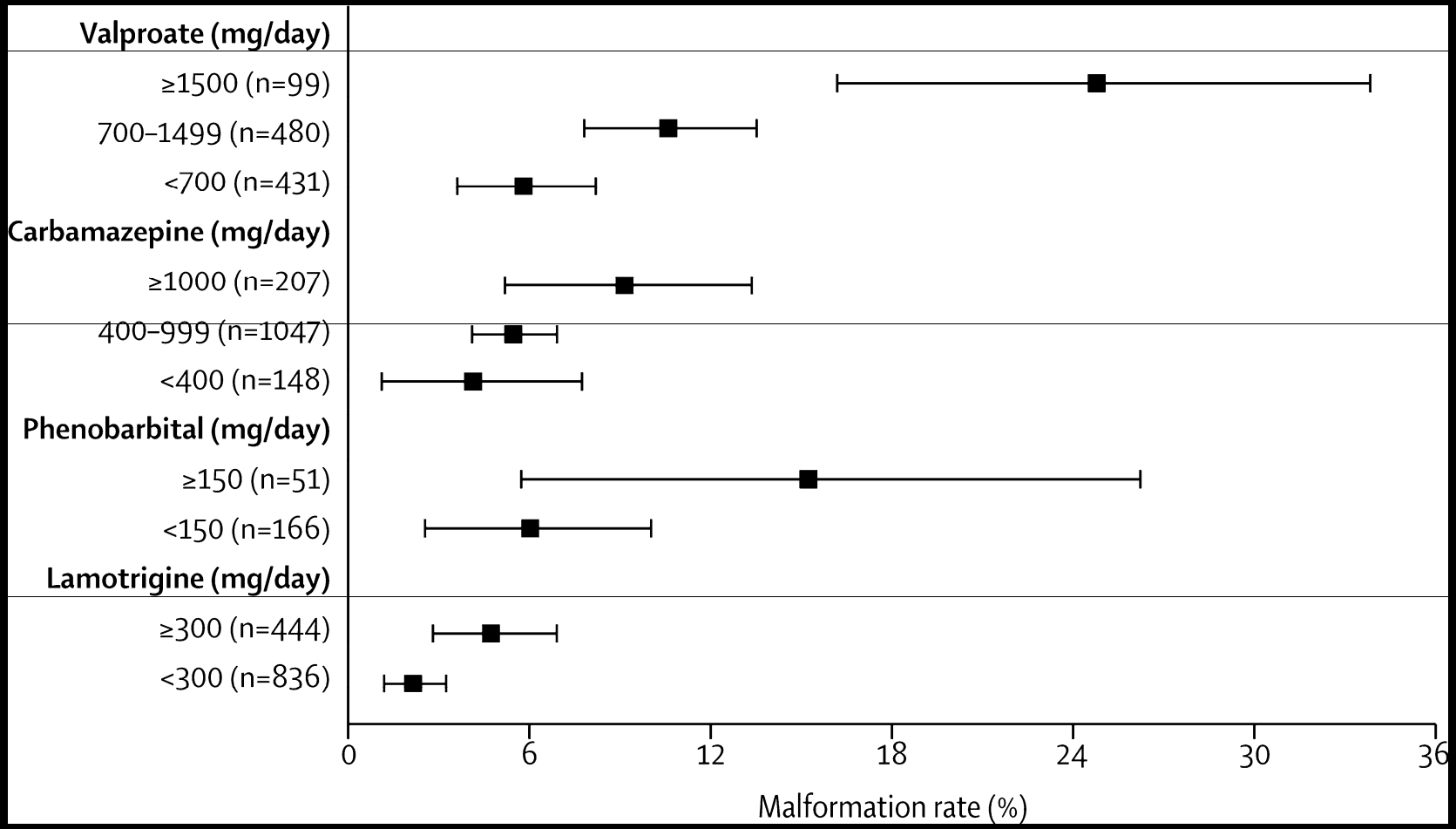


Figure 2 Rates of some specific major congenital malformations associated with exposure to monotherapy with antiepileptic drugs
The number of fetuses with specific malformations are shown on top of the bars. The figure is based on combined data from 21 pr...

Torbjörn Tomson , Dina Battino

Teratogenic effects of antiepileptic drugs

The Lancet Neurology Volume 11, Issue 9 2012 803 - 813


Valproate (mg/day)
≥1500 (n=99)
700–1499 (n=480)
<700 (n=431)
Carbamazepine (mg/day)
≥1000 (n=207)
400–999 (n=1047)
<400 (n=148)
Phenobarbital (mg/day)
≥150 (n=51)
<150 (n=166)
Lamotrigine (mg/day)
≥300 (n=444)
<300 (n=836)
0
6
12
18
24
30
36
Malformation rate (%)

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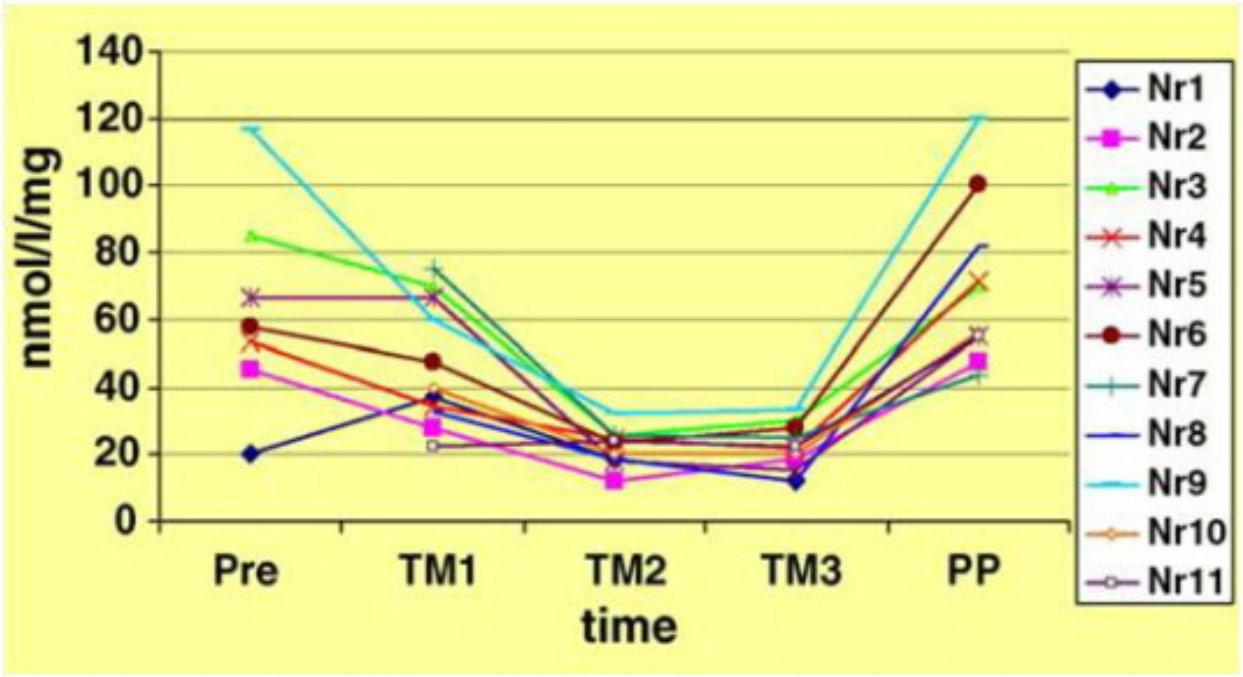
Cognitive Function at 3 Years of Age after Fetal Exposure to Antiepileptic Drugs

Kimford J. Meador, M.D., Gus A. Baker, Ph.D., Nancy Browning, Ph.D., Jill Clayton-Smith, M.D., Deborah T. Combs-Cantrell, M.D., Morris Cohen, Ed.D., Laura A. Kalayjian, M.D., Andres Kanner, M.D., Joyce D. Liporace, M.D., Page B. Pennell, M.D., Michael Privitera, M.D., and David W. Loring, Ph.D., for the NEAD Study Group*

Table 2. IQ Scores of Children at 3 Years of Age According to In Utero Exposure to Antiepileptic Drugs.*

Variable	Carbamazepine (N=73)	Lamotrigine (N=84)	Phenytoin (N=48)	Valproate (N=53)
Mean IQ (95% CI)†	98 (95–102)	101 (98–104)	99 (94–104)	92 (88–97)
Mean difference in IQ from valproate group (95% CI)‡	6 (0.6–12.0)	9 (3.1–14.6)	7 (0.2–14.0)	
P value§	0.04	0.009	0.04	

LMG plasma concentrations

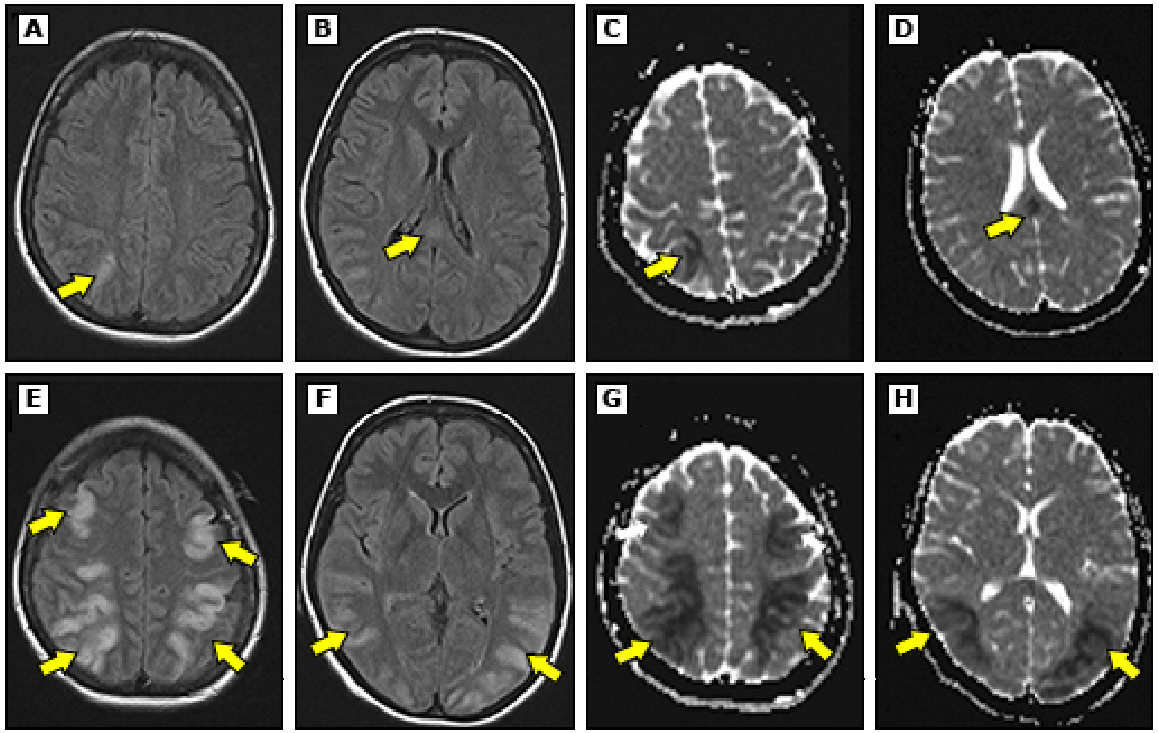


Petrenaite V et al. Epilepsy Research 2005;65:185-8

Thunderclap onset headache

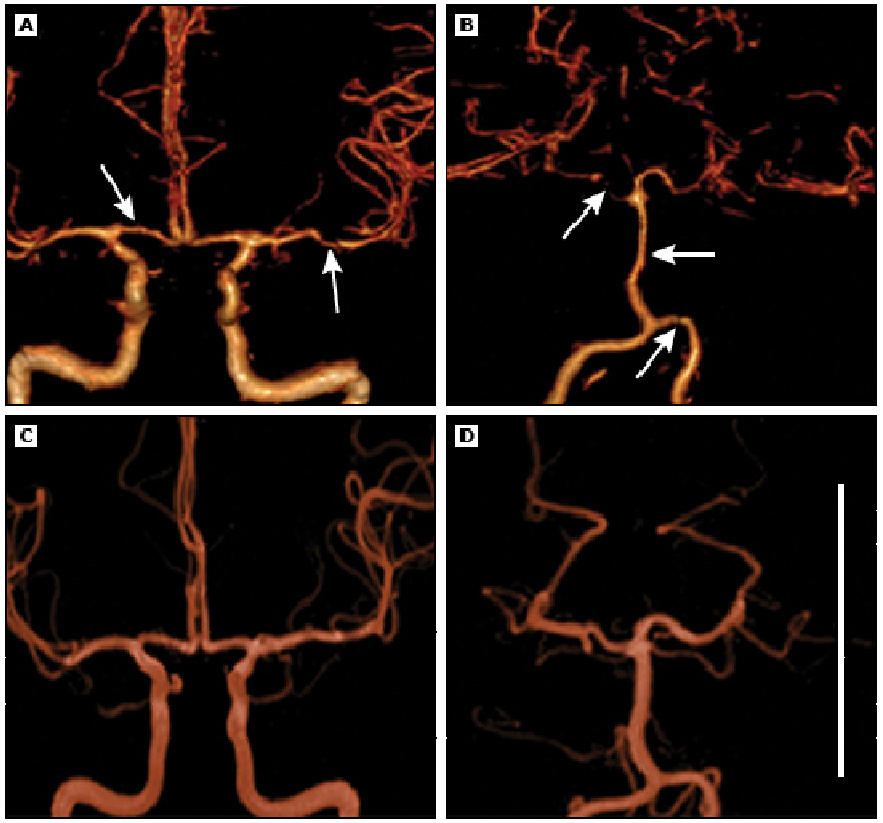
- ? SAH
  - CT
  - Lumbar puncture….. If negative….
- ? Intracranial venous thrombosis / Reversible cerebral vasoconstriction syndrome / Pituitary apoplexy
  - MRI / MRVenogram / MRA

Brain MRI of a 33 year old woman with postpartum angiopathy (reversible cerebral vasoconstriction syndrome)



Head MRI axial cuts: Fluid-attenuated inversion recovery (FLAIR) (A, B, E, F) and apparent diffusion coefficient map (C, D, G, H) sequences.
Upper panel MRI, performed on admission, showed FLAIR hyperintensities and diffusion restriction in the right parietal lobe and in the splenium of the corpus callosum (arrows). Lower panel, done on hospital day 3 when the patient deteriorated, showed worsening bilateral lesions involving the cortex and subcortical white matter of the parietal, posterior frontal, and occipital lobes (arrows).

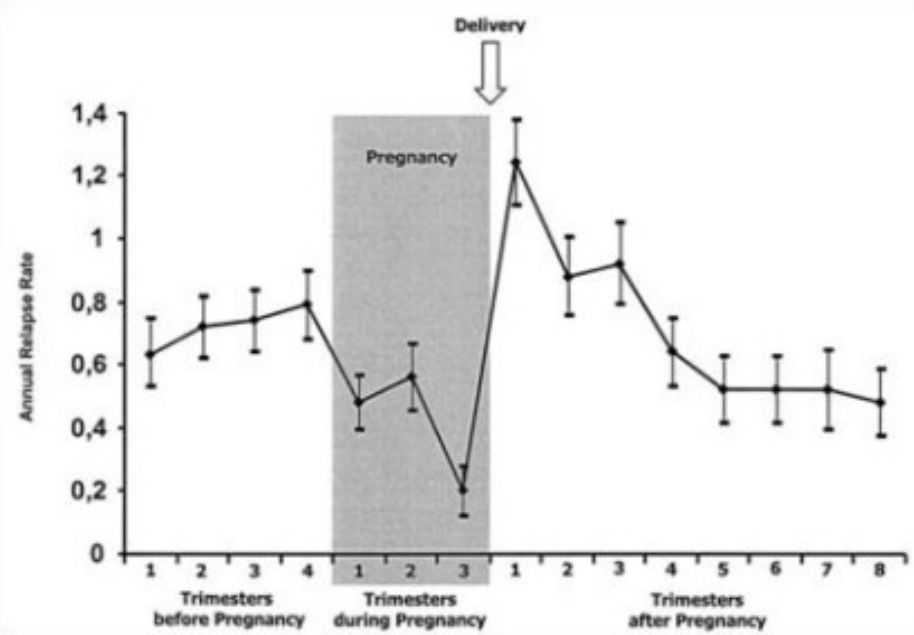
CTA showing segmental narrowing of intracranial vessels in a 33 year old woman with postpartum angiopathy (reversible cerebral vasoconstriction syndrome)



Head CT angiography (CTA) six days after onset of postpartum occipital headache reveals segmental narrowing of the left middle cerebral artery and the A1 segment of the right anterior cerebral artery (panel A, arrows); in addition, there is segmental narrowing of the posterior cerebral and left distal vertebral arteries with broad narrowing of the basilar artery (panel B, arrows). Head magnetic resonance angiography (MRA) two months after discharge shows complete reversal of arterial pathology (panels C and D). The magnification is similar in all parts of the figure; the white vertical band denotes 5 cm.

Multiple Sclerosis

- Symptoms tend to improve in pregnancy



S Vukusic et al. Brain 2004

Multiple Sclerosis

- Steroids safe if needed
- Immunomodulatory therapy
  - Interferon beta
  - Glatiramer Acetate
  - Natalizumab
- Benefit vs risk... Registers suggest no significant increase in risk, but current recommendations to discontinue disease modifying agents preconception

Idiopathic Intracranial Hypertension

- Preponderance in young obese females
- Pregnancy is not an independent risk factor
- Anecdotally often presents in second trimester
- Treatment:
  - Weight loss
  - Acetazolamide (exacerbates potassium loss and HCO3)(try to avoid in first trimester)
  - Diuretics – discouraged
  - Repeat LP
  - Optic nerve sheath fenestration

Conclusion

- Pregnancy is a special circumstance
- Pre-pregnancy counselling is imperative
- The order of the differential diagnosis may change in pregnancy
- Most neurological conditions are treated similarly in pregnancy
- Ideal is a multidisciplinary team (neurologist, obstetrician, obstetric anaesthetist, midwife)
- Consider:
  - Mode of delivery
  - Mode of anaesthesia
  - Management of second stage
  - Breastfeeding
- See patients more often not less often during pregnancy