



## **Association of British Neurologists Self Assessment Exercise 2006 - ANSWERS**

### **QUESTION 1**

A 40-year-old female gave a 4 month history of daily headache which had started during a bout of "flu". She described a bilateral pressure feeling, occasionally associated with nausea but no photophobia or phonophobia. She would awaken headache free, but the headache would evolve soon after getting up and worsen through the day. She did not usually suffer headaches other than occasional "tension" headaches, and there was no family history of headache. She was a non-smoker and drank 7 units of alcohol per week. She was not taking any regular medication but used ibuprofen 2-3 times per week. On examination there were no abnormal findings.

The following results were normal: CT brain scan, ESR and autoantibody screen.

Which of the following is the most appropriate next step?

### **ANSWER OPTIONS:**

- A: Trial of indomethacin
- B: Trial of a suitable migraine prophylactic agent
- C: Lumbar puncture
- D: MRI brain with gadolinium
- E: Withdraw ibuprofen

### **SUGGESTED ANSWER D - EXPLANATION / COMMENTS**

This lady has a chronic, bilateral, largely featureless headache with a distinctive postural pattern, suggestive of a low CSF volume (or pressure) headache.

MRI with gadolinium may show diffuse pachymeningeal enhancement occasionally with subdural collections, although it is often normal.

Whilst a lumbar puncture may confirm low pressure, it might further exacerbate the symptoms.

Indomethacin-sensitive headaches tend to be unilateral.

Although the patient is taking ibuprofen it is unlikely to be the cause of her daily headache.

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### **QUESTION SETTER:**

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**QUESTION 2**

History: A 30 year-old man presented with a 5-month history of a constant, dull frontal headache of moderate severity, worst when bending over. It was accompanied by nausea, phonophobia and photophobia. For 2 weeks prior to admission he had lost patches of hair over his scalp, some of his body hair, and his eyelashes. The week prior to presentation he had developed an evolving left hemiparesis, involving the left side of his face. Six months prior to presentation he noted a widespread skin rash with malaise and lymphadenopathy, but had not sought medical attention. He was homosexual, but had no sexual contact for 18 months. Examination: He had generalised alopecia, angular cheilitis, oral aphthous ulceration and ulcerative gingivitis. He had a mild dysarthria, left facial weakness sparing the forehead, and a left hemiparesis (grade 0 in the arm, and grade 2 in the leg). Deep tendon reflexes were brisk throughout and the left plantar response was extensor. The rest of the examination was normal.

Investigations: FBC normal other than lymphocytes  $0.95 \times 10^9/l$  (1.5 to 4.0); U&E, random glucose, LFT, TFT, B12 normal; CRP 18; hepatitis serology normal; serum EBV and CMV IgG antibodies positive; toxoplasma gondii IgG antibody negative; CT brain: normal; MRI brain: see figure; CSF: opening pressure 15cm, protein 2.31g/l, glucose  $<1.1$  mmol/l (paired serum glucose 6.7 mmol/l), WCC 165/mm<sup>3</sup> (polymorphs 90%, lymphocytes 10%), RCC 840/mm<sup>3</sup>, cryptococcal antigen negative, PCR for JC virus, CMV, HSV 1&2, and VZV negative.

Figure A: T1 sagittal non-contrast MRI

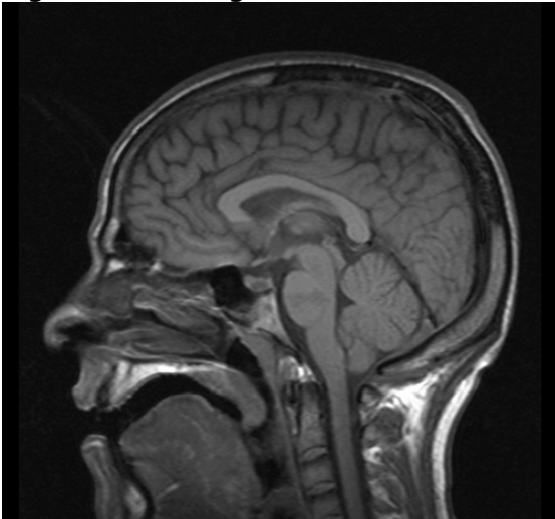


Figure B: T1 axial contrast enhanced MRI

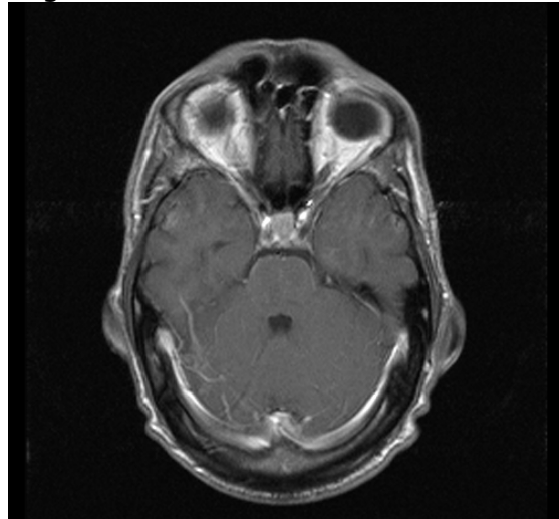


Figure C: T2 axial MRI

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: Progressive multifocal leukoencephalopathy
- B: HIV seroconversion
- C: Cerebral toxoplasmosis
- D: Meningovascular syphilis
- E: Tuberculous meningitis

SUGGESTED ANSWER D - EXPLANATION / COMMENTS

The serum anti-treponemal IgM was positive (6.384, positive >1.1), as was the CSF anti-treponemal IgM. The patient was also found to be HIV positive. CSF culture for mycobacteria was negative. He was treated with HAART and high dose penicillin with considerable improvement of his hemiparesis.

Syphilis is classified as primary, secondary, tertiary, or quaternary. Tertiary lesions are caused by obliterative small vessel endarteritis, which usually involves the vasa vasorum of the CNS. Tertiary syphilis comprises 3 types: neurosyphilis, cardiovascular syphilis, and late benign (gummatous) syphilis. Acute or subacute aseptic meningitis is present even in primary syphilis. The main types of neurosyphilis are: asymptomatic, acute syphilitic meningitis, meningovascular syphilis, tabes dorsalis, general paresis and optic atrophy. In meningovascular syphilis, there is typically a subacute meningoencephalitic prodrome, followed by a gradually progressive vascular syndrome.

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### QUESTION 3

In which of the following individuals would it be most appropriate to consider chronic subthalamic nucleus stimulation?

#### ANSWER OPTIONS:

- A: A 45-year-old man with a 14 year history of Parkinson's disease suffering from frequent 'on-state' freezing episodes each day, in spite of optimal medical treatment.
- B: A 52-year-old woman with a one year history of a rapidly progressive severe bilateral akinetic-rigid form of parkinsonism not responding to levodopa.
- C: A 72-year-old woman with an 18 year history of Parkinson's disease having frequent falls in spite of optimal medical treatment.
- D: A 59-year-old man with a 12 year history of Parkinson's disease experiencing severe frequent dyskinesias whilst in the 'on state' each day.
- E: A 45-year-old man with a history of hypertension having 'lower half' parkinsonism, consisting mainly of gait difficulties.

#### SUGGESTED ANSWER D - EXPLANATION / COMMENTS

STN stimulation does not help 'on-state' freezing.

The effects of STN stimulation correlate with the response to levodopa, so is unlikely to be effective for LD unresponsive forms of parkinsonism

Falls are not likely to be improved by STN stimulation and are a relative contra-indication to STN surgery – consider danger of sub-dural. However, there are some caveats for example falls caused by severe dyskinesia. Additionally, most centres have a cut off for STN stimulation at 60-65 years because the beneficial results of STN stimulation are inversely proportional to the patient's age.

STN stimulation is effective for dyskinesia. An alternative would be Globus pallidus internus stimulation.

Lower half parkinsonism suggests cerebrovascular parkinsonism which would not be expected to respond to STN stimulation.

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#### QUESTION 4

A 13-year-old boy presented with an 18 month history of failing at school, in part due to problems with bad behaviour and poor concentration. Of late it had also been noted that he had become slower in his movements. He had a normal birth and developmental history, but in the family history his father had died a year ago, at the age of 42, from a neurological disorder that had rendered him bed bound and demented over a 15 year period. His older sister and mother were well with no neurological problems.

On examination he was hard to engage, was bradykinetic with markedly abnormal eye movements, with an almost complete absence of saccades and a very unstable gait. On neuropsychological testing he had clear deficits in a number of domains, but especially with tasks sensitive to the frontal lobe.

His MRI brain was normal as was his routine blood testing including copper studies.

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: New variant CJD (nvCJD)
- B: Juvenile Huntington's disease (JHD)
- C: Metachromatic leukodystrophy (MLD)
- D: Attention deficit hyperactivity disorder (ADHD)
- E: Parkin positive Parkinson's disease

#### SUGGESTED ANSWER B - EXPLANATION / COMMENTS

The story is typical for juvenile HD with the major behavioural problems, bradykinesia, eye movement abnormalities, but little chorea. The family history would also be in keeping with HD, as in juvenile cases the inheritance is typically from the father, who in this case developed the disease early in life as well. Thus in cases such as this the CAG repeat length in the Huntington gene is typically >50, with <36 being normal, 36-39 affected with reduced penetrance and >39 being diagnostic of HD.

The normality of the scan and family history argues against a MLD, and the presence of neurological deficits means it cannot be ADHD. The history and examination is rather long and atypical for nvCJD, as is the age of the patient and the family history would then have to be irrelevant. In parkin positive PD cases, there are normally striking lower limb problems in the context of a parkinsonian phenotype, but the cognitive deficits in the patient are not in keeping with this condition. In addition the history in the affected father is not in keeping with this condition, which progresses very slowly.

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### **QUESTION 5**

A 63-year-old woman developed transient deafness on the left, followed 24 hours later by severe persistent left-sided deafness, vertigo, loss of balance and left-sided cerebellar signs.

Which of the following disorders best explains this syndrome?

ANSWER OPTIONS:

- A: Anterior inferior cerebellar artery (AICA) infarct
- B: Ménière's disease
- C: Posterior inferior cerebellar artery (PICA) infarct
- D: Ramsay Hunt syndrome (Herpes Zoster oticus)
- E: Vestibulo-cerebellar neuritis

### **SUGGESTED ANSWER A - EXPLANATION / COMMENTS**

The stuttering onset then sudden severe persistent features suggest a vascular cause. The internal auditory artery is usually a branch of AICA (sometimes it arises directly from the basilar artery). This patient has a partial AICA syndrome. The full-blown syndrome also involves damage to other inferior pontine structures.

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**QUESTION 6**

A 73yr old man presented with sudden-onset headache behind his right eye after cleaning his pond. The severe headache persisted for several days. He was otherwise asymptomatic. He had a CT scan of his head with contrast which showed the abnormality evident in Figure 1. There were no other abnormalities. His headache resolved and he was discharged.

Two weeks later he developed a similar, although milder, headache following sexual intercourse. The following morning he found he could not see all his fingers, missing those in the left visual field. On admission he was found to have a complete left homonymous hemianopia. A further CT scan of the head was performed (Figure 2). CT angiography was normal.

Figure 1: CT scan of the head with contrast (two cuts)

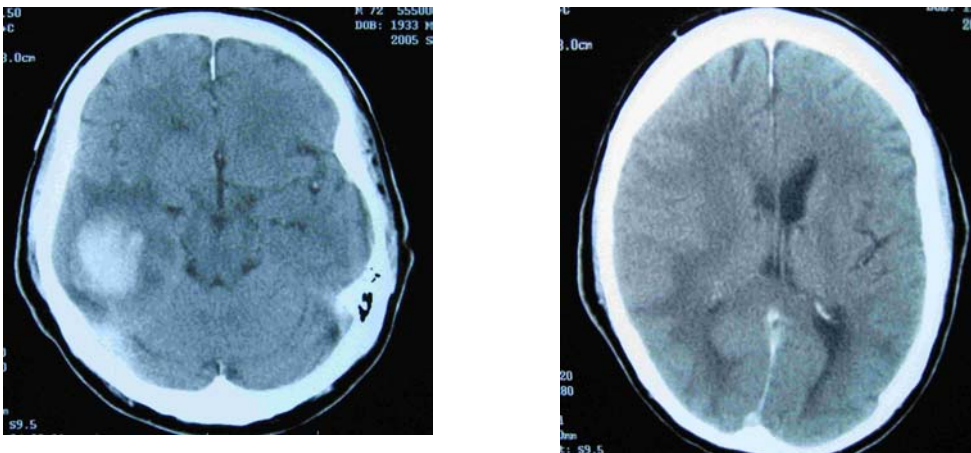
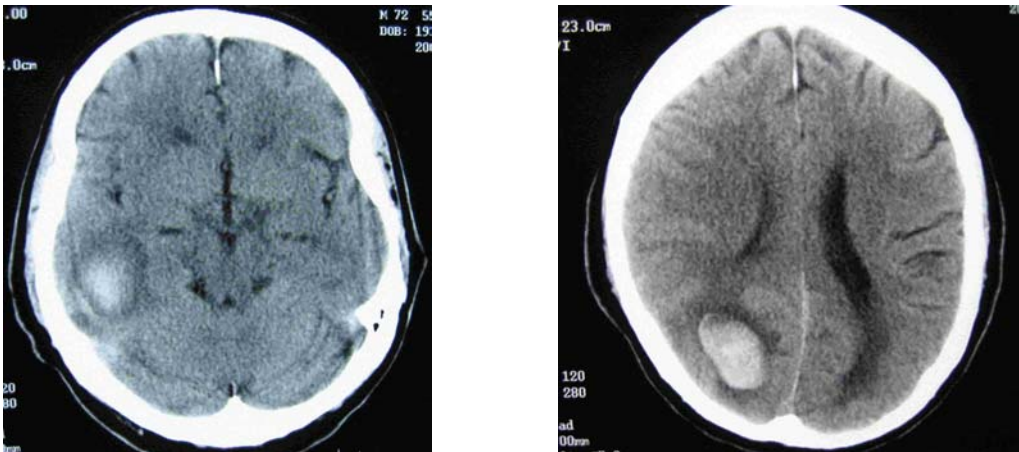


Figure 2: CT Scan of the head (equivalent cuts to original scan)



What is the most likely underlying diagnosis?

ANSWER OPTIONS:

- A: Aneurysmal bleed
- B: Arteriovenous malformation
- C: Cerebral amyloid angiopathy

- D: Hypertensive bleed  
E: Metastatic disease

### SUGGESTED ANSWER C - EXPLANATION / COMMENTS

Normal CT angiography and the intraparenchymal nature of the bleed make an aneurysmal source unlikely. Normal CT angiography also reduces the likelihood of these bleeds being due to underlying AVMs. The haemorrhages are not in a typical location for hypertensive bleeds, which are characteristically in the basal ganglia. The fact that the initial contrast CT did not demonstrate a right occipital lesion makes metastatic disease less likely.

Cerebral amyloid angiopathy (CAA) is estimated to account for up to 15% of all intracerebral haemorrhage (ICH) in patients older than 60 years and up to one half of nontraumatic lobar ICH in patients older than 70 years. CAA refers to the deposition of  $\beta$ -amyloid in the media and adventitia of small- and mid-sized arteries (and less frequently, veins) of the cerebral cortex and the leptomeninges. It is a component of any disorder in which amyloid is deposited in the brain, and it is not associated with systemic amyloidosis. CAA has been recognized as one of the morphologic hallmarks of Alzheimer disease (AD), but it also is found often in the brains of elderly patients who are neurologically healthy. While often asymptomatic, CAA can present as intracranial haemorrhage (ICH), dementia, or transient neurological events. ICH is the most consistent effect of CAA. Although the vast majority of cases are sporadic, two familial forms exist: Hereditary Cerebral Haemorrhage with Amyloidosis [HCHWA]-Dutch type and HCHWA-Icelandic type.

The most consistent clinical effect of CAA is lobar ICH. Lobar ICH is associated with a lower mortality rate (11-32%) and a better functional outcome than hypertensive deep ganglionic bleeds. Of individuals with CAA-related haemorrhage, 25-40% have a recurrence, with the highest risk in the first year. Recurrent haemorrhages can occur simultaneously or several years later. They are associated with a high mortality rate (up to 40%). Patients with a previous haemorrhage are at greater risk for subsequent haemorrhages than those with no history. Hypertension may exacerbate the tendency to CAA-related haemorrhage and vice versa. Cortical petechial haemorrhage can be epileptogenic. Cognitive impairment is a common feature of CAA. More than 40% of patients with ICH-related haemorrhage have some degree of dementia. In some cases, the cognitive changes can precede the ICH. The relationship between CAA and AD is close. CAA, which is present in 80-85% of patients with AD, is severe in one third to two thirds of these patients. Dementia may be manifested by any of several patterns of cognitive dysfunction. Some patients present with rapid progression from a normal baseline to profound dementia in a couple of years. Other patients can have a more protracted course, which is more typical of that seen in AD.

The management of CAA-related ICH is identical to the standard management of ICH, with special attention to reversing anticoagulation, managing intracranial pressure, and preventing complications.

#### REFERENCES:

<http://www.emedicine.com/NEURO/topic628.htm>

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**QUESTION 7**

You are asked to see a 56-year-old man on a general surgical ward.

He has Crohn's disease and ankylosing spondylitis. As a young man, he required multiple GI operations, but his inflammatory bowel disease has been relatively quiescent for some years. He had no family history of note and he takes NSAIDs and sulphasalazine.

He was admitted under the surgeons with a six month history of weight loss, abdominal pain and watery diarrhoea, which grew nothing on culture. Eventually, he had a laparotomy at which some adhesions were found, but no evidence of active inflammatory bowel disease. His symptoms settled, more or less, but he failed to mobilise after the operation, because of "dizziness".

You elicit a history of erectile impotence for five years and 10 years of urinary frequency and nocturia for longer, attributed by him to "prostate". He admits to having intermittently felt "dizzy" on standing for at least three years, and to "blacking out" on three occasions in the last year when getting out of bed at night.

On examination, lying down, there are no abnormal signs apart from poor constriction of the pupils to light. Power, sensation and reflexes are normal and there are no signs of parkinsonism. However, he is unable to stand for more than a few seconds, because of postural hypotension: 160/90 lying, 65/undetectable standing.

Blood and urine tests done on the surgical ward, including tests to diagnose diabetes, are normal or negative. An ECG shows sinus rhythm with no R-R variation on respiration.

Which diagnosis best accounts for the clinical picture?

ANSWER OPTIONS:

- A: Multiple System Atrophy
- B: Autonomic neuropathy due to primary amyloidosis
- C: Primary autoimmune autonomic neuropathy
- D: Autonomic neuropathy due to amyloidosis secondary to chronic inflammation
- E: Sjogren's syndrome

SUGGESTED ANSWER C - EXPLANATION / COMMENTS

He has pure autonomic failure, without clinical evidence of parkinsonism or neuropathy.

The first diagnostic issue is whether this is peripheral or central. The circumstantial evidence suggests that it is peripheral because a central aetiology (MSA/Shy-Drager syndrome) would, after ten years, have evolved definite symptoms and signs of parkinsonism and/or cerebellar deficits. A tyramine test can usefully distinguish these two on the basis that denervation of the vascular bed (in neuropathy) can lead to receptor hypersensitivity and hence a hypertensive response to tyramine that would not be seen in a central cause of autonomic failure.

Top of the list of causes of an autonomic neuropathy on most people's lists would be diabetes (which has been excluded here) and then primary amyloidosis. The median survival of patients with primary amyloidosis and a neuropathy is 13-35 months, so he is doing rather too well for that condition. Importantly, amyloidosis secondary to chronic inflammatory diseases does not cause an autonomic neuropathy.

A recent survey has highlighted the disproportionate autonomic involvement seen in the neuropathy associated with Sjogren's syndrome, but this was never seen as an isolated phenomenon for as long a time as in this case. The history is too long for an autonomic Guillain-Barre or a paraneoplastic autonomic neuropathy. The entity of "autonomic CIDP" does exist, but without clinical signs of a neuropathy, that seems a brave diagnosis. Rare and terribly unlikely causes in this context are the various hereditary autonomic neuropathies, infectious diseases with autonomic involvement (Chagas and HIV), and toxins (marine toxins, organic solvents).

Primary autoimmune autonomic failure is relatively newly described. It is caused by antibodies to the ganglionic acetylcholine receptor (a serum test for which is available from Prof. Angela Vincent's laboratory), which are definitely pathogenic as they cause a similar syndrome in animals. Patients can have autonomic failure for decades without clinical signs of a neuropathy. Even in the face of a long history, plasma exchange is well worth a shot. Reasonable responses have also been achieved with IVIG. As well as the standard treatments of orthostatic hypotension (amongst which should now be included midodrine), it has been suggested that L-DOPS (L-threo-3,4-dihydroxyphenylserine) is especially beneficial in these patients.

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### QUESTION 8

A 40-year-old man developed progressive weakness and numbness of the legs then arms over 8 weeks. On examination he was bed bound with symmetrical weakness of upper and lower limbs, MRC grade 2-3 proximally and distally. Tendon reflexes were absent. There was glove-and-stocking sensory loss to all modalities. Cranial nerves were normal apart from bilateral papilloedema. His spleen tip was palpable.

Investigations showed: full blood count, renal and liver function, calcium all normal; biochemical evidence of hypothyroidism; IgA lambda paraprotein 2g/L; immunoglobulin levels otherwise normal; CT brain scan normal; CSF pressure and contents normal; skeletal survey: solitary sclerotic lesion in right ilium.

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: Chronic inflammatory demyelinating polyradiculoneuropathy with monoclonal gammopathy of undetermined significance (CIDP-MGUS)
- B: Guillain Barré syndrome with MGUS
- C: Multiple myeloma
- D: POEMS syndrome
- E: Primary systemic amyloidosis

#### SUGGESTED ANSWER D – EXPLANATION / COMMENTS

POEMS syndrome is an acronym for polyneuropathy-organomegaly-endocrinopathy-M-band-skin changes. This patient had four of the cardinal features (all 5 need not be present). There is a strong association with osteosclerotic myeloma. Papilloedema may be present with normal CSF pressure and protein and may result from abnormal angiogenesis. The most common associated paraprotein is IgG lambda or IgA lambda. The history of progression is too long for GBS, which would also be expected to involve cranial nerves with such severe limb weakness. CIDP would not explain the endocrinopathy and organomegaly. Primary systemic amyloidosis usually presents with a painful predominantly sensory neuropathy with prominent autonomic features. Multiple myeloma would also be more likely to present with a painful sensory neuropathy and there were no lytic lesions on the skeletal survey.

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### QUESTION 9

A 27-year-old Vietnamese man presented to Casualty with rapidly progressive weakness of the limbs which had developed over the previous 3 hours, following a heavy meal. On examination, cranial nerves were normal. There was profound proximal and distal weakness of all 4 limbs. Tendon reflexes were absent. Sensory examination was normal. The admitting medical team managed him for Guillain-Barré syndrome but by the next morning he had returned to normal.

What is the most likely underlying endocrinopathy?

ANSWER OPTIONS:

- A: Hyperaldosteronism
- B: Hyperthyroidism
- C: Hypoaldosteronism
- D: Hypopituitarism
- E: Hypothyroidism

### SUGGESTED ANSWER B - EXPLANATION / COMMENTS

Though hyperaldosteronism may present with hypokalaemic periodic paralysis, it is very rare and the thyrotoxic form is seen in south-east Asian patients.

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**QUESTION 10**

An otherwise healthy man aged 26 was in a psychiatric hospital undergoing an addiction treatment programme for cocaine and alcohol for 10 days. He had been receiving multivitamins and thiamine. On day 11 he went for a fast swim, including a strenuous 25m underwater swim. The following day he passed dark urine on three occasions and his muscles felt a little sore. He had a serum creatine kinase of 30,000 U/L and when this result was discovered two days later he was admitted to the local district general hospital. He recalled having had at least three similar episodes of dark urine after exercise since the age of 20. There was no family history of relevance. General and neurological examination were normal. The serum creatine kinase was now 3,000. Urea and electrolytes and FBC and ESR were normal. He received 2.5 l of saline and was discharged on the following day. Five days later, the serum creatine kinase, electromyography and nerve conduction were normal. An ischaemic exercise test showed normal lactate elevation. A muscle biopsy was planned.

What is the most likely diagnosis at this stage?

ANSWER OPTIONS:

- A: Malignant neuroleptic syndrome
- B: Polymyositis
- C: A form of muscular dystrophy
- D: A disorder of muscle glycogen metabolism (e.g. phosphorylase deficiency)
- E: A disorder of muscle lipid metabolism (e.g. carnitine/carnitine palmitoyl transferase deficiency)

**SUGGESTED ANSWER E - EXPLANATION / COMMENTS**

There is no history of neuroleptic consumption or seizures. There is no clinical evidence of muscle weakness and no myopathic potentials on EMG, which would be expected on a form of muscular dystrophy and in an acute alcoholic myopathy and, usually with fibrillations, in polymyositis. The patient has the syndrome of Recurrent Paroxysmal Myoglobinuria triggered by exercise. Muscle disorders of glycogen metabolism (commonest is phosphorylase deficiency) result in an abnormal ischaemic exercise test with no rise in lactate whilst this test is normal in disorders of muscle lipid metabolism (commonest is carnitine palmitoyl transferase deficiency). It is unusual in the metabolic disorders for acute rhabdomyolysis to be followed by acute renal failure. The muscle biopsy can help to identify a number of different metabolic causes. In a proportion of cases of this syndrome (50%-60%), no cause is found. The muscle biopsy may fail deliver the diagnosis of CPT 2: a useful initial investigation here would be to measure carnitine: acylcarnitine levels and ratio and, if abnormal, do a skin biopsy and fibroblast culture to confirm the specific metabolic and enzyme diagnosis. CPT 2 activity can also be measured in muscle tissue.

REFERENCES:

Tonin et al. Metabolic causes of myoglobinuria. Ann Neurol 1990; 27: 181.

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### QUESTION 11

A mildly obese 70-year-old man presented with a one year history of episodes of movements in sleep, occurring most nights, sometimes on several occasions in one night. He himself was not aware of the movements but he was brought to medical attention by his wife, who described stereotyped repetitive flexion/extension movements, apparently confined to the legs, lasting for a few minutes at a time. They sometimes disturbed his sleep and, after bad nights, he felt tired the next day and fell asleep easily. He had a 10 year history of diabetes, treated with dietary restriction and an oral hypoglycaemic agent. Six years earlier, he had had a sudden onset of a left hemiparesis that resolved over two weeks, diagnosed as an ischaemic stroke without investigation. Five years previously, he had had a single generalised tonic-clonic seizure, assumed to be secondary to the stroke, without investigation or treatment. He was reported to snore on some occasions. Neurological examination was generally unremarkable, although the ankle jerks were absent and he had lost vibration sense below the knees.

Which one of the following statements, relating to the episodic movements, is most likely to be true?

ANSWER OPTIONS:

- A: The movements are likely to occur in REM-sleep phases.
- B: The most likely diagnosis is epilepsy.
- C: The symptoms may respond to an L-DOPA containing drug.
- D: The problem is likely to be secondary to sleep apnoea.
- E: A cause needs to be sought with cerebral MRI

### SUGGESTED ANSWER C - EXPLANATION / COMMENTS

The most likely diagnosis is that of Periodic Limb Movements of Sleep (PLMS). Such movements are generally linked to non-REM sleep phases and are generally absent in REM sleep phases. They can cause poor sleep with arousals and lead to excessive daytime drowsiness the next day.

PLMS is relatively common with aging and, while it can be associated with other conditions, including diabetic polyneuropathy, may occur in healthy individuals. Cerebral MRI is not a helpful in investigation. There is no compelling evidence for sleep apnoea in the presented history and the movements appear to be the primary problem. Some tendency to snoring is not uncommon. The story as presented is not suggestive of epilepsy. L-DOPA may be helpful in treatment.

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**QUESTION 12**

The general medical team requested a neurological review of a 49-year-old woman who had been admitted a week previously. She had been brought to casualty by her husband following repeated falls at home. Although the patient herself was alert and attempting to be co-operative, she was not able to provide a coherent history. Her husband said that she had, in retrospect, been having increasing difficulty for the previous year. Initially this had manifested with disengagement from her hobbies and friends. She had been treated for depression with fluoxetine by her GP but this had not helped. Things had worsened gradually such that in the week prior to admission she had begun to lose her way around the house, had become incontinent of urine and then started to fall frequently, culminating in her admission.

She scored 10 out of 30 on the Mini-Mental State Examination. Neurological examination was otherwise normal. Blood test results showed normal full blood count, urea and electrolytes, liver function, calcium, thyroid function, B12 / folate and VDRL. ESR was 28.

Plain CT scan performed on admission by the general medical team showed ventricular dilatation but no other changes. Cerebrospinal fluid examination had shown the following: Opening pressure 18 cm of water, 5 white cells (mononuclear), no red cells, protein 0.75 g/l, glucose 3.5 mmol / l (blood 5.2). No sample sent for cytology.

What is the most appropriate next management step?

ANSWER OPTIONS:

- A: EEG
- B: Removal of 30 mls of CSF followed by 10m timed walking test;
- C: MR brain imaging with gadolinium;
- D: Start treatment with cholinesterase inhibitor;
- E: Urgent referral to the neurosurgical team to request ventriculoperitoneal shunt placement.

**SUGGESTED ANSWER C - EXPLANATION / COMMENTS**

Presentation with cognitive impairment, urinary incontinence and gait instability is often thought to suggest normal pressure hydrocephalus but would seem quite unlikely at the age of 49, making B an unsatisfactory option. Similarly, one would wish to investigate further a woman of this age presenting with an apparent dementing illness before starting treatment with a cholinesterase inhibitor (D). The mildly raised ESR hints at an underlying cause, as does the borderline white cell count and mildly raised protein level in the CSF. It would be important to search for a malignant cause for her presentation, through at least one repeat CSF specimen sent for cytological examination, and probably including a "screen" for a primary tumour elsewhere. An EEG may show minor abnormalities but is likely to be non-specific (A) and there is no suggestion of seizure activity in the clinical details. Before referring her for neurosurgical intervention (E) in the absence of acute deterioration, it would be necessary to perform further brain imaging with MR and, most importantly, with gadolinium enhancement (C) to ensure that an underlying cause for her presentation was not missed.

This was a real case in which further imaging with gadolinium showed clear meningeal enhancement and patchy parenchymal change. The aqueduct was patent. CXR was normal as were pulmonary function tests but CT chest demonstrated marked hilar lymphadenopathy and reticular change in the lung fields. Old notes from another hospital revealed excision of a cutaneous sarcoid lesion 10 years previously. She was treated with steroids and her cognitive function improved dramatically over a number of weeks. Repeat CSF has shown resolution of the mild aseptic meningitis but the ventricular dilatation has not

diminished. A year later her cognitive function has returned to its expected pre-morbid level and her steroid treatment has been gradually withdrawn although she remains on a low dose. Further treatment options are being considered.

Hydrocephalus in neurosarcoidosis is rare but described. Speculation as to its aetiology caused vigorous discussion in our unit. Presumably, as there was no obstruction to the flow of CSF, one could postulate a problem with absorption through the arachnoid granulations being adversely affected.

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ACKNOWLEDGEMENT:

The patient was under the care of Dr Martin Prevett, Consultant Neurologist, Wessex Neurological Centre, Southampton.

QUESTION SETTER:

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**QUESTION 13**

A neurological review was requested for an unconscious 65-year-old man, who had been admitted 4 weeks before with a proven subendocardial myocardial infarction. Three weeks later he had had 2 coronary by-pass grafts, but his postoperative course had been complicated by a period of ventricular fibrillation lasting about 7 minutes. There had been subsequent haemodynamic instability requiring a temporary intra-arterial balloon pump.

On weaning him from the ventilator he had been found to be unresponsive to all painful stimuli. He made inadequate respiratory efforts, and coughed to suction; he had normal pupillary, corneal and doll's head movements. He had not had Propofol for 24 hours, and his urea, electrolytes, glucose and arterial gases were normal.

A representative slice of a CT brain scan is shown:-



What is the most likely cause of the patient's unresponsiveness?

ANSWER OPTIONS:

- A: Diffuse cortical ischaemia
- B: Brain stem ischaemia
- C: The Right frontal infarction
- D: Delayed excretion of anaesthetic drugs
- E: Critical illness neuropathy

**SUGGESTED ANSWER A - EXPLANATION / COMMENTS**

Focal supratentorial lesions do not affect consciousness until the reticular activating centres in the brainstem are distorted, and the brainstem is clearly functioning reasonably well here. The propofol will be long gone, and there is nothing to suggest a metabolic cause. His complete unresponsiveness, and the short history, are incompatible with critical illness neuropathy.

The prognosis must be 'guarded'. Many of these patients recover slowly, but often incompletely, and only too often the cardiological problems prove fatal during this time. This patient died a week after this assessment.

REFERENCES:

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**QUESTION 14**

A 48-year-old man was seen in clinic complaining of jerkiness of his arms and stiffness of his neck. He recalled being jerky as a teenager, without ever having had a seizure. He suffered from depression and anxiety in his early 20s, and was prescribed trifluoperazine for 9 months, after which he took diazepam regularly until his late 30s. During this time, his movements were much less prominent. Since stopping medication, his mental state had remained stable, although he admitted to being obsessional. He subsequently noted that his jerks, predominantly affecting the right arm, trunk and face and sparing the legs, had returned. Over the few years prior to referral he had noticed increased stiffness of his neck, which tended to turn backwards and to the right, and that his writing had become jerky. He did not smoke, but drank alcohol regularly. The family history was limited, but his father was said to have had limb jerks, to have been depressed, and to have died of liver failure.

On examination the MMSE was 28/30. There was a jerky torticollis to the right with a degree of retrocollis. The eye movements were normal. Intermittent brief facial jerks were seen, but there was no blepharospasm, or oro-facial dyskinesia, and tongue and palatal movements were normal. In the limbs there were prominent brief jerks of the right hand and arm on movement, which were present to a lesser extent on the left and trunk. Writing was effortful and jerky, but there was no bradykinesia or rest tremor. There were no cerebellar signs. Lower limb examination was entirely normal. The reflexes were all present and the plantar responses were flexor. The gait was normal.

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: Huntington's disease
- B: Myoclonus-dystonia
- C: Neuroacanthocytosis
- D: Tardive dyskinesia
- E: Tourette's syndrome

**SUGGESTED ANSWER B - EXPLANATION / COMMENTS**

The case presented is fairly typical for the myoclonus-dystonia syndrome. Patients present with predominantly upper body myoclonus in their childhood/teenage years. Patients commonly develop upper body dystonia, with cervical dystonia and writer's cramp being particularly common. The lower limbs are generally spared. Panic attacks, anxiety and obsessive compulsive disorders are associated features. The disease is inherited in an autosomal dominant fashion, usually due to mutations in the epsilon-sarcoglycan gene on chromosome 7q21. Symptoms frequently respond very well to alcohol, often leading to dependence, and to benzodiazepines.

Of the alternatives, Huntington's disease is unlikely given the prolonged disease course and absence of either chorea or significant cognitive disturbance. Tourette's syndrome is not usually associated with myoclonus or dystonia. The patient took neuroleptics for less than a year, and the temporal relationship makes tardive dyskinesia unlikely. Individuals with advanced neuroacanthocytosis, which is usually autosomal recessive, would be expected to have absent ankle jerks (associated axonal neuropathy and myopathy) and oro-lingual involvement or dysarthria; the involuntary movements rarely abate during treatment with benzodiazepines.

QUESTION SETTER:

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**QUESTION 15**

A 29-year-old Australian Caucasian female was admitted following a collapse. She lost consciousness for approximately one minute; there was no witnessed seizure activity. When she awoke she had expressive dysphasia but no other neurological symptoms. She had no relevant past medical or family history and the only regular medication was the oral contraceptive pill. She consumed alcohol occasionally, was a regular smoker (10/day) and admitted to smoking cannabis but denied any other recreational drug abuse.

On examination she was afebrile, in sinus rhythm with a BP of 120/65 mmHg in both arms. Examination of the cardiovascular and respiratory systems was normal. She had expressive dysphasia but no other neurological signs.

The only abnormal blood results were: ESR 66 mm/hour; total cholesterol 6.5 mmol/L. The following investigations were normal or negative: full blood count, renal, liver and thyroid function, CRP, syphilis serology, coagulation, vitamin B12, red cell folate, glucose, proteins C and S, activated protein C resistance, antithrombin III, autoantibody screen, lupus anticoagulant.

An initial CT demonstrated a left middle cerebral infarct. The patient was commenced on high dose aspirin and admitted for further investigations. The following morning she awoke with a dense right hemiplegia and complete aphasia. MRI confirmed a large left MCA territory infarct with a large clot in the left carotid artery. A transthoracic bubble echocardiogram was normal. A CT angiogram demonstrated a large ring of abnormal soft tissue surrounding the aortic arch, extending cranially along both the left common carotid and, to a lesser extent, the brachiocephalic artery, causing severe narrowing of the left common carotid artery.

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: Cerebral vasculitis
- B: Fibromuscular dysplasia
- C: Patent foramen ovale
- D: Takayasu's arteritis
- E: Todd's paresis

**SUGGESTED ANSWER D - EXPLANATION / COMMENTS**

A stroke in a young patient with a raised ESR with a normal CRP should suggest a vasculitic process. Cerebral vasculitis is a possibility but the absence of a headache and the large ring of abnormal soft tissue surrounding the aortic arch suggest a large vessel arteritis, such as Takayasu's.

A PET scan demonstrated increased uptake in the aortic root and ascending aorta in keeping with a large vessel aortitis.

Takayasu's arteritis is a rare form of chronic inflammatory arteritis affecting large vessels, predominantly the aorta and its main branches. Inflammatory infiltrates cause thickening of the affected artery wall with narrowing of the lumen and thrombosis. In addition, ectasia and aneurysm formation occur. Takayasu's is rare with an annual incidence of 2.6 per million in North America. It is rarely seen in Caucasians being more common in Japan, South East Asia, India and Mexico. However, this patient from Australia may have had some ancestral genetic mixing. There is a higher incidence in

females and it usually presents in the second or third decade. The subclavian artery is the vessel most commonly affected, with involvement in 90% of cases, almost two-thirds of cases involve the aorta and the common carotid is involved in 50% of cases, usually on the left side as in this case.

Clinical manifestations due to end-organ ischaemia are dependent on the vessels involved. Presentation varies from asymptomatic pulselessness to catastrophic neurological events. Neurological presentation varies between studies ranging from 10 to 20%.

Takayasu's is treated using steroids and immunosuppression and has a variable course. Although a rare cause of cerebrovascular disease it is important to consider the diagnosis in young patients.

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QUESTION SETTER:

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**QUESTION 16**

A 30-year-old woman presented with a two-month history of recurrent attacks of generalised shaking associated with loss of consciousness. These were happening up to four times a week. She said that she usually had no warning (although sometimes had had a weird 'aura' before them) and afterwards felt drowsy. She had been incontinent of urine on several occasions and had also sustained carpet burns to her face. Her partner, who had witnessed a number of them, said that she looked quite flushed and upset for several minutes before the attack. The shaking lasted on average around 10 minutes and could include pelvic thrusting. During an attack, her eyes and mouth tended to be shut and afterwards she was often tearful.

She had a history of irritable bowel syndrome and repeated laparoscopy for pelvic pain. She had been under psychiatric care and had received diagnoses of borderline personality disorder, depression and post-traumatic stress disorder. There was a history of recent domestic violence. Subsequent investigation with videotelemetry confirmed the clinical suspicion of non-epileptic attacks.

In hindsight, which of the following aspects of the history was most persuasive for this diagnosis?

**ANSWER OPTIONS:**

- A: Borderline personality disorder
- B: Pelvic thrusting during the attack
- C: The duration of the attacks
- D: The history of domestic violence
- E: The history of irritable bowel syndrome and pelvic pain

**SUGGESTED ANSWER C - EXPLANATION / COMMENTS**

There are many clinical clues here to a diagnosis of non-epileptic attacks or pseudoseizures. The point of the question is to emphasise that it is dangerous to use the presence of a psychiatric history, previous functional symptoms or recent life events to make a diagnosis of non-epileptic attacks. All of these things are fairly common in patients with epilepsy.

To make the diagnosis, you should always look at the features of the attack itself<sup>1</sup>.

Features that are common in pseudoseizures but rare in epilepsy include: prolonged duration of attack (over 2 minutes); eyes or mouth shut; post-ictal weeping and side to side head shaking.

Features that you might think suggest epilepsy but are in fact not helpful include urinary incontinence (which is relatively common in non-epileptic attacks); injury (minor trauma such as a carpet burn is common in non-epileptic attacks); the presence of an aura (which on closer questioning in patients with non-epileptic attacks is often a dissociative state related to a build up of panic); post-ictal drowsiness and the presence of attacks arising from apparent sleep (which in non-epileptic attacks is usually 'pseudosleep'). Pelvic thrusting is not helpful because of its occurrence during frontal lobe epilepsy.

No single feature should be used in isolation to make a diagnosis

Video EEG is the best way to make the diagnosis securely, but even here the semiology of the attack must be considered since some seizures, such as frontal lobe seizures,

may not be picked up with scalp electrodes. A 'suggestion protocol' may improve pick up rates at routine EEG testing<sup>2</sup>.

As it turned out, this patient had a number of clues to the diagnosis and her psychiatric history and history of previous functional symptoms is almost certainly relevant.

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QUESTION SETTER:

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**QUESTION 17**

A 54-year-old milkman was referred from the regional chest unit with a query whether he might have motor neurone disease. He had been referred from his local hospital because of daytime somnolence and found to have severe hypercapnia ( $PO_2=9.5$  kPa,  $PCO_2=11$  kPa). An overnight sleep study with video telemetry revealed frequent oxygen desaturation associated with periods of complete apnoea for up to 30 seconds. These episodes were followed by arousals with vocalisations and thrashing around. The patient had no recall for these events.

He was treated with nocturnal non-invasive positive pressure ventilation with complete resolution of daytime symptoms and the nocturnal desaturation. The chest physicians thought they could observe fasciculations in the arms and hands and referred him to the neurology department.

On examination he had a mild degree of cogwheel rigidity and unsteadiness when walking. What had been interpreted as fasciculation was in fact low amplitude myoclonus. A clinical diagnosis was made and the patient was discharged for outpatient follow up. Two weeks later he was found dead by his wife one morning.

Which of the following inclusion bodies was found at autopsy?

ANSWER OPTIONS:

- A: Glial cytoplasmic inclusions
- B: Hirano Bodies
- C: Lewy bodies
- D: Tau positive inclusions
- E: Ubiquitinated inclusions

**SUGGESTED ANSWER A - EXPLANATION / COMMENTS**

The diagnosis was multiple system atrophy. Sleep disordered breathing is common but was unusually dramatic and an early feature in this case. It is usually associated with stridor (and is therefore essentially a form of obstructive sleep apnoea) for which nocturnal CPAP can be a very effective therapy. Disorders of REM sleep latency (REM sleep behaviour disorder) are also very common in MSA.

The clinical diagnosis was made on the basis of a combination of Parkinsonism, ataxia and finger myoclonus on examination plus a drop of 30 mmHg in his blood pressure on standing and a history of urinary urgency. Vocal cord examination and spirometry did not reveal obvious adductor spasm of the vocal cord muscles and there was no history of stridor. The patient's nocturnal symptoms were interpreted as dysautonomia of breathing. His sudden and unexpected death would presumably only have been prevented by continuous mechanical ventilation via an elective permanent tracheostomy.

At post-mortem he had typical changes of MSA with widespread involvement including the basal ganglia, cerebellum and the brainstem. Loss of cholinergic neurons in the medulla is found at post-mortem in MSA patients with prominent sleep related symptoms.

QUESTION SETTER:

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### QUESTION 18

A 35-year-old woman presented with 3 drop attacks over a period of 6 years. These would occur without warning or provocation. Her legs would give way beneath her without any loss of awareness or consciousness and she would be able to rise immediately after. In addition she complained of feeling a little off balance when walking.

She walked at 11 months, was never good at sports at school but learned to ride a bicycle. There was no family history of neurological disease.

General examination was normal. Cranial nerves were normal. Muscle bulk and tone were normal in all 4 limbs. There was mild symmetrical weakness of hip flexion/extension, and knee flexion (MRC 4+). Upper limb reflexes were normal, knee jerks brisk, ankle jerks just present without reinforcement, plantars mute. There was mild 4 limb ataxia and mild gait ataxia. Romberg's test was negative. Sensory examination was normal.

The following investigations were normal: FBC, ESR, U&Es, LFTs, Calcium, TFTs, MRI brain and CSF analysis (protein, glucose, cell count), muscle biopsy (including oxidative stains).

Abnormal results: serum lactate: 3.00 mmol/l (0.5-2.00); EEG: markedly abnormal, with florid, generalised, short lived polyspike and wave complexes on a slow background.

What is the most likely diagnosis?

ANSWER OPTIONS:

- A: Baltic myoclonus
- B: MELAS
- C: MERRF
- D: SCA 2
- E: Sialidosis

### SUGGESTED ANSWER C - EXPLANATION / COMMENTS

The falls are due to negative myoclonus in the lower limbs. The long history, cerebellar signs, lactic acidosis, and epileptic features on the EEG all point to MERRF despite there being no overt seizures or myoclonus evident during the examination. 10% of patients with a confirmed mtDNA mutation may have no or borderline changes on muscle biopsy. In this case mtDNA analysis on blood was positive for the A8344G mutation.

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### QUESTION 19

A 45-year-old man presented with a history of evolving sensory disturbance in the lower limbs and a depressive illness, unresponsive to treatment. He subsequently developed memory problems and was seen in a neurology clinic by a specialist registrar, who included variant Creutzfeldt-Jakob disease in his differential diagnosis.

Regarding investigations, which of the following is the least compatible with variant CJD?

ANSWER OPTIONS:

- A: Generalised periodic EEG discharges
- B: Methionine homozygosity at codon 129 of the prion protein gene
- C: Negative CSF 14-3-3 protein
- D: Raised CSF protein
- E: Symmetrical posterior thalamic hyperintensity on MRI

### SUGGESTED ANSWER A - EXPLANATION / COMMENTS

With regard to variant CJD:

CSF 14-3-3 protein is positive in about 50%.<sup>1</sup>

Symmetrical posterior thalamic (pulvinar) hyperintensity on MRI occurs in about 90%.<sup>1</sup>

Raised CSF protein occurs in about one-third.<sup>2</sup>

Methionine homozygosity at codon 129 of the prion protein gene found in all cases tested to date.<sup>1</sup>

Generalised periodic EEG discharges not present in any UK case to date.<sup>1</sup>

REFERENCES:

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**QUESTION 20**

A 42-year-old scientist, presented to her General Practitioner with blurring of the vision in the infero-nasal quadrant of her right eye. This progressed over about a day, but never became a complete scotoma – there was just marked blurring. She had previously been well, there was no pain, and there were no other neurological symptoms. She had never travelled outside the country other than to attend conferences.

An optometrist was unable to find any abnormality on automated perimetry and sent her to an ophthalmologist. On examination, the ophthalmologist found her visual acuities to be 6/6 on the right and 6/5 on the left. She was able to see 15/17 Ishihara plates with the right eye, and 17/17 with the left. No abnormality was found to confrontational visual fields, and fundoscopy was normal. There was no relative afferent pupillary defect. The patient was reassured and discharged.

The visual disturbance settled after two weeks, but after another two weeks the lady returned to her General Practitioner, stating that the area of visual loss was now somewhat larger. A CT scan was organised by the General Practitioner. This showed some reduced attenuation in the left frontal lobe which was felt most likely to be due to demyelination. The patient was therefore referred as an emergency to the local neurologist. Like the ophthalmologist, the neurologist could find nothing on examination, but performed visual evoked potentials. In the right eye, the latency of the P100 was 123 msec, and that of the left eye was 106 msec (normal range 95 – 110 msec). Blood tests were normal, as was a lumbar puncture; in particular, no oligoclonal bands were found. A brain MRI showed the appearances in the figures below. An MRI scan of the spinal cord was normal. The visual disturbance subsequently resolved over the next few months and the patient felt her vision had returned back to normal.

Figure 1: Axial T2 and Gd-enhanced T1 weighted MRI scans

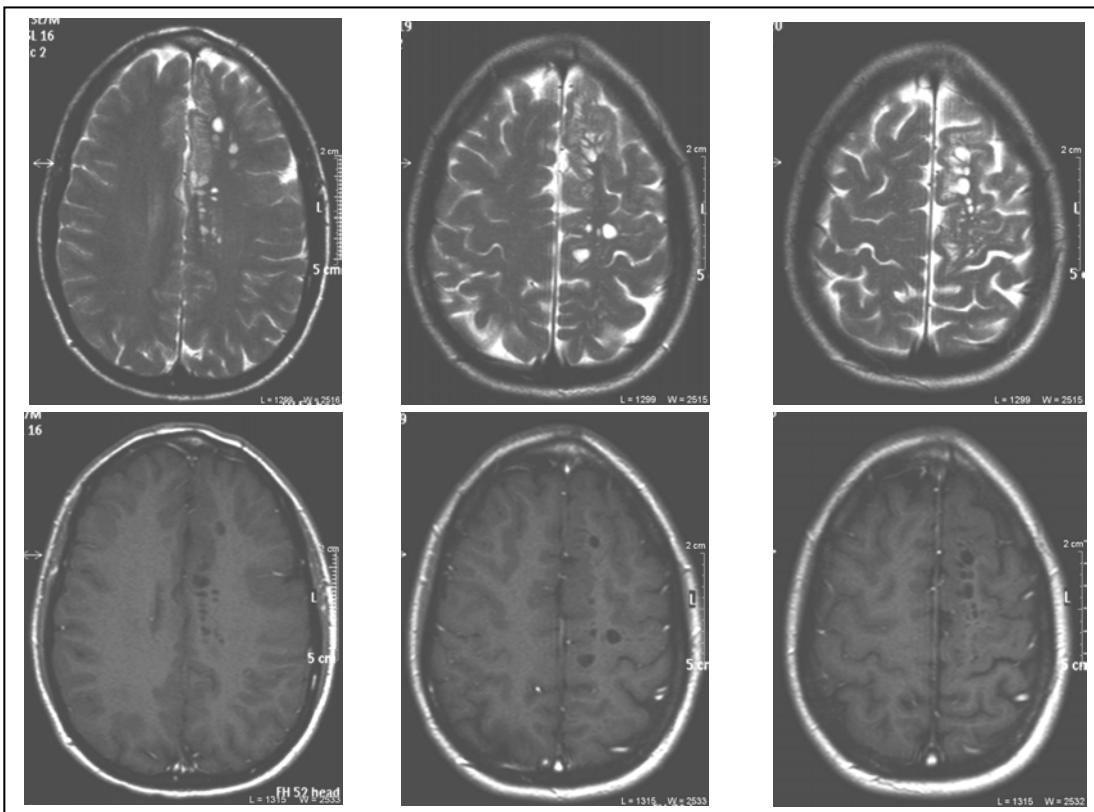
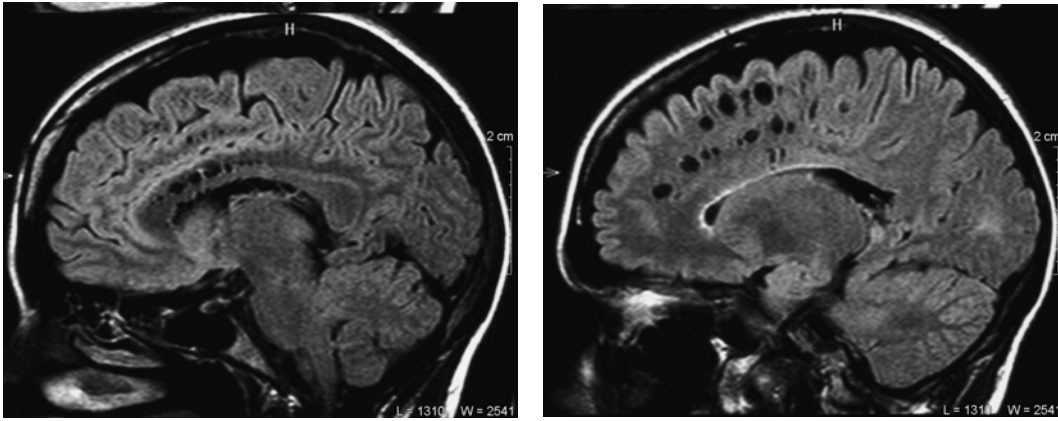


Figure 2: Unenhanced sagittal T1 images



Which of the following statements is correct about the diagnosis and management of this individual?

- A: The patient has multiple sclerosis according to the McDonald criteria, and should ideally be started on a disease-modifying agent (beta interferon or glatiramer acetate).
- B: The patient has multiple sclerosis according to the McDonald criteria, but should not be started on a disease-modifying agent (beta interferon or glatiramer acetate).
- C: The patient has multiple sclerosis according to the Poser criteria, and should ideally be started on a disease-modifying agent (beta interferon or glatiramer acetate).
- D: The patient has probably had a clinically isolated syndrome, and should be started on a disease-modifying agent (beta interferon or glatiramer acetate).
- E: The patient has probably had a clinically isolated syndrome but should not be started on a disease-modifying agent (beta interferon or glatiramer acetate).

#### ANSWER OPTION E - EXPLANATION / COMMENTS

The changes on the MRI scan are those of cystic white matter (sometimes called "état criblé"), and not those of demyelination. This appearance is thought to represent dilated Virchow-Robin spaces and multiple potential causes have been described in the literature, including prenatal or perinatal trauma,<sup>1,2</sup> and vascular dementia.<sup>3</sup> Dilated Virchow-Robin spaces are not necessarily associated with pathology.<sup>4,5</sup> Granted the patient was previously normal and of normal intellect, the striking MRI features are likely to be an incidental finding of no clinical significance.

The visual disturbance appeared, lasted for a few weeks, and then resolved completely. Even though there were no other typical associated features such as pain on eye movement, the time course, prolonged VER, and lack of any other explanation would make isolated optic neuritis the most likely diagnosis. The fact that the symptoms resolved and then reappeared in the same place does not constitute two separate lesions, and therefore she has had a clinically isolated syndrome. As above, the MRI scan is, from the purposes of diagnosing MS, normal, and therefore the McDonald criteria are not met.

Even allowing for recent studies such as CHAMPS6 which suggest that patients with clinically isolated syndromes do better on beta-interferon, the only objective abnormal finding here was that of a prolonged VER. The patient therefore does not fit into the

patient group studied in CHAMPS, and is therefore not a candidate for disease-modifying agents.

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